


Whither Nuclear Medicine Training in Pakistan?

Durr-e-Sabih

I hear there is stirring in the usually ossified halls of nuclear medicine higher learning and those at the helm of affairs are realizing, or saying that they are realizing, the importance of teaching cross-sectional anatomy to the young trainees of this fascinating specialty. This is the only way of keeping nuclear medicine physicians relevant.

Hats-off to the current PSNM executive council to have taken on this project with something of a missionary zeal, and thus the plethora of short courses in cross-sectional anatomy. While this is good, it does not replace need of formal training for young trainees and retraining with some sort of certification and assurance of basic competence of the practitioners of this art.

As an examiner of the Asian Nuclear Medicine Board, I get to interact with young (and some not-so-young) nuclear medicine physicians from many countries of Asia. I have yet to be impressed by a candidate from our country. In the small sample that I have had the privilege of interacting, I have realized that it is not only the lack of knowledge that distinguishes our candidates, it is the lack of "thinking", the lack of trying to use all of the available information and the lack of confidence in clinical problem solving and the lack of any understanding of a CT or MR image. Why is this resistance to learn cross-sectional imaging, hasn't it been an issue for almost 20 years [1].

It hurts because I see so many highly intelligent physicians doing nuclear medicine. That they should be so mediocre when reporting a nuclear medicine procedure is disappointing and even demoralizing.

Our statistics say a lot, something that I have been heckled at for quoting. Even today our trainee numbers show a depressing trend with only 17 FCPS trainees and 14 MS trainees; MD training positions remain unfilled as do the PET fellowship positions. Generally, we have had more faculty in nuclear medicine than trainees, and that is also true today. Being "faculty" looks good on your CV and who cares if you earn your title or not.

In a country that graduates over 14000 physicians annually, a country where radiology has about a thousand trainees at any given time, less than 30 nuclear medicine trainees means that this specialization is not attractive. Everyone who argues otherwise is misguided at best.

In fact we conducted a professional satisfaction survey in 2013 and found that almost 60% of practicing nuclear medicine physicians were unhappy professionally, most commonly with the quality of training they had received [2]. Of those who trained in nuclear medicine, almost a fifth changed their specialization [3], something quite unheard of in any other specialty. This was something that should have sent our faculty at institutes of training into a huddle. They did huddle, but to circle their wagons instead of trying to figure out what to do to address this issue. One gentleman from one institute suggested that the placement of nuclear medicine training opportunities in a shared newspaper ad was the reason for lack of interest.... I wish he was
joking but he wasn’t. Another very senior person starts all nuclear medicine training discussions with his opinion that the PAEC’s mandate does not include nuclear medicine or nuclear medicine training… another gentleman, again a shining tower of nuclear medicine training sat for several years on a file with a new training curriculum.

As we slowly reach a critical mass of PET scanners and, as attractive business models develop that can justify this investment, we will attract another kind of attention, that of our imaging big brothers, the radiologists…. I have heard the argument as I am sure all of you have too, that they are already trained in cross-sectional anatomy; they have trained in the PET technique and they can chase a hot spot as well as any nuclear medicine physician… so it makes sense for them to take ownership of this technique and the associated resources.

This has already happened in many places, and in the US there was a move to do away with nuclear medicine residencies altogether, thankfully this was aborted in the face of international opposition from the nuclear medicine community. The clamour has died down for now, but surely not for long and we will see turf battles and new wars for resources.

PET-CT will live on, patients will continue to get services, and very competently I am sure, but whereas radiology is solid, structured and overt, nuclear medicine is subtle and abstract and has one eye always on the lab bench.

Nuclear medicine physicians can join dots that are only faintly visible, their conclusions are often interpolative and their art is at acquiring moving targets, biochemistry, radiochemistry, pathology, physiology, etc., which all interplay before a nuclear medicine opinion is formed… it would be unfortunate if nuclear medicine physicians were to become extinct, to be replaced only by full time researchers in labs and full time radiologists in the imaging suites.

After this jeremiad, you would expect me to come up with solutions too…. Well here is what comes to mind. Strengthen, strengthen, strengthen the training programmes, make it more broad based. It takes time to overcome inertia of changing curriculum at the university or college level, but a Pakistan School of Nuclear Medicine, sponsored by the PSNM but not controlled by it so that it can remain non-partisan and focused only on its job, would be one solution. The only job that the school would have is look at the weaknesses in the current training programs and offer certification courses to fill these knowledge gaps. We can get this expertise locally or use our network with the Asian School of Nuclear Medicine to get faculty and courses. I am very happy that this idea (initially floated by the present President PSNM) is getting traction among those in the Pakistani nuclear medicine community who feel there is need to fix things.

Frankly I think those at the helm of training affairs have played their innings and need to go home. A changing of the guards is long due, let younger, more mentally agile, more committed members of the community take on the training challenge. We need someone new, someone who can rise to the challenge; design a new curriculum, weed out the obsolete and include the relevant. We should look at the success stories around us, even Iran, living under such heavy constraints for so long has managed to train superb nuclear medicine physicians (an Iranian lady physician stood first in the last year's ANMB exam); India can boast of world class facilities manned by world class personnel. What have we not that the others have? Only the will to give all; once we have that will, I am there will be no turning back.

PS: Please disagree, I would love to see opinion to the contrary and hope this would be published in these very pages.

References


Note

The views expressed in the Editorial are those of the author alone with the journal or the PSNM taking no responsibility for the contents or the opinion.
Estimation of time for release of patients after the administration of I-131 to thyrotoxicosis patients

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Abstract

Radioactive iodine (I-131) has been used for more than six decades for the treatment of thyrotoxicosis. Radiation safety is of paramount importance in I-131 based treatment of thyroid diseases, as treated patients become a potential radiation hazard for other individuals [1]. The purpose of this article is estimation of the time period for radiation safety restrictions through assessments of total effective dose equivalent (TEDE) in individuals exposed to I-131 for thyrotoxicosis therapy, by incorporating into the calculations, various factors such as relevant socioeconomic conditions.

For performing patient-specific dose calculations, we have used published data of uptake fractions & effective half-lives and triexponential model for total body clearance of iodine-131 [2].

Results obtained showed that the TEDE to other individuals (especially the family members, particularly children) and general public may be much higher than the annual dose limits recommended by the International Atomic Energy Agency (IAEA) and International Commission for Radiation Protection (ICRP) in some situation especially when the administered activity is greater than 15 mCi and occupancy factor greater than 0.125 and proper precautionary measures are not taken after the release from hospital [1, 3].

It is therefore suggested that a fixed dose limit of 15 mCi (550 MBq) instead of 30 mCi (1100 MBq) be recommended for release of I-131 thyrotoxicosis therapy patients in order to reduce undesired exposure to caregivers and general public in countries like Pakistan because of factors such as poor socioeconomic conditions and low literacy rates, etc.

Key words: Iodine-131 therapy, thyrotoxicosis, patient release

Introduction

Use of unsealed radionuclide therapy to treat a variety of diseases has become common throughout the world for several decades. I-131 is a useful reference therapeutic radionuclide because of its widespread use...
and the presence of an external radiation field from its energetic gamma emissions [1].

The only disadvantage of this method is that it may lead to higher radiation exposure to the family members of the patient and the general public if precautionary measures are not taken after release from the hospital.

The dose received by the family members and general public depends totally upon the conduct of the patient. This is because of the fact that a member of public will not realise that the person sitting next to them is highly radioactive [4].

The physical half-life of I-131 is about 8 days. The main decay product is xenon-31, which is rapidly washed out of the body. In addition, damaged thyroid cells lose their capacity to organify iodine and consequently, the iodine is released back to the blood stream, resulting in excretion. Thus, I-131 is removed from the body reasonably quickly, either due to radioactive decay or by metabolic excretion. The total amount of I-131 reduces to half its original value at a rate which depends on the state of disease: between 1 day, in the case of thyroid cancer and total ablation of thyroid tissue, and 7 days for patients with euthyroid goitre. In the case of hyperthyroidism, the effective half-life is about 4-5 days [2, 5].

When the patient is kept in the hospital following radionuclide therapy, the people at risk of exposure include hospital staff, who may or may not be radiation workers or carers. This is a significant problem. However, it is generally felt that it can be effectively managed with well-trained staff and appropriate facilities. On the other hand, once the patient has been released, the group at risk include members of the patient’s family, including children and carers. They may also include neighbours, visitors to the household, co-workers, those encountered in public places, on public transport or at public events and finally the general public. To avoid these problems, certain precautionary measures have to be taken to minimise the dose delivered to the general public. Therefore, to keep the doses to general public as low as reasonably achievable (ALARA), the patient and his/her attendant should be properly educated in this regard.

There are significant radiation protection problems relating to management of radioactive patients. The pattern of practice around the World with regard to the release of patients from hospital after therapy with unsealed radionuclides is quite varied. Specifically, there is no agreement on whether it is necessary to hospitalize patients undergoing therapy, and, if so, when and under what conditions they can be released. [1].

Current recommendations in accordance with regulatory requirements, regarding release of patients after therapy with unsealed radionuclides is based on one of the following options:

1. Release of patients based on patient-specific dose calculations/dose limits
2. Release of patients based on administered activity/residual activity
3. Release of patients based on measured dose rate at 1 m

The United States Nuclear Regulatory Commission (NRC) regulations for the release of patients administered radioactive material (10 CFR 35.75) authorize patient release according to a dose-based limit, i.e., the dose to other individuals exposed to the patient. A licensee may release patients, regardless of administered activity, if it can be demonstrated that the TEDE to another individual from exposure to a released patient is not likely to exceed 5 mSv and the TEDE to a member of the general public is not likely to exceed 1 mSv. Furthermore, in a case where the dose could exceed 1 mSv, the patient is also to be provided with instructions on how to maintain doses to others as per ALARA principle [2, 6].

The Radiation Protection unit of the European Commission, in its last guide, proposed dose limits related to age and family bonds. For family and close friends, the proposed limits were 1 mSv/y for children (including unborn
children), 3 mSv/y for adults ≤60y old, and 15 mSv/y for adults >60y old. For third parties or the general public, the proposed limit was 0.3 mSv/y [7].

The IAEA recommends that the dose to any comforter or visitor shall be constrained so that it is unlikely that his or her dose will exceed 5 mSv during the episode of a patient’s diagnostic examination or treatment. The dose to children visiting patients who have received radioactive materials should be similarly constrained to less than 1 mSv [1, 8].

This article provides some guidance/help to the medical professionals involved in release of patients after therapy with I-131. Also there is suggestion for local regularity body for re-considering of the existing release limit in the light of our own socioeconomic conditions, family traditions etc. instead of fixed limit of 1100 MBq (30 mCi).

Methods & Materials

The methodology for calculation of absorbed dose (or TEDE) from an external source, such as a patient or a spill on the floor, was described in Appendix-I of NCRP 37. Other methods were suggested in the more recent Appendix-U of NUREG-1556 Vol. 9 (the NRC guidance associated with the patient release rule pursuant to 10 CFR 35.75), NCRP Report No. 155, a Society of Nuclear Medicine (SNM) guidance document, and other references at the end of this document.

Equation to calculate the TEDE from a patient administered I-131 may have three components. Dose for the first eight-hour non-void period (pre-equilibrium period) with an occupancy factor of 0.75, the dose from the extrathyroidal component from 8 hours to total decay and the dose from the thyroidal component from 8 hours to total decay.

During the first 8 hours (0.33 day) after administration, little biologic elimination of I-131 occurs. Effective half-life of I-131 during this period is considered constant, although some inter-patient variability exists and estimated to be 80% of physical half-life [2, 5, 6].

After the pre-equilibrium period, the remaining I-131 is considered to be divided between thyroidal component and extrathyroidal component. The effective half-lives of I-131 in each of these components is different. The effective half-lives of I-131 for thyroidal and extrathyroidal components also vary from patient to patient but were assume to be constant in our calculations as given in Table 1.

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>Uptake Fraction (F₁)</th>
<th>Effective Half-life (T₁eff, day)</th>
<th>Uptake Fraction (F₂)</th>
<th>Effective Half-life (T₂eff, day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthyroidism</td>
<td>0.20</td>
<td>0.32</td>
<td>0.80</td>
<td>5.2</td>
</tr>
<tr>
<td>thyroid cancer *</td>
<td>0.95</td>
<td>0.32</td>
<td>0.05</td>
<td>7.3</td>
</tr>
</tbody>
</table>

*Post-thyroidectomy

These equations do not include the dose from internal intake by household members and members of the public, because the dose from intake by other individuals is expected to be small (less than a few percent), relative to the external gamma dose [5]. Specific gamma ray constants (Γ) for I-131 is 2.2 rem-cm²/mCi-h.

Occupancy Factor (OF) is the fraction of time, a person spends near the patient (~at 100 cm distance) in 24 hr cycle. OF is the estimate of the patient’s proximity to people at home or in the community after dose administration.

OF=0.125 (3 hr/24 hr) 12.5% time
OF=0.33 (8 hr/24 hr) 33% time
OF=0.5 (12 hr/24 hr) 50% time
OF=01 (24 hr/24 hr) 100% time
Equations

\[ D_{(0 \rightarrow t)} = \left\{ (1st - component) + (2nd - component) + (3rd - component) \right\} \]

\[ 1st = D_{(0 \rightarrow 8hr)} (rem) = \frac{34.6 \times \Gamma \left( \frac{rem - cm^2}{mCi-h} \right) \times A(mCi) \left( 0.75 \times 0.8 \times 8.04(d) \left( 1 - e^{-0.6930.33} \right) \right)}{r^2 (cm^2)} \]

\[ 2nd(extra-thyroidal) = D_{(8hr \rightarrow t)} (rem) = \frac{34.6 \times \Gamma \left( \frac{rem - cm^2}{mCi-h} \right) \times A(mCi) e^{-0.6930.33} \left( OF \times F_1 \times T_{eff-1} (d) \left( 1 - e^{\frac{-0.6930.33}{T_{eff-1}}} \right) \right)}{r^2 (cm^2)} \]

\[ 3rd(thyroidal) = D_{(8hr \rightarrow t)} (rem) = \frac{34.6 \times \Gamma \left( \frac{rem - cm^2}{mCi-h} \right) \times A(mCi) e^{-0.6930.33} \left( OF \times F_2 \times T_{eff-2} (d) \left( 1 - e^{\frac{-0.6930.33}{T_{eff-2}}} \right) \right)}{r^2 (cm^2)} \]

Where

- \( D_{(0 \rightarrow t)} \): Total effective dose equivalent at time t, in rem (1 rem=10 mSv)
- 34.6: Conversion factor, 24 hrs/day times the total integration of decay
- (1.44)
- 0.75: is the occupancy factor for first 8 hours
- 8.04 (d): physical half-life of I-131
- 0.8: factor of 80% for first 8 hours clearance through physical decay
- \( \Gamma \): Specific gamma ray constant in rem/mCi-h at 1 cm (2.2 for I-131)
- A: Activity in mCi at the time of the release
- OF: Occupancy Factor from 8 hours to total decay
- F_1: Extrathyroidal Uptake Fraction
- F_2: Thyroidal Uptake Fraction
- T_{eff}: Effective half-life in days
- T: Exposure time in days
- r: Distance from the source to the point of interest in cm (1 m=100 cm)

Results & Discussion

Figures 1 (a, b, c, d, e & f) are showing variation of TEDE with time for different administered activities (10, 15, 20, 25 and 30 mCi) at fixed distance of 100 cm (1m) and 0.125, 0.25, 0.33, 0.5, 0.75 & 1.0 occupancy factors respectively.

