www.jcimcr.org

JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Short Commentary

Open Access, Volume 2

Nuclear odontology: Pictorial essay

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Received: Mar 11, 2021

Accepted: Apr 26, 2021

Published: Apr 29, 2021

Archived: www.jcimcr.org

Abstract

There is increased demand by the general dentist and oral surgeon's for Nuclear Medicine (NM) imaging procedures both for initial diagnosis and follows up of patients with different dental and facial disorders. There are several procedures in NM including bone scan, gallium scan and PET scan which can offer important diagnostic information complementing the information obtained from other imaging modalities in particular a better understanding of the pathophysiology of the disease and therapy monitoring.

Introduction

During the last two decades, I have witnessed increased demand by the general dentist and oral surgeon's for Nuclear Medicine (NM) imaging procedures both for initial diagnosis and follow ups of patients with different dental and facial disorders. This fact inspired me to call this work 'Nuclear Odontology' terminology to the best of my knowledge not stated before.

Nuclear odontology is the use of Nuclear Medicine (NM) in the diagnosis of dental and oral disorders. NM is a branch of medicine in which small quantities of radioactive material is given to the patient mainly through an intravenous route to assess the function of organs rather than the structure which is best evaluated by anatomic imaging such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). Therefore if we want to assess the size and location of temporal condyle we perform a CT scan, however to assess the osteoblastic activity of the condyle bone scan gives the answer. The aim of this essay is to familiarize the general dentist and oral surgeon who are not acquainted and refresh those who are with the available NM imaging procedure which can help them in their daily practice. In addition we will discuss the application of NM in several disorders of the dental and oral cavity which the physician may face in daily practice of odontology.

Methods

There are several procedures in NM used for the diagnosis and follow up of dental and oral disorders including bone scan, gallium scan and PET scan.

Imaging techniques

The images obtained can be planar images (two dimension) or tomographic images (three dimension): Single Photon Emission Computed Tomography (SPECT) coupled with Computed Tomography (CT) and fused together to give SPECT/CT image. The other modality is Positron Emission Tomography (PET) and when fused to CT gives PET/CT image. The studies presented in this review were done in our department. Planar and SPECT/CT was performed using a dual head gamma camera (Philips' Bright View XCT). PET /CT performed using (General Electric Discovery ST 64-slice PET/CT machine system).

The radioactive materials used for diagnostic purposes are of short half-life and therefore there is no significant hazard to the patients or to the staff managing them.

Imaging protocols

Bone scan: Three phases bone scan (blood flow, blood pool and uptake phase) is performed when infection suspected and images obtained immediately post injection for blood flow and blood pool images and a delayed planar scan is obtained 2-3 hours post intravenous injection of 20-25 millicurie (mCi) 99mTC-methylene diphosphonate (99 mTC-MDP) which accumulates on the surface of the bone mineral matrix. The bone uptake of the tracer depends on blood flow and metabolic bone activity. No patient preparation is required. The patient is instructed to drink plenty of fluid and empty the urinary bladder frequently to reduce radiation dose. SPECT/CT is performed to the area of interest.

Gallium-67 scan: Gallium-67citrate (Ga-67) binds to transferring, lactoferrin, leukocytes and siderrophores produced by bacteria and accumulates in infection and inflammatory sites. The patient is injected intravenously 4.0-5.0 mCi Ga-67 and planar images obtained 48 hours postinjection coupled with SPECT/CT image to the area of interest.

PET/CT: F-18 FDG: Fluoro Deoxy Glucose (FDG) labeled with Fluorine -18 (F-18) is the most widely used PET radiopharmaceutical for tumor imaging. F-18 FDG is taken up by cells in proportion to their metabolic rate. In tumors there is increased glycolysis compared to normal cells leading to high target (tumor) non target (normal cells) ratio.

The patient in fasting state, PET/CT images are obtained 60 minutes post intravenous injection of 10 mCi F-18 FDG.