Fig. 1(a) shows that TEDE approaches to and exceeds from limit of 1 mSv (i.e. for children and general public) if patient with administrative activity of I-131 > 15 mCi, spends 3 hour per day (OF=0.125) close to other individuals for first 15 days after therapy. Similarly, from Fig. 1 (d, e, f) it is clear that TEDE to other individuals who spends more
Figure 1 Total Effective Dose Equivalent (TEDE) to other individual w.r.t time he/she spent with patient having I-131 therapy for different administered activities (10, 15, 20, 25 and 30 mCi) taking fixed distance of 100 cm and for Occupancy Factors (a) 0.125, (b) 0.25, (c) 0.33, (d) 0.5, (e) 0.75 & (f) 1.0
Figure 2  Total Effective Dose Equivalent (TEDE) to other individual w.r.t distance from patient having I-131 therapy for different administered activities (10, 15, 20, 25 and 30 mCi) during first 30 days from I-131 administration and for Occupancy Factors (a) 0.125, (b) 0.25, (c) 0.33, (d) 0.5, (e) 0.75 & (f) 1.0
time per day (i.e. OF>0.5) with I-131 (>15 mCi) therapy of patients, approaches to and exceeds from 5 mSv (limit for adult family members/caregivers) within 2-3 weeks.

Figure 2 (a, b, c, d, e & f) shows variation of TEDE (during first 30 days after I-131 administration) with distance from patient for different administered activities (10, 15, 20, 25 and 30 mCi) for 0.125, 0.25, 0.33, 0.5, 0.75 & 1.0 occupancy factors respectively.

Figure 2a shows that if the patient with administered activity of I-131 >15 mCi does not maintain the distance of 1m or greater from other individuals, the limit of 1 mSv (i.e. for children and general public) will exceed very quickly, even for OF=0.125 (i.e. if he/she spends 3 hour per day closer to other individual) for 1 month after I-131 administration.

Similarly, Figure 2(d,e,f) shows that for OF > 0.5, TEDE approaches to and exceeds 5 mSv when the patient does not maintain the distance of 1m or greater from other individual for administered activity of I-131 >15 mCi.

After I-131 therapy, doses to comforters & carers, family members, the public, co-workers and others need to be limited or constrained in accordance with the National and International Regulations. The control arrangements should focus on the dose limits or dose constraints that are generally applied. The decision to hospitalise or release a patient should be determined on an individual basis. Individuals differ not only in their social situations but also in the activity clearance rates from the body. This decision should take into account many factors, including the patient's wishes, their medical circumstances, the regulatory environment, occupational and public exposures, family considerations, cost and environmental factors [1].

The first few hours after administration of the I-131 are crucial. If someone spends 3 to 4 hours closer than 50 cm to the patient after administration, the dose limit could quickly be reached or exceeded. Exposures to other individuals can be effectively managed by the educated patient (or parent or guardian) after release if that patient follows the instructions provided. There are three major elements involved in successfully meeting a performance standard of maintaining exposure of members of the public to released I-131 therapy patients:

1. The evaluation of the patient's living and working conditions to ascertain whether or not a given patient can be safely released.
2. The appropriate performance of a patient-specific dose calculation to ensure that no individual member of the public will likely be exposed to a dose in excess of limits.
3. To provide verbal and written instructions that are simple in order for the patient to limit the radiation dose to others as per ALARA principle. This requires patient education and an assessment by the authorized physician that patient compliance with these instructions is highly likely.

**Conclusion**

Existing fixed release limit of 30 mCi (1100 MBq) for I-131 therapy of thyrotoxicosis patients may be re-evaluated and should be determined on individual basis, considering their life style, socioeconomic conditions and family background etc. for a country like Pakistan where mostly families do not have adequate facilities for isolating the patients at their home and many of them are unable to follow instructions given to them at the time of release from the hospital due to ignorance, i.e. low literacy rate. Alternatively, a fixed dose limit of 15 mCi (550 MBq) instead of the standard 30 mCi (1100 MBq) dose, may be recommended for release of I-131 thyrotoxicosis therapy patients.

**References**

2. US Nuclear Regulatory Commission. Specific Guidance about Medical Use Licenses (NUREG-1556, Vol. 9, Rev. 2) 2008


5. Radiation Safety in the Treatment of Patients with Thyroid Diseases by Radiiodine I-131: Practice Recommendations of the American Thyroid Association, THYROID Volume 21, Number 4, 2011


Lactate dehydrogenase (LDH) as predictive factor of the pain free syndrome duration after radionuclide treatment of bone metastases in patients with breast cancer

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Abstract

Aims The purpose of this study was to investigate a possible role of serum LDH as a predictor of cancer cell activity and to determine if serum LDH levels can prognosticate the duration of pain-free period after radionuclide therapy.

Methods The We selected 62 breast cancer patients with ages ranging from 29-67 years (mean age 53.2±9.5 years) who had a successful response to radionuclide therapy with ¹⁵³Sm-oxabifore and had their serum LDH levels determined prior to the therapy. Patients with a history of a benign disease, which could possibly influence the serum LDH levels, or those suffering from complications such as a vertebral fracture or impending cord compression, were excluded from the study.

¹⁵³Sm-oxabifore was administrated in a standard dose of 37 MBq per kg body weight. All patients were on bisphosphonate therapy, both before and after samarium-153 treatment. Group 1 comprised of 23 patients who had received combined ¹⁵³Sm-oxabifore and zoledronic acid therapy. Group 2 comprised of 39 patients who had additionally received therapy for their primary tumour. For

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each of these two groups, the correlation between serum LDH levels and duration of the pain-free syndrome was estimated.

**Results** There was a strong negative correlation (r = -0.84) between the serum LDH levels and the duration of pain-free period in Group 1, but no significant correlation (r = 0.1) was seen between the LDH levels and the duration of pain-free period in Group 2. The duration of pain-free period in the second group was longer in comparison to the first group and was statistically significant (p<0.0001).

**Conclusion** Serum LDH level can prognosticate the duration of the pain-free period after radionuclide therapy and could be useful in selecting patients who in addition to samarium-153 therapy may additionally benefit from treatment of the primary tumour.

**Key words:** Lactate dehydrogenase (LDH), breast cancer, bone metastasis, zoledronic acid, radionuclide therapy

**Introduction**

Breast cancer has a propensity towards skeletal metastases, leading to osteolysis and abnormal new bone formation. Within the first 2 years of diagnosis, 10 - 15 % of patients may have distant metastases, 27.9% of which are bone secondaries. [1] Bone pain is a common and significant cause of morbidity affecting 60-90% of terminal patients of breast cancer. [2]

Bisphosphonates and radionuclide therapy are the both widely used for the treatment of painful bone metastatic disease. While bisphosphonates are indicated for prevention of skeletal-related events, radionuclide therapy with bone seeking radiopharmaceuticals like $^{153}$Sm-EDTMP (ethylenediamine tetramethylene-phosphonic acid), Sr-89, etc., have affinity for skeletal tissue, and, after intravenously administration, concentrate in active bone turnover, mostly in metastatic lesions, allowing site-directed radiotherapy for painful bone secondaries. Combination of both treatments is more effective as compared to either one in isolation [3-5].

In our earlier studies, we have demonstrated that combined therapy of bone metastases by zoledronic acid together with radionuclide therapy by $^{153}$Sm-oxabifore, was an effective therapeutic approach with statistically significant reduction of the pain syndrome; however, the duration of pain-free syndrome was different in different patients [6].

It is known that most cancer cells have an altered metabolism involving a shift to aerobic glycolysis with lactate production coupled with a higher uptake of glucose as the main source of energy. Lactate dehydrogenase-5 (LDH-5) catalyzes the reduction of pyruvate by nicotinamide adenine dinucleotide hydrate (NADH) to maintain the continuity of glycolysis, being an important control point in the system of cellular energy release [7]. Inhibition of LDH-A has demonstrated marked changes in metabolic processes and overall survival in carcinoma cells [8-9]. LDH has also been included in prognostic scores for several types of cancer [10]. However, the value of LDH as prognostic impact factor is unclear [11-13].

Progression of the primary tumour may lead to progression of the bone metastases and development of new bone secondaries, which will lead to reappearance of the pain syndrome. Recurrent pain or new sites of pain, often are the first indications of cancer progression and should be promptly evaluated.

The objective of our study was to estimate if serum LDH level can play a role as a predictor of cancer cell activity and proliferation of the primary tumour, and also to evaluate its value in predicting pain-free duration after radionuclide therapy.

**Patients & Methods**

**Patients**

As 300 patients received radionuclide therapy
for the pain syndrome from November 2009 to July 2013 and were followed-up till July 2015. We selected 62 breast cancer patients according to the inclusion criteria: 1) patients with known serum LDH level before combined \( ^{153} \text{Sm-oxabifore} \) and bisphosphonate therapy, 2) without any non-cancer diseases which could influence the LDH level, 3) without complications such as vertebral fractures or of impending cord compression, and 4) with complete or almost complete response to therapy and being on follow-up with documented duration of pain-free period after radionuclide treatment.

The patients were divided into two groups: Group 1 (n=23) included patients who had received treatment of bone metastases by zoledronic acid and \( ^{153} \text{Sm-153 oxabifore} \); Group 2 (n=39) included patients who had received radionuclide and bisphosphonate therapies together with the treatment of the primary tumour according to individual situation.

\( ^{153} \text{Sm-oxabifore} \) and bisphosphonate therapy

Inclusion criteria for radionuclide therapy were: 1) intense uptake in projection of painful bone metastases on recent (2-4 weeks prior to therapy) \(^{99m} \text{Tc-methylene diphosphonate (MDP)} \) whole-body (WB) bone scan; 2) satisfactory routine haematology (haemoglobin level >90 g/L; white blood cell count >4x10^9/L; platelet count of >100 x10^9/L); and 3) sufficient renal function according to Cockroft and Gault formula - creatinine clearance >50ml/min.

Prior to the administration of the radiopharmaceutical, the patients received verbal as well as written instructions and information about the procedure. This included: a) an explanation of the therapeutic procedure and radiation protection guidelines; b) estimated time when to expect possible pain relief; c) a warning that a transient flare effect of pain may occur; and d) a note on general radiation protection guidelines.

\( ^{153} \text{Sm-oxabifore} \) was administered to all patients at the standard bone palliation dose of 37 MBq/kg body weight. Whole-body post-treatment scans were obtained within 3-6 hours after \( ^{153} \text{Sm-oxabifore} \) administration.

All patients received zoledronic acid before (2-6 months) and after (whole period of follow-up) treatment as per protocol in the standard dosage, 4 mg every 28 days under control of serum urea and creatinine levels. The period of time between the administrations of zoledronic acid and \( ^{153} \text{Sm-oxabifore} \) was approximately ±2-7 days.

Pain assessment was based on visual analog scale (VAS), with 0 representing no pain and 9 representing intolerable pain. The time period between the occurrence of pain relief (when the patient stopped receiving analgesics) and the onset of pain syndrome recurrence was monitored and recorded by the local oncologists.

Statistical analysis

The results are expressed as the mean ± SEM for each index. Comparison of data among various groups was performed with Student’s unpaired \( t \)-test. \( P <0.05 \) was considered statistically significant. For calculating correlation between the LDH level and the duration of pain-free period, the Spearman’s rank correlation coefficient and simple linear regression for building the curves were used.

Results

The patient’s ages ranged from 29–67 years (mean age 53.2±9.5 years). Initial therapy for all patients included mastectomy, chemotherapy, radiotherapy and hormonal therapy (where receptor status was positive). See Table 1.

Time to developing bone metastases was between 2-7 years after initial treatment. Bisphosphonate and radionuclide therapy was given to all the patients; however, the second
additionally received therapy for the primary tumour. Between the patient’s groups (Table 2) there was no statistically significant difference in T or N stages, visual assessment scores (before and after therapies) and LDH levels. However, the pain-free period was almost twice as long in the second compared to the first group.

We found a strong negative correlation (R= -0.84) between the LDH levels and the duration of the pain-free period in the first group of patients (Figure 1a) but there was no correlation (R=0.1) between the LDH levels and the duration of the pain-free period in the second group (Figure 1b).

21 out of 39 patients in the second group restarted to receive hormonal therapy after developing bone secondaries. On follow-up scans, one patient from the first group had significant progression of bone metastases in the left sacroiliac area and thoracic vertebrae 5 months after radionuclide therapy (Figure 2). Figure 3 shows a patient from the second group, who received chemotherapy and

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**Table 1** Treatment characteristics of the patients

<table>
<thead>
<tr>
<th>Initial therapy</th>
<th>Group 1</th>
<th>Group 2</th>
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<tbody>
<tr>
<td>Mastectomy</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hormonal therapy</td>
<td>±*(6/23)</td>
<td>±*(21/39)</td>
</tr>
</tbody>
</table>

**Table 2** Patients’ characteristics and results

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDH level in IU/L</td>
<td>631.7±213.7 (284-918)</td>
<td>566.2±183.6 (244-985)</td>
<td>0.2</td>
</tr>
<tr>
<td>T</td>
<td>2.6±1 (1-4)</td>
<td>2.46±0.78 (2-4)</td>
<td>0.31</td>
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<tr>
<td>N</td>
<td>1.47±0.5 (1-2)</td>
<td>1.25±0.84 (0-3)</td>
<td>0.26</td>
</tr>
<tr>
<td>VAS pre therapy</td>
<td>7.56±1.34 (5-9)</td>
<td>7.87±1.32 (5-9)</td>
<td>0.38</td>
</tr>
<tr>
<td>VAS post therapy</td>
<td>1.04±0.82 (0-2)</td>
<td>0.85±0.75 (0-2)</td>
<td>0.33</td>
</tr>
<tr>
<td>Pain-free period (months) post 153Sm therapy</td>
<td>10.6±9.06 (3-36) CI-95%±3.68 (6.9-14.3)</td>
<td>25.5±13.04 (5-57.9) CI-95%±4.09 (21.41- 29.5)</td>
<td>0.00001</td>
</tr>
</tbody>
</table>

VAS- visual assessment score
restarted hormonal treatment, has some progression of bone metastases (together with signs of regression) 36 months after radionuclide therapy.

**Discussion**

The synergetic and simultaneous influence on bone metastases of medications like the last generation of bisphosphonates (Zoledronic acid) and radionuclide therapy, can be beneficial in treatment of the bone pain, especially in the earlier stage, before development of complications such as a vertebrae fracture or impending cord compression. Moreover, some authors report that Zoledronic acid may have some anti-tumour effect on disseminated tumor cells [15].

**Figure 1** Correlation between LDH level and the duration of the pain-free period after $^{153}$Sm-oxabifore therapy: (a) in Group 1 and (b) in Group 2

**Figure 2** Example whole-body bone scan of a patient from Group 1 (57-year-old female 4.5 years after mastectomy for T2N1 adenocarcinoma; LDH level before $^{153}$Sm-oxabifore therapy 800IU/L; pain-free period after $^{153}$Sm-oxabifore plus bisphosphonate therapy 5 months) showing progression of metastatic disease

**Figure 3** Example whole-body bone scan of a patient from Group 2 (55-year-old female 5 years after mastectomy for T2N1 adenocarcinoma; LDH level before $^{153}$Sm-oxabifore therapy 886 IU/L; pain-free period after combined $^{153}$Sm-oxabifore plus bisphosphonate plus chemotherapy at >36 months) showing regression
Possible mechanism of pain relief using radionuclide therapy was described by Kairemo et al. [16] suggesting that β-particles may irradiate the red bone marrow (cancer cells), and specific populations of nerve fibers that innervate skeleton; both these mechanisms may lead to disruption of the “vicious circle” [17-18] with possible termination of VEGF production and production of growth factors. According to Warburg's observation, cancer cells have a high consumption of glucose and produce large amounts of lactate [19]. LDH plays an important role in the final step of aerobic glycolysis by converting pyruvate to lactate, which is coupled with oxidation of NADH to NAD+ and allows maintaining the continuity of glycolysis [20]. Glycolysis is the main route of energy production with a minor use of oxidative phosphorylation.

In a meta-analysis conducted by Zhang et al. [21], high LDH level was associated with poor prognosis, suggesting that LDH may be a useful biomarker for therapeutic selection of high-risk patients who would need an intensive therapy. Elevated LDH level is thought to reflect tumour aggressiveness and high tumour burden. Dynamic measurement of LDH level could be a useful tool in outcome prognosis after therapy.

In our study, the patients who received combined treatment with bisphosphonates and radionuclide therapy only, the progression of bone metastasis and recurrence of the pain syndrome were faster in comparison to the group of patients who additionally received chemotherapy and hormonal therapy. This difference was presumably due to the fact that only 26% of the patients in the first group had responded to hormonal therapy versus 53% in the second group.

Our study demonstrates that there is strong negative correlation between LDH level and duration of the pain-free period after radionuclide therapy and no correlation in group of patients whom therapy of primary tumour was added. Since LDH levels reflects cancer progression, according to our data, patients even with high LDH level who received treatment for their primary tumour, had longer pain-free periods and reduction in bone metastases as documented on the WB bone scans. This underscores the importance of the elevated LDH levels prognosticating the need for more intensive treatment of the primary tumour.

The two limitations of our study are the study sample heterogeneity and the small number of patients in our study. In the first group of patients, initially 74% had no favourable prognosis since they were triple negative versus 46.3% in the second group. Initial stage for developing metastases also could play a role. Further investigation on a larger and more heterogeneous group is needed.

**Conclusion**

Based on the results of this study of breast cancer patients, serum LDH levels can prognosticate the duration of the pain-free period after radionuclide therapy. Further, as evidenced by the significantly longer pain-free period in Group 2, it appears that serum LDH levels could be useful in selecting patients who may need treatment for their primary tumour in addition to samarium-153 therapy.

**References**

4. Koutsikos J, Leondi A. Treatment efficacy of combined bisphosphonates and 186Re-


Assessment of renal parenchymal damage by DMSA after PCNL procedure in children using adult-sized equipment

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Abstract

Aims Percutaneous nephrolithotomy (PCNL) is an established technique for the management of renal calculi. The recent advances in this procedure in children include miniaturizing the endoscopic instruments used for renal access. However, there is limited data on the functional effects of PCNL on the renal parenchyma, performed using adult-sized equipment in the paediatric population. This study was therefore aimed to determine the effects of PCNL on the renal parenchyma in children with renal calculi using technetium-99m labelled dimercaptosuccininc acid (99mTc-DMSA) scans.

Methods Pre and post-surgery DMSA scans of 26 paediatric patients who had undergone PCNL over a five-year period were reviewed. The ages of the patients ranged from 1 year to 12.5 years (median: 3.75 years) at the time of PCNL. The procedures were done with 18 Fr or higher sized Amplatz sheath. DMSA scans was performed from 1 day to 47 months before the PCNL and 2 months to 27 months after the procedure and interpreted by two independent observers. Regions-of-interest around each kidney were drawn to determine differential renal function (DRF) of the kidneys.

Results Twenty patients (77 %) showed no change or showed improvement in post-procedure scans. Mean±SD DRF was 44.1±9.7% before and 44.6±10.6% after the procedure (p=0.52, n=21).

Conclusion We conclude that the PCNL procedure in children undertaken with adult-sized equipment may show renal defects in nearly one-fourth of children but there is no significant change in their global renal function.
**Key words:** Percutaneous nephrolithotomy; $^{99m}$Tc-DMSA; children; adult-sized equipment

**Introduction**

Open surgery for the management of upper urinary tract calculi has been largely replaced by percutaneous nephrolithotomy (PCNL) or extracorporeal shock wave lithotripsy (ESWL). PCNL is a surgical procedure in which renal calculi are removed through a one centimeter skin puncture. A track down to the kidney is established under x-ray guidance and a nephroscope is passed into the kidney. Small stones are removed directly and the larger ones are broken into small pieces with an ultrasonic or electrohydraulic probe, or a holmium laser lithotripter. ESWL due to its lower morbidity is the procedure of choice but PCNL is preferred for calculi more than 2 cm in diameter. In children, the latter is performed cautiously due to the concerns of damage to renal parenchyma when it is pierced by nephroscope. PCNL was first performed in paediatric patient in 1985 and with the advances in the technique the frequency has significantly increased since then [1-3]. Nephroscopes of sizes ranging from 19.5 to 27-Fr were used initially while 17-Fr was introduced in late 1980s [2]. Today, 15-Fr nephroscopes are easily available. Smaller nephroscopes may theoretically cause lesser damage to the renal parenchyma; however, their benefit in children is yet to be established. Traxer et al. reported no significant difference in scar tissue measured in sacrificed pigs with right kidney nephrostomies by 30-Fr Amplatz sheath than left kidneys punctured with 11-Fr sheaths [4]. The growing child’s kidney may be affected more by the PCNL size than full-grown kidneys. Although several studies have reported that the adult-sized PCNL equipment is safe in children [5-8], other researchers in contrast, have reported significant complications [9-11]. The assessment of safety of the procedure in all these studies was undertaken by measuring parameters like stone-free rates and the need for blood transfusions. Scanning with technetium-$^{99m}$ labelled dimercaptosuccinic acid ($^{99m}$Tc-DMSA) is a practical option for the assessment of renal parenchymal damage before and after the procedure. Identifying new photon-deficient areas or significant reduction in differential renal function of the operated side, indicates renal parenchymal damage. We visually and quantitatively compared pre- and post-PCNL $^{99m}$Tc-DMSA scans of paediatric population who had procedures performed with adult-sized PCNL tracts.

**Materials and Methods**

Medical records of four consecutive years of Urology and Nuclear Medicine departments at Great Ormond Street Hospital, London, UK, were examined retrospectively from 1999 to 2003, and 37 patients who had undergone PCNL with $\geq$18-Fr Amplatz sheath were selected. Patients who had either preoperative with postoperative, or a normal postoperative DMSA scan were included. Eleven patients were excluded due to lack of adequate details of imaging. Twenty-six patients with ages ranging from 1 to 12.5 years (median: 3.75 years) were therefore available for the review. Twenty-one patients had both pre- and post-procedure scan available, while 5 patients had only post-procedure scans, which were normal. 62% patients had calculi in the left kidney. The PCNL tracts were established and the stones were disintegrated with ultrasonic probe and removed. The size of the Amplatz sheath used varied from 18-Fr to 28-Fr (median: 24-Fr). After the PCNL a nephrostomy tube was placed (range 6-Fr to 28-Fr; median 24-Fr) in 22 patients; 4 patients did not have a tube placed after the procedure. Thirty-three punctures were attempted, with 7 kidneys perforated both in the upper and the lower poles. Five perforations were made in upper poles only, 6 in lower only and 8 in the midportion of the kidneys. In those cases where both the poles were punctured, Amplatz sheaths of the same size were used except in one case in which upper pole was perforated with a 26-Fr and the lower with a 24-Fr sheath.
DMSA scans were performed from 1 day to 47 months (median = 2 months) before the PCNL and 2 months to 27 months (median = 3.5 months) after the procedure. The child was injected using an intravenous line, with a maximum of 80 MBq of $^{99m}$Tc-DMSA and scintigraphy was started 2-4 hours after the injection. Images were acquired on one of two single-headed gamma cameras fixed with high-resolution parallel-hole collimators. Posterior and both posterior-oblique, i.e. left-posterior-oblique (LPO) and right-posterior-oblique (RPO) projections were recorded for 250-500 k-counts on digital matrix of 256×256.

Visually, DMSA scans were interpreted for any abnormality by two independent observers. The decision on any disagreement in interpretation was established after mutual consensus. The scans were also assessed semi-quantitatively by measuring differential renal functions (DRF) of the two kidneys and compared where both pre- and post-PCNL scans were available. Student's $t$ test was applied for this comparison and $p$-value less than 0.05 was considered significant.

**Results**

Table 1 shows the patients grouped on the basis of visual interpretation and comparisons of pre-procedure and post procedure DMSA scans. Twenty patients (77%) had either normal post-procedure scans ($n=12$, 46%) or had no change in pre-procedure abnormal scans ($n=8$, 31%). In those with normal post-procedure scans, the pre-PCNL scans were normal in five, abnormal in two and not available in five patients. Remaining 23% ($n=6$) patients showed new areas of uptake defects in previously normal or abnormal

**Pre procedure scan** | **Post procedure scan** | **No. of patients** | **Outcome**
---|---|---|---
Normal | Normal | 5 | Favourable
No scan available | Normal | 5 | $n=20$
Abnormal | Normal | 2 |
Abnormal | No change from previous | 8 |
Normal | Abnormal | 3 | Deteriorated
Abnormal | Abnormal with new defects | 3* | $n=6$

![Figure 1](image)

**Figure 1** $^{99m}$Tc-DMSA scans comparing pre and post PCNL images. (A) normal; (B) uptake defect in pre-procedure (arrow) and normal post-procedure; (C) same defect (arrow) in pre and post procedure; (D) normal pre-procedure and new defect (arrow) in post-procedure; (E) persistent defect in pre-procedure (arrow) and a new defect in post-procedure (arrowhead)
scans. Images of selected case are shown in Figure 1.

Pre-procedure scans had 44.1±9.7% DRF which after the procedure was 44.6±10.6% ($p=0.52$, $n=21$). DRF of the cases having favourable outcome on visual analysis was 43.5±11.3% before and 44.3±12.1% after the procedure ($p=0.83$, $n=15$). Those cases showing deterioration of DMSA scans on visual analysis had DRF 45.7±3.7% before and 44.7±5.0% after PCNL ($p=0.54$, $n=6$). Figures 2 and 3 demonstrate these changes individually.

**Discussion**

The pros and cons of Percutaneous Nephrolithotripsy (PCNL) versus Extracorporeal Shockwave Lithotripsy (ESWL) have often been highlighted when one discusses the management of renal stones. ESWL has an
advantage over PCNL of not requiring general anaesthesia. However, this advantage does not exist in case of children. There are controversial reports published regarding the safety of renal parenchyma during ESWL in adults as well as children [12, 13]. In case of PCNL, there is limited data available regarding the direct assessment of renal parenchymal damage caused when adult-sized nephroscopes are used.

$^{99m}$Tc-DMSA is an effective and reproducible method for evaluating regional and global renal function [14, 15]. It has been used for assessing damage to the renal parenchyma that may follow the PCNL procedure [16-18]. Regional assessments on $^{99m}$Tc-DMSA scans are usually performed by identifying the photon-deficient areas in the renal parenchyma. Global function may be assessed by visual analysis as well as quantitative analysis by measuring differential renal function [19-21].

After evaluation of our study data, it was found that 5 patients had normal scans before and after the procedure; 5 patients had only one normal post procedure study available; 2 patients showed improvement and 8 had abnormal pre-procedure scans with no change seen on the post- procedure scans. All of these 20 (77%) cases had a favourable outcome in renal function after PCNL. The other group consisted of 3 patients with normal pre-procedure scans and photon-deficient areas in scans done after the procedure and 3 patients with previously abnormal scan and deterioration seen visually in the renal scans after PCNL. In our study 23% of the patients showed new or additional regions of absent uptake of DMSA. This is in contrast to Samad et al. who demonstrated only 5% [22], but their data was based on only four children who had a pre-procedure scans available. In contrast, our study was designed to compare pre- and post-procedure scans. Pre-procedure scans were not available in our study only where they were not required, i.e., normal post-procedure scans. Moreover, Samad et al. used 17-Fr nephroscopes in 75% of their population while we used Amplatz sheaths of more than 18-Fr in all our patients. To our knowledge there is no study that compares pre- and post-PCNL DMSA scans in children where adult sized equipment has been used. Many studies have evaluated the use of such equipment in children by assessing the stone-free rates and complications like the need for blood transfusions, but the reported results are conflicting [5-11].

DRF of both pre and post studies were available in 19 patients. There was no significant change seen in DFR in the operated kidneys before and after the procedure. There was a slight increase in DRF in patients who showed favourable changes visually but was not statistically significant ($p=0.83$). Similarly, the DRF decrease in the patients showing deterioration visually was also not significant. In a study performed in an adult population, Demirtas et al. found significant differences in differential functions before and after PCNL [23]. The possible reason is the growing kidneys in children. This may cause compensatory change in overall renal function despite the fact that the scars may persist regionally.

**Conclusion**

The study demonstrated that PCNL procedure with adult-sized equipment may cause regional uptake defects on the DMSA scan in nearly one-fourth of children without a significant change in global differential function.

**References**


Vitamin B12 deficiency: prevalence and evaluation of a reversible co-morbidity in hypothyroid patients

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Department of Nuclear Medicine, Atomic Energy Medical Centre, Jinnah Postgraduate Medical Centre (JPMC), Karachi

Abstract

Aims The study aimed at assessing the prevalence and clinical features of vitamin B12 deficiency in hypothyroid patients and to evaluate clinical response to vitamin B12 replacement therapy.

Methods A total of 204 vitamin B12 deficient patients with primary hypothyroidism who attended the thyroid clinic at the nuclear medicine department of Atomic Energy Medical Centre Karachi, were included in the study. Signs and symptoms, haemoglobin (Hb), mean corpuscular volume (MCV), thyroid function tests and B12 levels were recorded. Patients with low levels of B12 or who had symptoms suggestive of B12 deficiency were given oral vitamin B12 treatment and monitored for improvement.

Results A total of 204 hypothyroid patients (197 females, 7 males) were evaluated. 92 of 204 patients (45.09%) had low vitamin B12 levels. Depression (p value 0.000082), weakness (p value 0.0018), numbness (p value 0.022), paraesthesia (p value 0.018), and impaired memory (p value 0.027) were statistically significant in B12-deficient hypothyroid patients. B12-deficient patients had increased prevalence of anaemia than the sufficient group (32.6% vs. 22.02%). 92 B12-deficient and 70 B12-sufficient patients with symptoms of B12 deficiency were started on oral vitamin B12 and improvement noted.

Conclusion There is a high (45%) prevalence of B12 deficiency in hypothyroid patients. Screening of vitamin B12 levels should be undertaken in all hypothyroid patients in the early course of the disease as it is a potentially reversible condition. Weakness, numbness and neuropsychiatric symptoms point towards B12 deficiency. Replacement of B12 leads to improvement in symptoms; however, placebo effect should be taken into consideration.

Key words: Anaemia, hypothyroidism, neuropsychiatric symptoms, vitamin B12 deficiency

Introduction

Vitamin B12 (cobalamin) is one of the complex water soluble vitamins. Several critical biological processes such as cellular metabolism, DNA replication and red blood cell formation depend on vitamin B12. Vitamin B12 deficiency occurs in about 3.8% of the population. Diverse religions, ethnic
and socio-economic heterogeneity of the people of Asian countries leads to under recognition of its deficiency [1].

Pernicious anaemia is present in subjects with primary autoimmune hypothyroidism with a reported association in up to 12% of patients [1]. Vitamin B12 deficiency may also be due to the high prevalence of H. pylori infections [2], use of oral contraceptive pills [3], diabetic medication like metformin [4], malnutrition and malabsorption. In developing countries, the deficiency is much more common starting in early life with the prevalence increasing with age. Classic cobalamin deficiency is associated with megaloblastic anaemia and neurological symptoms [8]. The typical haematologic changes are easy to detect but they occur at a later stage and may even be absent [9].

Hypothyroid patients often present with weakness, fatigue, paraesthesia, numbness or tingling in the fingers and toes, poor balance and coordination, depression, dementia, and a decline in mental abilities that is severe enough to interfere with daily life, despite being euthyroid on adequate doses of thyroxine.

The increasing frequencies of these symptoms in hypothyroid patients led us to evaluate for this co-morbid condition as it is a potentially reversible burden.

**Materials and Methods**

Patients with primary hypothyroidism who attended the thyroid clinic at the nuclear medicine department of Atomic Energy Medical Centre Karachi, from October 2015 to march 2016 were evaluated. Patients who were strict vegetarians, had history of gastric or ileal resection or malignancies were excluded.

Clinical features including weakness, numbness, abdominal pain, depression, impaired memory, paraesthesia and decreased reflexes were noted. The presence of pallor and impaired reflexes was recorded. A note of concomitant illnesses and medications including gastric acid inhibitors and metformin was made. Haemoglobin level, mean corpuscular volume, thyroid function tests, thyroid antibodies and vitamin B12 levels were measured.

Patients who had low levels of vitamin B12 or who had symptoms suggestive of vitamin B12 deficiency, were given oral vitamin B12. The patients were followed for 6 months and a note was made of any improvement in symptoms.

Haemoglobin was checked by spectrophotometer using cyanide-free technique with patients with Hb levels of <11 mg/dl in females and <13 mg/dl in males were considered as anaemic. Vitamin B12 levels were estimated by the radioimmunoassay technique by a gamma counter using the Diagnostic Product Cooperation (DPC) method, with the normal range of 200-900 pg/ml.

Results were expressed as mean ± standard deviation, median for all continuous variables and number (percentages) for categorical data. Statistical analysis was performed by chi-square test where appropriate and p value <0.5 was taken as significant. Statistical interpretation of data was performed using SPSS 10.0.

**Results**

204 hypothyroid patients were evaluated including 197 (96.5%) females and 7 (3%) males. The patients' age ranged from 14-80 years with a mean age of 37.24 ± 11.61 (44.28 ± 16.93 for males and 36.99±11.35 for females); 117 (57.35%) patients were below 40 years of age.

A total of 92 (45.09%) of 204 patients had vitamin B12 levels <200 pg/ml (normal 200-900 pg/ml); 75 of the 92 patients had levels between 100-200 pg/ml, and 17 with levels <100 pg/ml. There was no significant difference in mean age and sex ratios between the groups with vitamin B12 deficiency and those with normal vitamin B12 levels (Table 1).

Symptoms of depression, weakness, numbness, paraesthesia, impaired memory and hair loss were seen more commonly in vitamin B12-deficient patients. The frequencies of common symptoms recognized in our hypothyroid patients are seen in Table 2. Twenty hypothyroid
patients with vitamin B12 deficiency were seen to have pallor. Impaired reflexes were recorded in 15 of the hypothyroid vitamin B12-deficient patients.

Haemoglobin value was noted in all patients. The mean Hb in vitamin B12-deficient group was slightly lower than in B12-sufficient group (10.61 ± 1.82 vs. 11.84±1.54). 5 (71%) males had Hb <13.5 while 53 females (57.6%) had Hb <11g/dl. B12-deficient patients had increased prevalence of anaemia compared with the non-deficient group (32.6% vs. 22.02%).

### Table 1  Mean age and sex demographics in vitamin B12-deficient and B12-sufficient groups

<table>
<thead>
<tr>
<th></th>
<th>B12 &gt;200 pg/ml</th>
<th>B12 &lt;200 pg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>112</td>
<td>92</td>
</tr>
<tr>
<td>Age</td>
<td>37.47±11.2 yrs</td>
<td>36.96±12.1 yrs</td>
</tr>
<tr>
<td>Sex</td>
<td>male 1</td>
<td>male 6</td>
</tr>
<tr>
<td></td>
<td>female 111</td>
<td>female 86</td>
</tr>
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</table>

### Table 2  Frequency of symptoms in B12-deficient and B12-sufficient patients

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Total patients (n= 204)</th>
<th>B12&lt;200 pg/ml</th>
<th>B12&gt;200 pg/ml</th>
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</thead>
<tbody>
<tr>
<td>Depression</td>
<td>150</td>
<td>80 (53.3%)</td>
<td>70 (46.6%)</td>
</tr>
<tr>
<td>Weakness</td>
<td>144</td>
<td>75 (52.0%)</td>
<td>69 (47.9%)</td>
</tr>
<tr>
<td>Numbness</td>
<td>136</td>
<td>69 (50.7%)</td>
<td>67 (49.2%)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>99</td>
<td>53 (53.5%)</td>
<td>46 (46.4%)</td>
</tr>
<tr>
<td>Impaired memory</td>
<td>87</td>
<td>47 (54.0%)</td>
<td>40 (45.9%)</td>
</tr>
<tr>
<td>Hair loss</td>
<td>65</td>
<td>35 (53.8%)</td>
<td>30 (46.1%)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>80</td>
<td>34 (37.5%)</td>
<td>46 (57.5%)</td>
</tr>
<tr>
<td>Retrosternal burning</td>
<td>57</td>
<td>22 (38.5%)</td>
<td>35 (61.4%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>31</td>
<td>15 (48.3%)</td>
<td>16 (51.6%)</td>
</tr>
<tr>
<td>Decreased reflexes</td>
<td>21</td>
<td>10 (47.6%)</td>
<td>11 (52.3%)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>11</td>
<td>6  (54.5%)</td>
<td>5  (45.4%)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>3</td>
<td>1  (33.3%)</td>
<td>2  (66.6%)</td>
</tr>
</tbody>
</table>
Associated diseases among the 204 hypothyroid patients included diabetes (n=15), hypertension (n=34), ischaemic heart disease (n=3) and dyslipidaemia (n=6). Six of the 15 diabetic patients were vitamin B12-deficient but 2 of them were taking metformin, which may have contributed to the vitamin B12 deficiency. Four out of 25 patients who were on proton pump inhibitors or H2 receptor blockers, were found to be vitamin B12 deficient. Replacement therapy with oral vitamin B12 was instituted and the patients were followed up subsequently. Ninety-two vitamin B12-deficient and 70 vitamin B12-sufficient patients with symptoms suggestive of vitamin B12 deficiency were started with oral vitamin B12 replacement therapy. Improvement in symptoms was documented in 122 patients. 87 out of 92 (94.5%) was B12-deficient while 35 out of 70 (50%) were B12-sufficient. Forty patients did not show any improvement in symptoms of which 5/40 (12%) were B12-deficient and 35 out of 40 (87.5%) were B12-sufficient.

Discussion

Vitamin B12 or cobalamin, is one of the B complex water soluble micronutrient chiefly available in animal protein. Several critical biological processes such as cellular metabolism, DNA replication, red blood cell formation depend on vitamin B12; furthermore, metabolism of B12 is essential for myelin synthesis and maintenance of neuronal integrity as well as neurotransmitter regulation [10, 11]. Our study estimated the prevalence of B12 deficiency at 45.09% (92 of 204 patients hypothyroid patients), which is higher than the 39.6% prevalence reported by Jabbar et al. [12].

Most people obtain sufficient vitamin B12 from their diet. However, in the developing countries, B12 deficiency is much more common, starting in early life, with an increase in prevalence with age in certain groups of people, such as people of low socioeconomic status who rely more on a vegetarian diet and people older than 50 years of age. In the developed countries 6% of those aged 60 years and above are B12-deficient, with the prevalence in elderly varying from 3-40% likely due to malabsorption [7].

Metformin can cause malabsorption secondary to its effect on ileal mucosa. Proton pump inhibitors and H2 receptor antagonist cause gastric hypochlohydria and malabsorption of vitamin B12. Pernicious anaemia in hypothyroid patients may be part of an autoimmune polyglandular endocrinopathy [13]. Intrinsic factor and gastric parietal cell antibody were not available locally and patients were unable to get tests done due to socioeconomic constraints; therefore, despite association of hypothyroidism and vitamin B12 deficiency, the underlying aetiology was difficult to determine.

Vitamin B12 deficiency causes haematological, neurologic, cognitive problems and mood symptoms. Severe cobalamin deficiency is associated with megaloblastic anaemia; however, it can occur without the classic signs of anaemia or macrocystosis. The typical haematologic changes associated with vitamin B12 deficiency are easy to detect but these develop at a later stage and may even be absent [9, 14].

In our study haemoglobin value was recorded in all patients. The mean Hb in vitamin B12-deficient group was slightly lower than in B12-sufficient group (10.61 ± 1.82 vs. 11.84 ± 1.54). 5 (71%) males had Hb <13.5 while 53 (57.6%) females had Hb <11g/dl. B12-deficient hypothyroid patients had increased prevalence of anaemia than the patients in the non-deficient hypothyroid group (32.6% vs. 22.02%). The MCV value was however the same for both groups (80.79±9.8 vs. 80.17±10.87). Unexpectedly, macrocystosis was rare in the current study population, even among those with very low cobalamin concentrations. One possible reason may be that an adequacy of folate intake, which protects against macrocystosis and thereby masks the effect of cobalamin deficiency [8, 15].

Hypothyroid and vitamin B12-deficient patients have similar symptoms of weakness, lethargy, memory impairment and tingling.
We noted that several patients, despite having adequate thyroxine treatment, had persistence of symptoms and these were later found to be vitamin B12-deficient. In our study, we noted that weakness and numbness, although present in both groups, was significantly higher in the vitamin B12-deficient hypothyroid patients, with p values at 0.0018 and 0.022 respectively.

Clinical signs of vitamin B12 deficiency may take long to manifest; however, neuropsychiatric symptoms occasionally present as the earliest clue to B12 deficiency. Vitamin B12 deficiency in hypothyroid patients can be one of the most important causes of reversible cognitive decline acting as a second hit in hypothyroid patients. In our study, statistically significant neuropsychiatric manifestations were seen between the B12-deficient hypothyroid patients and the B12-sufficient patients: including depression (p=0.000082), paraesthesia (p=0.018), and impaired memory (p=0.027). Other complaints like hair loss, nausea/vomiting, abdominal pain and decreased reflexes were common in both sets of patients; however, they were not statistically significant in vitamin B12-deficient patients.

There was a significant improvement reported in symptoms within 2-3 months of initiating oral cobalamin in hypothyroid B12-deficient patients. Although some of the B12-sufficient patients who had symptoms suggestive of vitamin B12 deficiency, also had improvement in the symptoms, this may likely be due to placebo effect but this needs to be further investigated and determined by a placebo-controlled study.

Measurement of serum cobalamin is the most commonly used biochemical test for diagnosing cobalamin deficiency, but it lacks sensitivity. Studies in the past has established that markers of cobalamin function, particularly total homocysteine (tHcy) and Methylmalonic acid (MMA) are elevated in subtle cobalamin deficiency states not characterized by the typical clinical symptoms [9]. Recently, it was reported that plasma tHcy concentrations are higher in vegans than in omnivores [16]. A similar finding of elevated tHcy and MMA was observed in infants in a macrobiotic (vegan) community [17]. Determination of these levels can lead to early detection of vitamin B12 deficiency and can prevent morbidities in hypothyroid patients. Metabolism of homocysteine and methylmalonyl acid (MMA) involves cobalamin, which is associated with atherosclerosis [18, 19]. Although we did not measure homocysteine levels but other studies have shown a relationship with hypothyroidism which improves with treatment to euthyroid status [20, 21].

In developing countries flour fortification would potentially be helpful in improving the vitamin B12 status in the population at large because of low intake of vitamin from animal source foods. It could benefit across the life span and it would especially be beneficial for pregnant and lactating women, children and elderly.

**Conclusion**

Our study has shown that vitamin B12 deficiency is common in hypothyroid patients as well as in patients rendered euthyroid by thyroxine replacement. Screening for vitamin B12 should be undertaken early in the diagnosis of hypothyroidism. Patients with suggestive symptoms should be evaluated and followed up. Neuropsychiatric symptoms usually act as surrogate markers. Anaemia and macrocytosis cannot be relied upon to point towards vitamin B12 deficiency as it may develop in much later stages of B12 deficiency. Since there is a marked improvement after replacement therapy, early diagnosis and treatment is essential in preventing the long-term sequelae and morbidities of vitamin B12 deficiency.

**Acknowledgements**

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References


Validation of Ottawa ankle rule utilizing radionuclide skeletal scintigraphy

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Abstract

Aims Ankle and foot injuries, especially among teenagers and young adults, are frequently encountered by the primary care physicians. Most common ankle injuries are sprains due to inversion injuries to the lateral ankle ligaments. It has been observed that the overall number of ankle radiographs in the ER is around 15-20%, which includes about 30-40% unnecessary radiographs. Ottawa Ankle Rule (OAR) was first established in 1992, to reduce that unnecessary load on x-ray departments. In light of the current universal practice of evidence-based medicine it is important to undertake verification of the subjective OAR. Bone scintigraphy by merit of its high sensitivity was chosen as the imaging modality of choice to validate the accuracy of OAR.

Methods The study population comprised of 50 OAR-positive cases and 10 normal controls. Each case was scanned using 3-phase bone scintigraphy (TPBS), following a preliminary radiograph.

Results Out of 50 OAR-positive cases, x-rays showed frank fractures in only 12 cases, whereas bone scan was positive in 45 cases, out of which 43 had active bone lesions, the remaining 2 had a soft-tissue injury. By considering the TPBS bone scan as the gold standard, we found the sensitivity of OAR was 95% and specificity 61.5% with PPV and NPV at 90% and 80% respectively.

Conclusion We conclude that there is a high concordance between the OAR and the bone scan and that the OAR is evidence-based as determined by the successful verification of the OAR by the TPBS in 95% of the cases. Based on our findings we recommend the routine practice of the OAR in all emergency departments. In patients with acute ankle/foot injuries, with a positive OAR, even with a negative x-ray, the injury should not be taken lightly and if required, a bone scan should be performed for confirmation of lesion. Bone scintigraphy rather than plain radiography appears to be the modality of choice in this situation being cost- and time-effective without compromising the quality of medical care.

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**Key words:** Ottawa ankle rule, radionuclide bone scan, x-ray, radiograph

**Introduction**

Ankle and foot injuries, especially among teenagers and young adults, are commonly encountered by the primary care physicians. The commonest ankle injuries are sprains due to inversion injuries to the lateral ankle ligaments [1]. It has been observed that the overall number of ankle radiographs in the emergency room (ER) is around 15-20% [2], which includes about 30-40% unnecessary radiographs [3].

Although at first glance, ankle injuries may appear to be minor, up to 44% of patients may have persistent symptoms one year after the injury. Though only a few of these cases suffer a fracture, nearly all are investigated through plain x-rays of the ankle or foot, or both [4]. To deal with this clinical problem, a set of guidelines known as the Ottawa ankle rules, were first developed at the University of Ottawa in Canada in 1992 [5], stating that ankle x-rays are only required if there is any pain or tenderness at posterior edge or tip of either of the malleoli, and foot x-rays are only required if there is any pain or tenderness at the base of 5th metatarsal or the navicular bone or the patient is unable to bear weight both immediately post injury and in the emergency department.

Stiell et al. in 1994 [6] showed that by proper implementation of this rule there was a reduction in ankle radiography by 28%. Pigman et al. [7] also studied acute ankle injuries in emergency departments of three hospitals during the pre-intervention and intervention periods and observed significant reduction in radiographic requests.

The impact of the Ottawa ankle rules in a US Army troops medical clinic in South Korea was studied by Springer et al. [8] who reported a sensitivity and specificity for the rules at 70% and 73% respectively. The positive and negative predictive values were 31.8% and 93.3% respectively. Leisey et al. in 2004 observed that correct implementation of the OAR has a definite potential to decrease the use of radiographic resources in deployed military population [9]. Papacostas et al. (2001) studied Ottawa ankle rules protocol in Greek athletes and concluded that the Ottawa ankle rules protocol is 100% sensitive [10]. Karpas et al. (2002) studied the application of OAR in paediatric emergency department and found that the use of the OAR had reduced the radiography rate by 21% [11].

All prior reported studies were aimed at utilizing these rules for the prediction of frank fractures by plain radiography. In contrast, we have attempted to validate the OAR through bone scintigraphy, the most sensitive diagnostic modality for skeletal trauma. This first reported study of its type compared the OAR findings with x-ray and bone scan results with an aim to validate the sensitivity and specificity of OAR.

**Patients and Methods**

The study was carried out at Nuclear Medical Center, Armed forces Institute of Pathology, Rawalpindi. The patients were referred from the orthopaedic department of the Combined Military Hospital, Rawalpindi. A total of 60 subjects were studied, which included 10 normal controls (6 males, 4 females) and 50 patients with acute ankle or mid foot injuries (41 males, 9 females) fulfilling the criteria for a positive Ottawa ankle rule. The age of the subjects ranged from 12 to 64 years (mean 29±12 years). Each patient was examined by 3 doctors including a general physician, a surgeon/orthopaedician and a nuclear medicine physician. The study exclusion criteria were more than 30 days since injury, pregnancy, an obvious deformity of ankle or foot, crush injuries, diabetic foot, and children below 12 years of age.

After routine history taking and clinical examination, fresh ankle and foot x-rays (AP and lateral views), were advised. The study procedure was explained to the patient and
informed consent was taken. A 3-phase bone scan was performed on the next working day using dose injected in each case was 16 mCi. The patient was positioned supine under the gamma camera fitted with a low-energy general-purpose collimator and 16 mCi (~600 MBq) of technetium-99m labelled methylene diphosphonate ($^{99m}$Tc-MDP) was injected intravenously. A dynamic flow study (1st phase) was obtained at 1-sec/frame for 60 seconds. This was followed by a blood pool image at 2 minute (2nd phase), for 1 min. Four delayed static images in the anterior, posterior, right-lateral and left-lateral projections were subsequently at 3 hours postinjection (3rd phase). The delayed spot views were count-based with 300 k-counts per image. The scan were interpreted independently by three nuclear medicine specialists.

Statistical analysis The data was tabulated and the means and standard deviations (S.D.) were calculated for each group and the chi-squared test applied to obtain statistical inference considering $p$ value of <0.05 as significant. Taking the bone scan as the gold-standard, the sensitivity, specificity, PPV and NPV of Ottawa ankle rule were calculated.
**Results**

Out of the 50 OAR-positive patients, only 12 cases had a complete fracture detected by x-rays, with the patients complaining of pain, swelling and tenderness and all of them were unable to bear weight on the affected side. Rest of the clinical findings, x-rays and bone scan results are shown in Table 1.

Out of the 50 OAR-positive cases, 45 had positive scans, i.e. 90% of lesions were picked up by bone scan, while only 10% of OAR-positive cases had a normal bone scan.

Figure 1 shows the ability of various diagnostic modalities to pick bone and soft-tissue lesions. In this study, out of 50 OAR-positive cases, x-ray could pick only 24% of the lesions (12 out of 50) and missed 76% of the lesions, whereas in contrast 90% of the lesions (45 out of 50) were picked up by bone scintigraphy which also included two soft-tissue injuries, that were picked up by Ottawa ankle rule and were confirmed by the bone scan.

For our control group we selected 10 OAR-negative individuals as control subjects, 7 out of 10 of whom were army personnel.

Optimisation of results was performed to determine the best technique for the diagnosis of acute ankle/foot injuries or arrive at the best possible combination (see Table 2).

Chi-squared test applied to obtain statistical inference considering p value of <0.05 as significant considered the null hypothesis, i.e. x-ray and bone scan are equally good for validation of Ottawa ankle rule. With the degree of freedom 1 and p value as <0.05, we found that our calculated value (22.7) was much higher than tabulated value (3.84), thereby rejecting the null hypothesis and allowing us to conclude that the bone scan was significantly superior to x-ray for validation of Ottawa ankle rule.

Since OAR is a set of clinical criteria based on subjective finding, it cannot form a criterion for evidence based medicine. For its validation we selected the most sensitive imaging modality, i.e. bone scan, as the gold standard and determined the sensitivity of OAR at 95%, specificity at 61.5%, positive predictive value (PPV) at 90%, and negative predictive value (NPV) at 80%.

**Discussion**

Ankle and foot injuries are very common in clinical practice, constituting a major proportion of cases in emergency medicine. X-Ray is considered to be the most important method of evaluation of bone lesions, but most of the times, it just increases the work

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**Table 2 Optimisation of the results**

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>X-Ray Findings</th>
<th>Bone scan Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Fracture</td>
<td>NAD</td>
</tr>
<tr>
<td>Patient (OAR +ve)</td>
<td>50</td>
<td>12</td>
<td>38</td>
</tr>
<tr>
<td>Control (OAR -ve)</td>
<td>10</td>
<td>-</td>
<td>10</td>
</tr>
</tbody>
</table>

NAD: No abnormality detected. A.B.L.: Active bone lesion.

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**Figure 1** Comparison between clinical evaluation criteria (OAR), x-ray and bone scintigraphy
load on x-ray department [2]. The Ottawa ankle rule (OAR) was introduced in 1992 to cope with this problem. The OAR incorporates guidelines for ordering x-rays in acute ankle and mid-foot injuries [5]. Appropriate utilization of OAR can reduce the number of radiographic requests by 22.4% [12].

These days evidence-based medicine is stressed by the medical professionals. The OAR, being only a set of clinical criteria, could be called as subjective only [15]. This is one of the reasons that children below 12 years of age were not included in the study, as OAR is a clinical judgement, which is difficult to appreciate in children correctly and there is always a chance of over estimation. Though Dayan et al. in 2004, observed malleolar zone and mid-foot zone fractures in children and found the rule to be reasonably sensitive [14].

In this particular scenario, it was essential, that there should be an evidence-based study for validating these rules, and for this purpose we chose the highly sensitive imaging technique of the radionuclide bone scan. Thus to fulfil the criteria of evidence-based medicine for the validation of OAR, we utilized the radionuclide bone scan, which has proven high sensitivity and a reasonably high specificity [16,17] and found that the sensitivity of the Ottawa ankle rule came out to be 95%, positive predictive value and negative predictive value were 90% and 80% respectively.

We performed x-rays and bone scans on all of the 50 OAR-positive patients and observed that that out of 50 cases only 12 (24%) had fractures on x-rays whilst 45 (90%) had positive bone scans and out of these 45, 43 had active bone lesions and 2 had soft-tissue injuries.

Our control group included 10 volunteers, all OAR negative. But out of these 10, 7 were military personnel, who routinely undertake physically stressful activities [13] with the result that 2 (20%) subject (Table 2), had a false-positive scan. We presume that if we could take a larger control group and all were selected from the general public rather than a fixed occupational group, the results could be even better.

Our study is an analytical study in which we validated the OAR using the radionuclide bone scan. In the study, out of the 50 OAR-positive cases, only 12 (24%) came out to be frank fractures picked up by the plain radiographs (Table 1). The rest of the 38 cases were sprains, confirming the fact that a sprain is much more common problem that can be easily missed by an x-ray, but can be picked up by clinical assessment criteria i.e. OAR.

In this study, we could detect a wide range of lesions with fixed assessment criteria used. Figure 2 shows an intensely hot lesion at the base of the 5th metatarsal in the left foot, which was due to a fracture picked up by plain radiography. But on the bone scan, it was observed that adjacent talus also had an active bone lesion, which was not detected by plain x-ray, indicating the usefulness of bone scan in the diagnosis of such cases.

Another important finding was presence of soft-tissue lesions (Figure 4) indicating that OAR criteria are so valid and significant and that they can even pick up soft-tissue injuries, which definitely needs early identification and management in order to avoid long-term complications [18].

In our control group, we have seen that the false-positive rate was rather high (20%) representing 2 out of 10 cases. This could be due to high bone scan sensitivity [19], that can even pick up mild, localized inflammatory lesions, associated with routine stress (as in our case of military personnel) who were otherwise asymptomatic. This results in high false-positive values, reducing the specificity of the rule, which in our study came out to be at 61.5%. We think that if we have to apply OAR randomly on the general public, the specificity will be definitely higher due to lower false-positive rate.

It was observed that, in almost all the cases there was increased perfusion and blood pool
Figure 2 A 52-year-old male (case 1) with a history of trauma to the left foot with tenderness at base of the left 5th metatarsal and navicular bones. Bone scan (left) shows active bone lesions at the base of left 5th metatarsal and the adjacent talus, with the x-ray (right) showing fracture at the base of the left 5th metatarsal.

Figure 3 A 34-year-old female (case 2) with history of trauma to the right foot with tenderness over the right navicular bone. Bone scan (left) shows an active bone lesion in the right talus, with a normal x-ray (right).

Figure 4 A 41-year-old male (case 3) with history of trauma to the left foot with tenderness below and behind the lateral malleolus. Bone scan (left) shows increased uptake in lateral malleolus on the perfusion and blood pool images with normal delayed views consistent with soft-tissue injury; the x-ray is normal (right).
on the contralateral side and delayed static views also showed slightly raised tracer uptake. We know that whenever there is increased pressure or weight bearing at any site, this initiates a remodeling process in the bone, causing increased radiotracer uptake [20], but such uptake is physiological.

One may query the importance of a set of clinical criteria. The answer to that question is cost, time and convenience. A simple but thorough clinical examination involves minimum time and cost equivalent to a single visit to a physician and with no radiation exposure. We may wonder that on a simple clinical examination one may somehow miss some important findings. However, we have seen that by simply utilizing the OAR criteria, we can pick as minute bone lesions, stress fractures, and even soft-tissue injuries, which can only be detected by bone scintigraphy. These stress-related injuries, if missed, can transform into more serious lesions such as conversion of stress fractures into frank fractures, which can be avoided by utilizing the OAR [21].

Another important aspect is the cost effectiveness of the implementation of the rule. We have made a rough estimate of cost for unnecessary x-rays in this study, and it was observed that at least 20-30% of the total cost and a lot of precious time can be saved, if the OAR is properly utilized.

One thing that is worth mentioning is that, we are not recommending bone scan for every patient with a positive OAR, rather we are suggesting that there is no need of any diagnostic test after a positive OAR in a patient with acute ankle injury. We can directly switch on to the management, which in most of the cases is conservative and involves immobilization, analgesics and anti inflammatory drugs for 3-6 weeks [22]. But if for some reason confirmation of lesion is essential, for example for some documentation like job requirements, insurance purposes, etc., one should go for bone scintigraphy as it will most accurately pick up all types of bone lesions.

We therefore strongly recommend that with a OAR is positive, a person should be considered as an injured person and he/she should receive optimal treatment. But if the physician himself is not very confident in declaring the patient as OAR-positive, in mild cases, only 1-2 weeks immobilization with mild analgesics will be enough and neither x-ray nor bone scanning is recommended [19].

The discussion above may give a false impression that perhaps we totally negate the

**Figure 5** A 16-year-old female (case 4) with history of trauma to the left foot with tenderness over the lateral malleolus. Bone scan (left) shows an active bone lesion in the left lateral malleolus; the preliminary x-ray was reported to be normal but a repeat x-ray confirmed the lesion.
Acute ankle / foot injuries

History and Clinical examination

OAR positive
- Go for Management

OAR negative
- Observe

For confirmation of lesion

X-Ray (very low sensitivity): 24%

Bone scan (very high sensitivity): 90%

Doubtful cases

Well localized, intense uptake
- x-ray indicated

Mild uptake
- No need of x-ray

Figure 6  An algorithm for assessment of the patients with acute ankle/foot injuries
importance of plain radiograph. This is not the case as x-rays are definitely indicated in some cases where we need a higher specificity rather than high sensitivity. So whenever an orthopaedician is suspecting a frank fracture that may need some intervention like open reduction or internal fixation, x-ray is strongly indicated.

Now the question arises when one should go for x-ray after bone scintigraphy? The answer is, when the lesion is very hot and well localized in all the 3 phases of 3-phase bone scan. This is an indication for plain radiograph after bone scintigraphy but the simple visual impression will not be enough. Semi-quantitative analysis should decide the cutoff point in such cases. A bone scan will then compliment the x-rays. Another possibility could not be excluded was that fractures were present and radiologist was unable to see the fractures. Even in our study, we had 2 cases, one of which is shown in Figure 5, where the patient had a twisting eversion injury of left foot and the initial x-ray was reported as normal whereas bone scan detected an intense, well-localized lesion at left lateral malleolus. Repeat x-ray was then performed, of the specific site with a specific zoom and it was then reported to have a hairline fracture at the level of the lateral malleolus.

We propose an algorithm for the assessment of the patients with acute ankle/foot injuries (Figure 6) and we expect that if the physicians follow this algorithm for evaluation of patients with acute ankle/foot injuries, there will be a minimum chance of missing a significant lesion and the quality of medical care will definitely improve.

We recommend extensive utilisation of the Ottawa ankle rule in surgical emergency departments, to detect all sorts of bone lesions in acute ankle/foot injuries. The emergency staff should be properly trained to learn and implement OAR in all the cases with acute ankle and foot injuries.

Conclusion

Evidence supports the Ottawa ankle rule as an accurate and very effective instrument for detection of the ankle and midfoot injuries. The OAR has a sensitivity of 95% which is comparable to bone scintigraphy and reasonably high specificity of 61.5%. Therefore in patients with acute ankle/foot injuries, with positive OAR, even with a negative x-ray, the injuries should be taken seriously. However, in difficult cases, bone scan can play a complementary role to plain radiographs. The widespread application of OAR can save both time and money without compromising quality of medical care.

References


Radiosynoviorthesis in pigmented villonodular synovitis using Re-188 labelled tin colloid: a case report

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Abstract

Radiosynoviorthesis (RSO) is an attractive alternative to surgical synovectomy for controlling symptoms of rheumatoid arthritis and many other chronic proliferative joint diseases. The procedure is not widely used in our country because of the non-availability of suitable radionuclides and radiopharmaceuticals. The production of rhenium-188 (¹⁸⁸Re) from ¹⁸⁸W/¹⁸⁸Re generator and by labelling it with particles of appropriate size, has a promise to offer. We labelled ¹⁸⁸Re with tin colloid and analyzed its biodistribution and clinical efficacy after injecting it to a patient with recurrent pigmented villonodular synovitis. Gamma camera imaging performed after 1, 24 and 48 hrs showed no leakage of the radiopharmaceutical from the injected joint. The clinical outcome of this study was also excellent, which suggests that ¹⁸⁸Re labelled tin colloid is a potentially effective radiopharmaceutical for recurrent PVNS and can be used for other chronic inflammatory joint diseases.

Key words: PVNS, Particle size, Radiosynoviorthesis, ¹⁸⁸Re tin colloid

Introduction

Radiosynoviorthesis (RSO) is an effective alternative tool for restoration of synovium in chronic inflammatory joint diseases (CIJD) in carefully selected patients. The procedure is based on an intra articular injection of β-emitting radiopharmaceuticals directly into the affected joint space in an effort to ablate the synovium [1-3]. The radiopharmaceutical deposits almost all of its β energy on the internal lining of the inflamed and proliferative synovium. This destroys the proliferating synovial cells of the involved joint and will enable it to restore a near normal lining. RSO can be helpful in a number

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of conditions including rheumatoid arthritis (RA), osteoarthritis, haemophiliac synovitis, synovial chondromatosis, PVNS and some other rare inflammatory arthritic diseases [2-4].

PVNS is a rare, aggressive, non-malignant proliferative histiocytic joint lesion that causes swelling, pain and loss of mobility in the affected joint [5]. The disease poses challenges in the management. It is primarily treated by open or orthroscopic synovectomy with reasonable success rates but there is a high risk of recurrence ranging from 8-46% depending on extent and severity of disease [6, 7].

In such conditions, RSO plays an appealing role in that it selectively irradiates the proliferating synovium without any significant radiation burden to the rest of the body [8]. Radiopharmaceuticals with strong β emissions and soft-tissue penetration are ideal for RSO [4, 9]. The most commonly used radio pharmaceuticals for RSO along with their physical properties are presented in Table 1.

188Re has excellent nuclear and chemical properties, therefore its potentials are being explored in a variety of clinical settings. 188Re is available from 188W/188Re generator which offers significant advantages in terms of in-house availability and convenience with low cost as compared to other therapeutic radionuclides [10]. Owing to its deep tissue penetration (10 mm), 188Re is considered suitable for treatment of large and some time medium joint diseases. In this study, 188Re Tin colloid was prepared and its biodistribution was assessed after intra articular injection into the knee joint affected by PVNS under ultrasound guidance.

**Case Report**

A 17-year-old girl was referred to the nuclear medicine department of Institute of Radiotherapy and Nuclear Medicine (IRNUM) for treatment of PVNS. She had undergone multiple open surgical synovectomies over the last 18 months. On examination, she had a large swollen right knee joint with multiple scars of past surgical synovectomies [Figure 1]. The joint had a limited mobility and was tense and tender. The patient had undergone debulking surgery and removal of septations prior to 188Re-RSO. After four weeks of the debulking synovectomy, the patient underwent RSO. 185 MBq (5 mCi) of 188Re tin colloid was injected into the right knee joint under ultrasound guidance at 2 sites. After 1 hour, an image of the knee was acquired to look for biodistribution of the radiopharmaceutical (Figure 2).

<table>
<thead>
<tr>
<th>Radiopharmaceuticals</th>
<th>β E_{\text{max}} (MeV)</th>
<th>γ E_{\text{max}} (KeV)</th>
<th>T_{1/2} (d)</th>
<th>Penetration (mm)</th>
<th>Particle size (µm)</th>
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<tbody>
<tr>
<td>32P chromic phosphate colloid</td>
<td>1.71</td>
<td>--</td>
<td>14.3d</td>
<td>7.9</td>
<td>500-2000</td>
</tr>
<tr>
<td>90Y citrate or silicate</td>
<td>2.27</td>
<td>--</td>
<td>2.7d</td>
<td>11</td>
<td>100</td>
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<tr>
<td>165Dy FHMA</td>
<td>1.29</td>
<td>95</td>
<td>2.33h</td>
<td>5.7</td>
<td>3000-8000</td>
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<td>155</td>
<td>17h</td>
<td>10</td>
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<tr>
<td>169Er citrate</td>
<td>0.34</td>
<td>--</td>
<td>9.4d</td>
<td>1.0</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 1 Radiopharmaceuticals clinically used in radiosynovectomy
Injection technique

The involved joint was draped and prepared according to standard sterile techniques. A 185 Mbq dose was then injected into the affected knee joint of the patient under ultrasound guidance using a 20-gauge needle. The joint was brought through a full range of motion to improve distribution of the radiopharmaceutical and was then splinted for comfort and for limiting the extra articular leakage of the radiopharmaceutical.

Follow-up procedure

We evaluated our patient for pain relief, swelling and quality of life at 2, 4, 6 and 8 weeks, and then after every 2 months until one year. At the time of injection, the patient complained of tolerable pain, which subsided after the needle was removed. After 2 weeks, the patient had mild reduction in the pain, effusion and size of the joint swelling. After 4 weeks, the knee circumference was markedly reduced from 30.9 cm to 27.3 cm (Figure 3). The joint mobility was also improved from completely immobile to flexion of about 450 at the affected knee joint. After eight weeks the patient was completely asymptomatic (pain free).
without taking any analgesics and the swelling subsided over the next six months. The patient is still free of symptoms and at times complains of slight pain which subsides after some rest.

**Biodistribution**

Early 1-hr and delayed 24-hr & 48-hr anterior and posterior images of the knee joint and pelvis (Figure 2) were acquired to see if there was any leakage of the radiocolloid especially into the regional lymph nodes. The biodistribution study was performed on Siemens Orbiter gamma camera with low-energy all-purpose (LEAP) collimator with energy window of 15% centered at 155 KeV photo peak. We found no focal area of abnormal tracer accumulation and all the $^{188}$Re labelled colloid was found localized to the injected joint space.

**Discussion**

PVNS is a rare, aggressive but benign proliferative histocytic joint lesion, which results in various degrees of villous and/or nodular changes in the affected joint structure [2, 11]. It poses serious challenges in the management because surgical attempts are not successful in most of the cases and frequent recurrences are common. Repeated surgeries are associated with greater morbidity and may result in complications like infections and limitation of movement [12]. With recent advances in the field of therapeutic nuclear medicine, in such scenarios, RSO offers a quick and economical solution [3, 10].

In this process mostly β-emitting radionuclides labelled with particulate compounds are introduced into the affected joints. As there is presumably no leakage outside the joint cavity, the radiolabelled colloid deposits most of its β-energy on the internal lining of the joints when these are phagocytosed by the free floating fluid macrophages [4, 13].

RSO is regularly practiced in Australia and Canada as well as in other Western European countries but it is very common in Germany. According to an estimate, RSO is performed in about 70,000 joints per year in Germany [4]. However, it hasn’t gained widespread acceptance in the developing or under developing countries where its clinical benefits can be better utilized, mainly due to the non-availability of the isotopes and resulting lack of expertise in the field.

The physical and chemical properties of the radionuclide as well as the particle size of the labelled colloid, are important factors considered for RSO. The availability of $^{188}$Re from $^{188}$W/$^{188}$Re generator, has made the nuclear medicine community take interest in this isotope because of its favourable physical properties. $^{188}$Re ($T_{1/2}=16.9$ hrs) is the decay product of its parent $^{188}$W ($T_{1/2}=69.4$ d). It has a β energy of 2.12MeV (70%) accompanied by a 155 KeV γ-rays. The additional 155 KeV γ-ray emission can be helpful for imaging or biodistribution studies. It has a deep tissue penetration of 10 mm as compared to other isotopes. These physical properties and its potential low cost associated with a long-lived parent makes it a suitable candidate for radionuclide therapies in large joint RSO.

Similarly various size particles ranging from 11000 μm has been applied for RSO in the literature. But for homogenous distribution and to be phagocytosed easily by the lining
cells of the synovium, particles with small size are preferred [13]. However, they have an associated high risk of leakage from the treated joints resulting in a higher radiation dose to the non-target organs. To overcome this problem, radionuclide particles of 210μm size are considered suitable [14].

In this case, we selected tin colloid as a carrier with particle size 0.1–2±0.2 μm. To avoid leakage, the larger labelled particles were isolated from the smaller ones through centrifugation. The biodistribution studies (imaging at 1, 24 & 48 hours) showed that following intra-articular injection, $^{188}$Re tin colloid is retained in the knee joint throughout the study. The 24-hr and 48-hrs postinjection images prove the efficacy of $^{188}$Re tin colloid as a better radiation synovectomy agent.

This particular patient had undergone multiple repeated surgical interventions, which had caused some degree of scarring and pocket formation in the joint space that was treated by pre RSO surgical de-bulking and removal of intervening septa. The double site of injection ensured adequate distribution of the tracer. The clinical response at two years of follow-up is satisfactory. The patient married after one year of treatment and has recently given birth to a healthy male child. She has slight limitations of movements with no swelling and occasional slight pain. The limitation of movement is attributed to scarring due to previous surgery.

The clinical outcome, ease of administration and comparatively lower cost than surgical synovectomy, make RSO a reasonable option in the therapy of PVNS. This is however a single case and further studies are needed to better define the role of $^{188}$Re labelled tin colloid in PVNS.

**Conclusion**

PVNS is a slow growing but challenging joint lesion and RSO remains a viable option for its management [15]. In this connection $^{188}$Re labelled tin colloid is an economical and readily available radiopharmaceutical for patients with recurrent PVNS who are unresponsive to traditional therapy.

**References**


Unusual spinal metastases from an adenoid cystic carcinoma of the maxillary sinus seen on a bone scan: a case report

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Abstract

Adenoid cystic carcinoma (ACC), the second most common cancer occurring in the sinonasal tract, is an aggressive malignancy that presents itself insidiously and is generally advanced when diagnosed. Current treatment modalities include surgery and irradiation. Despite advanced successful therapies, these tumours are notoriously associated with locoregional recurrences. This report presents the original case of a patient with adenoid cystic carcinoma of the maxillary sinus with an unusual clinical course and a thoracic vertebral metastases, with spinal cord compression revealed by a bone scan, occurring only nine months after stopping treatment. The aggressive nature of the tumour and the skull base invasion at the time of diagnosis probably explains the rapid onset of this unusual site of metastases.

Key words: Adenoid cystic carcinoma, bone scan, maxillary sinus tumour, radio biphosphonates, spinal metastases

Introduction

Adenoid cystic carcinoma (ACC) is a rare malignant tumour which represents less than 1% of head and neck malignancies, and 10% of salivary gland tumours [1]. ACC most commonly occurs in the major and minor salivary glands of the aerodigestive tract and skin [3]. The ACC are tumours with slow and insidious growth, often discovered at a late stage and locally evolved. The sinonasal locations of ACC have the worst prognosis. Surgery is often complicated by the importance of the local extension. Recurrence is common and late and can occur many years after the initial treatment [1]. Spinal metastasis of ACC of the maxillary sinus, have only been rarely reported in the literature. We present a case of a patient with maxillary sinus carcinoma with vertebral metastases revealed by $^{99m}$Tc-HMDP bone scan.

Case report

A 45-year-old woman developed ACC of the right maxillary sinus, which was treated by surgery and radiotherapy. The patient presented 9 months later with limb weakness, which had progressed moderately over time. Neurological examination revealed paraparesis with preserved tendon reflexes and sensation.
$^{99m}$Tc-hydroxyl-methylene diphosphonate ($^{99m}$Tc-HMDP), bone scan revealed increased uptake of the right maxillary sinus, the right orbital roof, and also heterogeneous aspect of C7-T1 vertebral bodies (Figure 1).

SPECT-CT confirmed increased uptake in the right wing of sphenoid bone with cheekbone lysis (Figure 2) together with increased uptake in C7 & T1 vertebral bodies (Figure 3). A follow-up MRI of face and neck with and without contrast injection, showed two lesions: one in the right maxillary sinus extending to the pterygopalatine fossa, and the second affecting the right wing of sphenoid bone with cheekbone lysis, and orbital and temporal soft-tissues extension (Figure 4). It also shows the
the presence of a lesion in the T1 vertebral body, with extension to the anterior paraspinal and epidural soft-tissue (Figure 5), causing a compression of the spinal cord at this level, with infiltration of the adjacent vertebral bodies.

An open surgical biopsy of spinal cord lesion was carried out with laminectomies from the 7th cervical to the 2nd thoracic vertebrae. Histopathological examination revealed a metastasis of the known ACC of the maxillary sinus in the vertebral column. Palliative local radiotherapy with chemotherapy was initiated. The patient died two months after completion of chemotherapy.

Discussion

Malignancies arising from the sinonasal tract are uncommon. Carcinoma of the maxillary sinus comprises 0.2% to 0.5% of all cancers
of the head and neck [4]. According to Wang [2], squamous cell carcinomas are the most common form of maxillary sinus tumours, followed by adenoid cystic carcinoma and adenocarcinoma. The choice of optimal therapy for ACC of the head and neck is affected by site, stage, histologic grade, and biologic behavior of the ACC. There are a number of publications that address the efficiency of surgery and radiation therapy in the treatment of ACC of the head and neck [4-6].

ACC of the head and neck, and specifically of the nasal cavity and paranasal sinuses, poses numerous treatment challenges for several reasons: it has a high propensity for local invasion to adjacent structures, making resection more difficult; it is commonly diagnosed late due to its insidious growth; and in 50% of cases it has caused perineural spread at the time of diagnosis [7]. Furthermore, ACC is associated with high rates of distant metastases, which have been noted to occur as late as 10 years after the diagnosis of the primary lesion [8]. Clinicians are all too aware that distant metastases often defeat successful treatment of patients with ACC, despite locoregional control, and are associated with a low long-term survival rate.

Histologically, ACC can be categorized into 3 growth patterns: cribriform, tubular, and solid. In most studies, a solid growth pattern is associated with a worse prognosis, caused by advanced stage and development of distant metastases [9, 10]. A unique feature of ACC is the propensity for perineural invasion, even with early-stage tumours. The tumour is graded according to Szanto et al. [11] as cribriform or tubular (grade I), less than 30% solid (grade II), or greater than 30% solid (grade III). In our report the histopathology revealed a solid subtype. This is probably one factor contributing to the bad outcome.

The reported incidence of spinal epidural compression from head and neck cancer is around 1% [12], which is much lower than that of compression by metastasis from breast (20-26%) or lung cancer (12-13%). Compression of the spinal cord or cauda equina by metastatic disease is almost always extradural [13]. This condition usually results from tumour involvement of the vertebral column affecting either a vertebral body or a neuronal arch, as is the case in our patient. According to literature data, only four patients with carcinoma of the maxillary sinus with spine metastases have been reported: with compression of the cauda equina in two of them. Survival was short (three months) for both [14,17,18].

The clinical course, in our reported case, was atypical in terms of its chronology. The diagnosis of spinal cord metastasis from ACC of the maxillary sinus only nine months after completion of radiotherapy illustrates the highly aggressive nature of this tumour. Decompression and stabilization of the spinal cord can maintain or improve quality of life. The role of decompression and/or fusion in spinal metastases with neurologic deficits is still under debate, although recent studies have confirmed the beneficial role of surgical intervention in selected patients [15, 16]. According to Patchell et al. direct decompressive surgery plus postoperative radiotherapy seems to be superior to treatment with radiotherapy alone for patients with spinal cord compression caused by metastatic cancer [15].

In this reported case, the aggressive nature of the tumour and the presence of intracerebral invasion of the skull base at the time of diagnosis probably explains the rapid onset of this unusual site of metastasis. The presence of perineural invasion on the initial histological examination should have been considered to be a predictive factor of this progression.

**Conclusion**

Spinal metastases of maxillary sinus ACC are uncommon. Decompression and stabilization of the spinal cord can maintain or improve quality of life. The clinical behavior of ACC, and its high propensity for local invasion to adjacent structures makes obligatory a periodic examination throughout life.
References


CASE REPORT

SPECT/CT imaging of primary mediastinal goitre: case report and literature review

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Abstract

Primary mediastinal goitre (PMG) is an ectopic thyroid in a rare location, even more so when associated with an anomaly of the native thyroid gland. It should be considered in the differential diagnosis of all mediastinal masses.

We report the case of a 74-year-old woman presenting primary anterior mediastinal goitre with a toxic multinodular goitrous thyroid gland located in the thyroid bed in the anterior neck. 99mTc pertechnetate scintigraphy (planar and SPECT/CT) confirmed the uptake of the radiotracer in the mediastinal mass, showing the mass to be separate from the cervical thyroid gland, thus confirming an ectopic PMG. A surgical resection of the cervical multinodular goitre and the intrathoracic mass was performed. Histopathology showed a multinodular adenomatous goitre without signs of malignancy. The patient has had an unremarkable postoperative recovery.

99mTc scintigraphy with SPECT-CT imaging seems to be the most important diagnostic tool for the detection of ectopic thyroid tissue and shows the absence or presence of thyroid in its normal location. The technique is not only important for establishing the diagnosis, but crucial in deciding upon the correct therapeutic strategy, including the surgical approach.

Key words: Primary mediastinal goitre, 99mTc scintigraphy, SPECT/CT imaging

Introduction

Primary mediastinal goitre (PMG) or true ectopic mediastinal goitre in presence of a multinodular native thyroid is an exceedingly rare entity representing less than 1% of all endo thoracic tumours with only a few cases reported in the literature [1]. The diagnosis may be difficult and is based on the imaging data. We present a case of a female with a toxic multinodular goitre located in the

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anterior neck with a separate large anterior mediastinal ectopic goitre, imaged by hybrid SPECT-CT imaging and subsequently treated successfully with surgical removal. bone scan.

Case report

A 74-year-old woman was admitted with complaint of dyspnoea and slight dysphagia. She had a history of hyperthyroidism treated by antithyroid drugs. Physical examination revealed a thyroid goitre. Ultrasonography of neck was performed which showed a multinodular goitre without any evidence of retrosternal extension. A chest x-ray (Figure 1) revealed marked mediastinal widening and predominant right with a tracheal deviation. Cervical and thoracic CT scan (Figure 2) showed a multinodular cervical goitre, with a large retrosternal mass (12.8 x 6.6 x 5.3 cm) with well defined borders, in the upper and middle mediastinum containing microcalcifications and showing an enhancement after iodinated contrast administration, without signs of infiltration. The appearances were compatible with a diagnosis of thymoma, teratoma or an intrathoracic goitre.

Figure 1 Chest x-ray showing tracheal deviation (red arrow) and marked mediastinal widening with a prominent right atrium (white arrow)

Figure 2 CT scan showing: (a) a multinodular orthotopic goitre (white arrow) and; (b) a large mixed density mass lesion in the anterior mediastinum containing microcalcifications showing enhancement after iodine contrast administration without vascular invasion (yellow arrow)
Laboratory tests showed normal thyroid function with the patient on anti-thyroid medications. Anti-thyroperoxidase and anti-thyroglobulin antibodies were absent, with normal serum calcitonin concentration and normal βHCG and αFP levels.

Thyroid scintigraphy was carried out 20 minutes after an intravenous injection of 185 MBq of $^{99m}$Tc pertechnetate. Imaging was performed using a dual-headed hybrid (SPECT/CT) gamma camera fitted with parallel-hole, high-resolution low-energy collimators, with 20% energy windows centered at 140 keV. SPECT/CT images were obtained according to predetermined parameters including 64 steps (20 sec/step), 360° orbit and reconstruction in a $128 \times 128$ matrix with a three-dimensional ordered-subset expectation maximization (OSEM) algorithm. Low-dose CT parameters included 120 kV and 100 mAs, and images were reconstructed with a section thickness of 5 mm in a $256 \times 256$ matrix. A CT-based attenuation correction algorithm was applied. The acquisition in planar mode highlighted an intense uptake in the cervical multinodular thyroid gland (Figure 3), with less intense and heterogeneous uptake at the upper and middle mediastinal regions but without any continuity between the mass and the cervical thyroid gland. SPECT-CT complement confirmed the uptake of radiotracer in the mediastinal mass, attesting the diagnosis of primary intrathoracic goitre (Figure 4). CT scan guided mediastinal biopsy confirmed the mass to be a benign colloid goitre. The multinodular orthotopic goitre and the intrathoracic mass were completely resected through a cervicotomy and a total median sternotomy. There were no tissue or vascular connections between the mass and the cervical thyroid gland. Histopathology showed a multinodular adenomatous goitre without signs of malignancy. Antithyroid drugs were replaced by thyroid hormone replacement therapy and the patient had a remarkable postoperative recovery.

Discussion

Primary mediastinal goitre (PMG) or true ectopic mediastinal goitre is a rare developmental abnormality involving aberrant embryogenesis of the thyroid gland during its passage from the floor of the primitive foregut to its final pre-tracheal position [2, 3]. It corresponds to a rare location of ectopic thyroid where the intra-thoracic thyroid tissue is independent of the native cervical thyroid gland. It represents about 0.2 - 1% of intra-thoracic tumours with a female preponderance (female/male ratio: 3). It is localized primarily in the anterior mediastinum (85% of cases). The middle and posterior mediastinum are less frequent locations in 15% of cases [4].
Most ectopic goitres are asymptomatic at the time of diagnosis but when they occur, clinical manifestations such as dysphagia, dyspnea, superior vena cava syndrome, are mostly related to the compression of adjacent organs. Chest pain may be present in case of nerve compression. Also, some cases of hyperthyroidism have been reported in the literature including certain forms of lymphocytic thyroiditis or toxic nodular goitres as in the present case.

A chest x-ray is the initial investigation showing mediastinal widening and perhaps compression signs like tracheal deviation. Ultrasound permits excellent characterization of cervical thyroid tissue, but it is not very effective in the evaluation of the PMG.

Computed tomography (CT) of the thorax, in addition to suggesting the thyroid origin of the mediastinal mass, often in the form of multicystic appearance with calcifications in its interior, may show a lack of continuity between PMG and the cervical thyroid gland.

Magnetic resonance imaging may be useful in more precisely defining the relationship of the tumour to the adjacent structures. However,
the definitive diagnosis is made only by means of histopathological analysis, often achieved only after removing the tumour. In some cases, biopsies can be obtained successfully using CT-guided puncture, as in our patient [11].

Further diagnostic tools are needed for deciding upon the appropriate management. Scintigraphy can be useful for the differential diagnosis of thymoma and teratoma [12]. Indeed, radionuclide scintigraphy using 99mTc, 131I, or 123I, is the most important diagnostic tool for detecting ectopic thyroid tissue and shows the absence or presence of thyroid in its normal location. It provides an excellent estimate of the functional status of a mediastinal goitre, its nature and extent. Also, it is very useful for confirming a discontinuity between the mediastinal mass and the cervical thyroid gland in the PMG and for delineating additional sites of thyroid tissue. It is considered the best preoperative investigation as it can be performed quickly, reliably, and with very low radiation exposure [13-16].

Although compared with other radioisotopes 131I is the preferred radionuclide for thyroid scintigraphy for imaging an intrathoracic goitre due to its low background activity, we currently prefer 99mTc to 131I/123I for several reasons including its low expense, ready availability, and the short time between injection and imaging. Radioiodine thyroid imaging, however, is preferred to 99mTc for the management and the follow-up of patients with well differentiated thyroid carcinoma.

Hybrid SPECT/CT combined with planar diagnostic 99mTc scintigraphy allows precise localization and accurate characterization of foci of radioactivity in the head, neck and thorax. Equivocal findings on planar imaging may be clarified on SPECT/CT, with subsequent changes made to treatment plans [17, 18] as in the present case. The ability to fuse functional data provided by SPECT slices and morphological images provided by CT, combines physiologic information of one method with the superior anatomic resolution of the other. In many cases, this allows more definitive diagnosis than can be obtained by simple visual comparison of nuclear medicine images and conventional cross-sectional imaging [19].

Surgical resection is advocated for relieving compressive symptoms, and for ruling out the diagnosis of malignancy [20, 21]. The specific surgical modality depends on the goitre location, size and its relationship to adjacent structures. Secondary intra-thoracic goitres are usually resected through an inferior cervical collar incision; nevertheless, extended mediastinal tumours beyond the aortic arch may require additional extra-cervical incisions including sternotomy, clavicular resection, anterior and posterolateral thoracotomy or video-assisted thoracoscopic surgery [22].

Conclusion

PMG is a rare condition, even more so in the presence of a native multinodular toxic goitre. This case demonstrates the importance of considering an ectopic thyroid in the differential diagnosis of mediastinal masses. 99mTc scintigraphy with SPECT-CT imaging is not only helpful in determining the aetiology of the mediastinal mass but also helps in the therapeutic strategy including the surgical approach. Surgical resection is advocated for relieving compressive symptoms, and for ruling out the presence of malignancy.

References


SPECT/CT for the accurate localization of $^{67}$Ga uptake in mycotic abdominal aortic aneurysm

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Abstract

We report a case of mycotic abdominal aortic aneurysm where the use of hybrid imaging with gallium scan demonstrated increased uptake in the infected aneurysm and aided in differentiating physiological uptake in the bowel from pathological uptake.

Key words: Gallium-67, SPECT, SPECT/CT, mycotic aortic aneurysm

Introduction

The term 'mycotic aneurysm' has been used since the 1800s for infected aneurysms resulting from bacterial endocarditis complicated by septic arterial emboli [1, 3]. Wilson et al. classified the infected aneurysms according to their clinical characteristics: mycotic (endocarditis-related), microbial arteritis, infection of existing aneurysm and post-traumatic infected false-aneurysm [4]. However, the majority of vascular surgeons nowadays keep to the commonly used definition of mycotic aneurysm to include all kind of infected aneurysms.

We report a case of mycotic abdominal aortic aneurysm where the use of hybrid imaging with gallium scan demonstrated increased uptake in the infected aneurysm and aided in differentiating physiological uptake in the bowel from pathological uptake.

Case report

A 61-year-old male with hypertension and a recent travel history to Cuba presented with a 3 week history of mild but unremitting pain in the lower abdomen and an episode of fever and chills 2 weeks prior to presentation. CT angiography of the abdomen was ordered for further evaluation of the pain, which revealed aortitis at the level of the infrarenal aorta with a pseudoaneurysm and small penetrating ulcer (Figure 1). A whole-body gallium-67 scan was ordered to assess for infection,
which showed focal accumulation in the aneurysmal sac (Figure 2). The patient was treated with broad-spectrum antibiotics for one week. A repeat CT of the abdomen was performed to assess the evolution of the infection, which showed expansion of the aneurysmal sac (Figure 3).

**Figure 1** Contrast-enhanced CT of the abdomen showing a pseudoaneurysm at the anterior right lateral aspect of the infrarenal aorta measuring approximately 0.8 cm. The aortic lumen is patent and of normal calibre. Computed tomography with contrast is the first choice of imaging modalities for the evaluation of vascular and perivascular abnormalities [2]

**Figure 2** A whole-body gallium-67 scan and SPECT/CT were acquired on the same day as the first CT to assess for infection, which showed focal intense increased uptake in the known pseudoaneurysm sac in the infrarenal abdominal aorta. Gallium-67 planar images of the abdomen show physiological activity in the abdomen (left) with the SPECT/CT scan (right) demonstrating increased uptake in the aneurysmal sac (white arrows), which is distinct from bowel activity (red arrow)
The patient underwent an operative procedure to repair the contained ruptured mycotic aneurysm with neo-aortic in-situ repair with right superficial femoral vein.

Microbiological examination and cultures of the resected aorta grew salmonella species, resistant to trimethoprim and ciprofloxacin, sensitive to ceftriaxone and ampicillin. He was started on Ceftriaxone intravenous antibiotic therapy, and continued for 6 weeks, then was switched to oral cefixime for a duration of 6 months.

**Discussion**

Organisms have been isolated from aneurysmal tissue in up to 76 percent of patients with mycotic aneurysms [5]. Staphylococcus spp. and Salmonella spp. remain the most common [6, 7]. The diseased aorta appears to be vulnerable to Salmonella, and this pathogen is frequently isolated in infected aneurysms due to bacteraemic seeding of atherosclerotic plaque [8].

The role of gallium-67 uptake in infected aortic aneurysms was previously described [9] on planar imaging with the aid of 3-phase $^{99m}$Tc-MDP bone scan. Aneurysms have been reported as incidental findings on the blood flow and blood pool images of $^{99m}$Tc-MDP or $^{99m}$Tc tagged erythrocytes [10, 11]. Infected aneurysms have been previously described in the literature with several radiotracers, such as gallium-67, In-111 tagged leukocytes, $^{99m}$Tc-hexamethylpropylene amine oxime (HMPAO) labelled leukocyte and $^{18}$F-FDG. [12-16]. Gallium-67 scan is considered not reliable in the abdomen because of physiological bowel activity. In this case, hybrid imaging with SPECT/CT was able to differentiate physiological gallium-67 uptake in the bowel and pathological uptake in the abdomen and also localized the uptake to the aortic pseudoaneurysm, which indicated the presence of an infected pseudoaneurysm, a potentially life-threatening condition [17].

**References**

1. Osler w. the Gulstonian lectures on malignant endocarditis. BMJ 1885; 1: 467.
1. Osler w. the Gulstonian lectures on malignant endocarditis. BMJ 1885; 1: 467.


CASE REPORT

Functional ectopic cystic parathyroid adenomas: case reports and literature review

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Abstract

Parathyroid adenomas are the commonest cause of primary hyperparathyroidism. About 10 percent of the parathyroid adenomas are ectopic in location. Cystic degeneration in parathyroid adenomas is seen in 4% of the cases and represents 1-2% of the cases with primary hyperparathyroidism. Hence, the combination of parathyroid cysts, which are both ectopic and functional is extremely rare. Functional parathyroid cysts can be either "silent" or associated with a wide range of clinical symptoms. We present two cases of functional mediastinal parathyroid cysts, one with and the other without clinical manifestations.

Introduction

Cysts of parathyroid glands occurs in less than 0.001% cases of the neck mass [1]. The majority of parathyroid cysts (PCs) are non-functioning and presents as an asymptomatic nodule(s) in variable locations extending from the cervical to the mediastinal regions, with 10% of the ectopic PCs located in the mediastinum [2].

Parathyroid cysts do not have a specific sonographic appearance [3] and in some cases definitive differentiation of these rare lesions on the basis of sonographic appearance and location alone may not be possible [4]. Since the ectopic locations are variable and the results of radiographic and cytologic modalities may lead to confusion, in patients with hypercalcaemia and hyperthyroidism, dual-phase technetium-99m sestamibi (99mTc-MIBI) scan is the method of choice for the accurate localization of ectopic functional parathyroid cysts. The treatment of choice is complete surgical removal of the cyst and therefore pre-surgical localization of the functional parathyroid cysts by dual-phase MIBI scan can be extremely helpful to the surgeon. 99mTc-MIBI parathyroid scintigrapy accurately localizes the tumour in 90% of cases and simplifies the surgical management [5].

We present 2 cases with ectopic mediastinal functional parathyroid cysts both with and without clinical manifestations.

Key words: 99mTc-sestamibi, SPECT/CT, parathyroid adenoma, parathyroid cyst

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Case 1

A 46-year-old lady presented in the emergency department with severe abdominal pain associated with vomiting and fever. A diagnosis of acute pancreatitis was established and the patient managed conservatively. Her routine laboratory results raised WBC counts and raised CRP, and also showed high serum calcium 4.14 mmol/L (normal range: 2.2-2.6). Serum parathormone (PTH) level was raised at 25.1 pmol/L (normal range: 1-7.5). Chest x-ray showed a mass in the right mediastinum (Figure 1). Contrast-enhanced CT (Figure 2) showed a fairly well-defined cystic lesion in the right paratracheal region measuring 5.5x4.0x3.7 cm with marginal enhancement and fine internal septations.

The patient's MIBI parathyroid scan (Figure 3) showed a large doughnut-shaped lesion in the right upper mediastinum characterized by increased uptake at the periphery, which was seen to correspond to the lesion seen on CT. Pre-surgical serial PTH levels showed a rising pattern with the highest value of 125.40 pmol/L. A diagnosis of bronchogenic cyst was made and video-assisted thoracoscopic surgery performed. Excision biopsy of the lesion confirmed parathyroid adenoma. PTH level fell to 38.3 following surgery. A repeat dual-phase MIBI scan was negative (Figure 4).

Figure 1 Chest x-ray of Case 1

Figure 2 Contrast-enhanced CT scan showing the mediastinal cyst

Figure 3 Early (left) and late (right) baseline ⁹⁹mTc-MIBI scans showing a doughnut-shaped mediastinal lesion

Figure 3 Early (left) and delayed (right) postoperative ⁹⁹mTc-MIBI scan showing normal uptake
Case 2

A 16-year-old male was found to be hypercalcaemic with a corrected serum calcium of 4.14 mmol/L (normal range: 2.2-2.6). Serum parathormone (PHT) level was subsequently also found to be raised at 50 pmol/L (normal range: 1-7.5). Chest X-ray showed mediastinal widening and a right sided shadow suggesting a tumour (Figure 5).

Figure 5  Chest x-ray showing mediastinal widening

The contrast CT showed a multicystic mass lesion in the mediastinum measuring 6x5x7 cm located between the sternum and the great vessels, with well-defined low-attenuation fluid density areas and tiny foci of fat density suggesting a thymic neoplasm (Figure 6).

Figure 6  Contrast-enhanced CT scan showing a mediastinal mass

The patient's planar $^{99m}$Tc-MIBI scan images showed a large eccentric rim of increased uptake, with the SPECT/CT scan (Figure 7) showing central photopaenia with increased uptake in periphery corresponding to the multicystic mass on the CT component (Figure 8).

Figure 7  Planar early (left) and late (right) MIBI scan showing a half doughnut lesion in the mediastinum

Figure 8  Fused SPEC/CT scan showing a peripheral rim of increased MIBI uptake in

Discussion

Only about 10% parathyroid cysts (PCs) are reported to be functional associated with hypercalcaemia and primary hyperparathyroidism which can manifest as fatigue,
weakness, polydipsia, polyuria, depression, nephrolithiasis, osteoporosis, peptic ulcer disease, abdominal pain, in some cases resulting to parathyroid crisis [6, 7].

These so-called functional parathyroid cysts are in essence parathyroid adenomas with secondary cystic changes within the adenoma. The non-functional parathyroid cysts are not associated with increased serum calcium and PTH levels but are identified by a raised level of PTH in the cystic fluid [8]. These functional PCs have reported to present as parathyroid crises [A, B]. There are only a few published case reports on this entity in the radiology literature [6, 7].

The heterogeneous clinical presentation of PCs is determined by their hormonal activity, size and location. The clinical manifestation of disease in case 1 was acute pancreatitis. Acute pancreatitis secondary to hypercalcemia is an uncommon presentation of primary hyperparathyroidism and has been reported in 1-8% of cases [10-13]. Previous publications about acute pancreatitis induced by primary hyperparathyroidism suggest that the relationship between the two clinical conditions is not incidental [14-21]. Hypercalcaemia induces pancreatic injury via a secretory block, accumulation of secretory proteins, and possibly activation of proteases [22]. In cases of metabolic pancreatitis, in addition to standard routine management of pancreatitis, a careful monitoring of metabolic abnormalities is crucial due to the danger recurrent bouts of acute pancreatitis which may be life threatening [23]. Increased levels of serum calcium documented in a patient presenting with an episode of acute pancreatitis should raise the suspicion of primary hyperparathyroidism [24].

In Case 2 patient, who was clinically asymptomatic, routine pre-operative screening x-ray showed mediastinal widening with routine biochemical testing showing incidentally raised serum PTH and calcium levels. CT examination however was suggestive of a possible thymic neoplasm. The presence of parathyroid and thymic tissue in the same locations may be explained on embryological basis as thymus and inferior parathyroids both usually develop from the third pharyngeal pouch with the inferior parathyroids separating from the thymic tissue but remaining close to lower pole of the thyroid, whereas the thymus descends into the mediastinum. During thymic migration, small fragments of thymus may separate and attach themselves to any site along this route, with the parathyroid tissue either close to or embedded within the thymus as a result of their common origin and path of descent [25].

Functional hybrid imagine technique such a SPECT/CT with $^{99m}$Tc sestamibi of the neck and chest allows accurate preoperative localization of ectopic parathyroid adenomas, both cystic and non-cystic [26]. In our cases Tc99m Sestamibi SPECT/CT scan showed increased tracer uptake in periphery with photopenic defects at the centre confirmed by the CT component. In both cases $^{99m}$Tc-sestamibi SPECT/CT was more specific than x-ray and CT scan.

**Conclusion**

Functional mediastinal parathyroid cysts are an extremely rare cause of primary hyperparathyroidism, which in our opinion can only be diagnosed correctly *in vivo* by functional radionuclide imaging. The dual-phase MIBI parathyroid scintigraphic technique is valuable not only in pre-surgical localization but also helps in the differential diagnosis.

**References**


22. Frick TW, Mithöfer K, Fernández-del


Pulmonary arteriovenous malformation diagnosed on a $^{18}$F-fluorodeoxyglucose PET/CT scan

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**Key words:** AV malformation, PET/CT scan

**Background** A 68-year-old female with known gastric cancer in 2011 had a routine follow-up CT scan in Nov 2016, which showed a pulmonary nodule in the right lung. The patient was referred to the nuclear medicine department for an $^{18}$FDG-PET scan to investigate the nature of the lesion.

**Procedure** $^{18}$F-flourodeoxyglucose (277 MBq) was injected intravenously and PET/CT imaging performed after 60 minutes. PET, CT and fused images were reconstructed in the transaxial, coronal and sagittal axes (Figure 1).

**Findings** The PET-CT scan showed a hypermetabolic lesion in the lateral segment of the lower lobe of the right lung with SUV$_{\text{max}}$ of 4.3 (Figure 1a). This mass-like lesion was seen to be interposed between the right inferior pulmonary vein and branches of the right interlobar artery (Figure 1b) with the CT appearance of fingers-in-a-glove, a sign in keeping with a pulmonary arteriovenous malformation (AVM). This was seen to correspond to the hypermetabolic lesion (Figure 1c). The scan was otherwise normal.

**Conclusion** The PET/CT scan findings were consistent with a hypermetabolic right lung mass suspicious of an AVM. A contrast-enhanced CT confirmed this impression (Figure 2).

**Comments** Pulmonary AVM is a rare congenital anomaly with uncertain aetiology [1]. Since the patients are usually asymptomatic and an undiagnosed AVM may be associated with serious complications [2] it is important to make an early diagnosis for instituting correct and timely treatment.

In a patient with known previous gastric carcinoma, an FDG-avid mass-like lesion could have raised the possibility of malignancy and may have resulted in misdiagnosis leading to further unnecessary bronchoscopic biopsy. There are however several benign conditions which show increased FDG avidity. A literature search revealed a previous report of a patient with AVM showing increased FDG uptake [3].

This case underscores the importance of careful evaluation of both the CT and the PET images taking into consideration the entire...
Figure 1  PET-CT scan showing PET image (left row), the CT image (middle row), and the fused image (right row) in the transaxial (a), coronal (b) and sagittal (c) axes. The PET component shows an FDG-avid (SUV$_{\text{max}}$ 4.3) nodule in the lower lobe of the right lung. The CT component shows a mass-like para-hilar lesion in the lateral segment of the right lower lobe of the lung. The fused images shows the focal increased FDG uptake to correspond to the mass-like lesion.
gamut of the reported benign pulmonary pathologies, which may show increased $^{18}$F-fluorodeoxyglucose uptake to avoid making a misdiagnosis.

References


Multifocal osteomyelitis on bone scan performed for mandibular mass with uncertain malignancy

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Key words: Osteomyelitis, Bone scan

Background A 10-years-old boy presented with a mandibular mass and pain in the right leg. The patient had a suffered from a benign mandibular tumour, an ameloblastoma, which is a rare disorder of the jaw involving abnormal tissue growth. MRI centered on the right inferior member showed osteomyelitis in the right lower extremity involving the femoral diaphysis with a subperiosteal abscess. Bone scan with radiobiphosphonates was performed to investigate the possibility of bone metastases and to confirm the presence of musculoskeletal infection [1].

Procedure The Planar whole-body bone scan was performed in the anterior and posterior projections 3 hours after an injection of $^{99m}$Tc-hydroxymethylene diphosphonate. Single-photon emission computed tomography (SPECT-CT) was additionally performed to investigate the nature of the hot-spots documented on the whole-body bone scan.

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Figure 1 Whole-body bone scan showing multifocal osteomyelitis of the lower third of the left forearm, the right and the left femoral diaphyses (black arrows). Note the intense uptake in the right mandible related to the mandibular mass with uncertain malignancy (red arrow)
Findings  The whole-body bone scan images showed intense uptake in the right mandibular mass at the site of the known tumour (Figure 1). The bone scan additionally showed a linear area of intense uptake involving the medial cortex of the middle one-thirds of the left femoral shaft with a similar but smaller lesion seen at the junction of the middle and the lower thirds of the right femoral shaft medially. There was also a fusiform focus of increased activity seen two-thirds down the left ulnar shaft (Figure 1). These lesions were confirmed as multifocal osteomyelitis on the SPECT-CT scan, which showed subperiosteal abscesses in these locations (Figure 2).

Figure 2  (A) SPECT / CT centered on the left femoral diaphysis in transaxial sections showing intense uptake related to osteomyelitis with subperiosteal abscess. (B) SPECT / CT centered on the left forearm showing uptake in the left ulna related to another focus of osteomyelitis with subperiosteal abscess

Conclusion  The bone scan findings were consistent with multifocal osteomyelitis, of the lower third of the left forearm, the right and the left femoral diaphyseal with subperiosteal abscesses. SPECT-CT has also eliminated septic arthritis and possibility of fractures. These diagnoses were confirmed by MRI acquisition centered on the two femoral diaphyseal (Figure 3). The patient was taken for incision and drainage and was also treated with intravenous antibiotics.

The histologically confirmed mandibular mass, an ameloblastoma, also required surgical treatment (Figure 4).

Comments  3-phase bone scintigraphy with radiobiphosphonates is particularly recommended for the diagnosis of multifocal osteomyelitis and septic arthritis [2]. Hybrid imaging (SPECT-CT) is useful in confirming the clinical diagnosis of osteomyelitis and also
provides essential information on the site and extent of the infection, which helps the clinician in planning medical and surgical treatment [3].

References


Unsuspected chronic multifocal osteomyelitis diagnosed on a whole-body $^{18}$F-FDG PET/CT scan

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**Key words:** Osteomyelitis, PET/CT, $^{18}$F-flourodeoxyglucose

**Background** A 24-year-old male with prune belly syndrome suffering from end-stage renal disease for which he was undergoing routine haemodialysis reported with a 2-week history of swelling of the left knee associated with fever. Blood culture revealed gram +ve cocci (*s. aureus*). The patient was referred to the nuclear medicine department to investigate the possibility of septic arthritis of the left knee and to rule out any osteomyelitis.

**Procedure** $^{18}$F-flourodeoxyglucose (245 MBq) was injected intravenously and PET/CT imaging performed after 60 minutes. PET, CT and fused images were reconstructed in the transaxial, coronal and sagittal axes.

**Findings** The whole-body PET/CT scan images (Figure 1) showed mild increased soft-tissue uptake ($\text{SUV}_{\text{max}}$ 2.4) above and at

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**Figure 1** PET whole-body MIP scan image
the lateral aspect of the left knee without evidence of any increased bone uptake seen to suggest local osteomyelitis (Figure 2).

The whole-body PET/CT scan images additionally showed focal increased uptake ($SUV_{max}$ 3.8) in the right 3rd rib anterolaterally with the CT component showing fusiform local expansion of the rib and cortical disruption (Figure 3).

There was intense focal FDG uptake ($SUV_{max}$ 8.2) in the left pelvis corresponding to the left pubic body, the inferior pubic ramus and the adjacent ischium, with the CT component showing medullary expansion and cortical destruction (Figure 4).

A focus of intense uptake ($SUV_{max}$ 6.0) was seen in the right distal fibula with the CT component showing medullary expansion, bone destruction and fracture at this site (Figure 5).
Figure 4  PET/CT scan with the CT (left), PET (middle) and the fused CT & PET (right) images showing intense focal FDG uptake ($SUV_{max}$ 8.2) in the left pelvis corresponding to the left pubic body, the inferior pubic ramus and the adjacent ischium, with the CT component showing medullary expansion and cortical destruction.

Figure 5  PET/CT scan with the CT (left), PET (middle) and the fused CT & PET (right) images showing intense focal FDG uptake ($SUV_{max}$ 6) intense focal increased uptake in the distal right distal fibula with the CT component showing medullary expansion, bone destruction and fracture at this site.
Conclusion The PET/CT findings were consistent with soft-tissue infection/inflammation in the symptomatic left knee region. However, the other multiple hypermetabolic osseous bone lesions documented on the PET/CT scan seen involving the right 3rd rib, in the left pelvis and the right fibula, were consistent with chronic polyostotic osteomyelitis.

Comments Positron emission tomography/computed tomography (PET/CT) with the glucose analogue, $^{18}$F-fluoro-2-deoxyglucose ($^{18}$F-FDG), has an established role in oncological imaging but is being increasingly used for the diagnosis of musculoskeletal infection. The accumulation of FDG at sites of infection/inflammation is due to its uptake by the activated granulocytes, which use glucose as an energy source. Inside the cells, the FDG is phosphorylated by hexokinase to $^{18}$F-fluoro-2-deoxyglucose-6-phosphate, which is not further metabolized. Increased cellular metabolism in the activated inflammatory cells results in an increased expression of glucose transporter (GLUT) proteins by these cells, which coupled with an increase in the affinity for glucose by the glucose transporters secondary to the effects of cytokines and growth factors results in high FDG uptake at sites of infection/inflammation [1]. FDG-PET imaging is particularly useful for diagnosing chronic and low-grade infection because of the high uptake of FDG in activated macrophages, the predominant cell type present in chronic infection [1].

The sensitivity and specificity of FDG-PET for diagnosing chronic osteomyelitis is reported at 100% and 92%, respectively by Guhlmann et al. [2], with de Winter et al. [3] reporting a sensitivity, specificity, and accuracy of 100%, 88%, and 93% respectively. Zhuang et al. [4] reported similar results.

The superior imaging characteristics and the shorter imaging time span of positron imaging coupled with its higher spatial resolution compared to conventional nuclear medicine infection imaging techniques such as labelled white cells or the gallium scanning, is a distinct advantage. Also, the combination of functional and morphological imaging provided by the hybrid techniques is evidently superior to either the structural imaging modalities such as the CT or MRI or the conventional nuclear medicine imaging of infection alone. The PET/CT technique not only proved highly sensitive in confirming the soft-tissue infection/inflammation in the region of the left knee and excluding the presence of local osteomyelitis, but also additionally identified previously unsuspected multifocal osteomyelitis. The presence of concomitant structural changes also proved very specific in establishing the chronic nature of the osteomyelitis.

References


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