Clinical applications

Plain radiograph, panorama imaging, cone beam CT, CT and MRI are the most commonly used techniques by dentists and oral surgeons. However, these are anatomic imaging techniques which reveal changes in structure and they have some limitations in post-operative conditions where differentiation between residual or recurrent disease from scarring is a challenge. Nuclear medicine and after the recent introduction of hybrid imaging (SPECT/CT, PET/CT and PET /MR) has the power to solve this dilemma hence it evaluate changes in function (which precedes changes in structure) and structure as well to determine disease extent and in neoplastic lesions assess local extension and distant metastases at initial stage of the disease (staging), monitoring therapy (therapy response) and follow up and detection of recurrence(re-staging).

Several disease conditions can be evaluated by NM imaging such as: Condylar hypoplasia, condylar hyperplasia, osteomyelitis, osteonecrosis, metabolic bone disorders (fibrous dysplasia, Paget's disease, hyperparathyroidism), graft viability and oral cavity tumors.

Condylar hypoplasia: Condylar hypoplasia or aplasia is an abnormality caused by underdevelopment or non-development of the condyle. It can be congenial either unilateral or bilateral or acquired secondary to local (trauma, infection or irradiation) or due to systemic causes (toxic agents or rheumatoid arthritis) [1].

The diagnosis is usually by clinical examination, conventional radiographs, and 3dimensional CT. Bone scan is used to assess osteoplastic activity at initial diagnosis and on post -operative follow up of the affected condyle which appears underactive compared with the contralateral normal one. Figure 1 is a bone scan of a 21 year old female complaining of mandible deviation and right hypotrophic condyle since puberty, bone scan requested for confirmation and assess osteoplastic activity.

Bilateral aplasia is a congenital abnormality where both condyles are undeveloped and therefore underactive and are non-visualized on SPECT/CT. Figure 2 is a bone scan of a 24-year-old female patient with bilateral hypoplasia of the mandibular condyles (Mandibulofacial dysostosis)**.** Bone scan ordered to assess condyles osteoplastic activity.

Condylar hyperplasia (CH): Condylar hyperplasia is a disorder characterized by overgrowth of the condyle. The main consequence of CH is unilateral facial asymmetry deformity, which combined with alteration of the dental occlusion with unilateral cross bite or open bite [2]. The disorder can present at any age and is more frequent in women [3]. Diagnosis of CH is based on clinical and radiographic findings [4]. Bone scan is used to assess condylar osteoplastic activity as base line and for follow up [5]. The affected site shows higher tracer uptake (overactive) on planar images (more than 10%) compared to the contralateral normal one [4]. SPECT CT has higher sensitivity than planar image with the added detection of structural changes. Figure 3 is a bone scan of a 23 years old male complaining of enlarged lower jaw in left temporomandibular area. Bone scan requested to assess osteoplastic condyles activity.

Osteomyelitis (OM): Osteomyelitis is an inflammatory condition of the bone marrow, which starts as an infection of the medullary cavity and extends thereafter to the haversian systems to involve the bony cortex and periosteum of the affected area [6]. OM of the jaws is mainly caused by spread of adjacent odontogenic infection. Several causes have been demonstrated, such as dentoalveolar infection, trauma, operative procedures, radiation, neoplasia, systemic bisphosphonate use, and genetic conditions [7,8]. Depending on clinical presentations, osteomyelitis is classified into acute, subacute and chronic [9]. The time of onset of symptoms is a key point to differentiate acute from chronic osteomyelitis while the former occurs within one month of the onset of symptoms the latter takes more than one month [10,11]. The signs and symptoms of chronic osteomyelitis probably less severe than those of an acute form, however most patients present with jaw pain, swelling and suppuration [12]. Diagnosis is usually based on history, clinical examination and radiology (panoramic x-ray, cone beam CT) and in some cases nuclear medicine studies are required to confirm diagnosis and monitor antibiotic therapy.

The NM criteria of active osteomyelitis of the jaw is matched increased uptake of tracer on both bone and gallium scan. Gallium scan is used to monitor therapy and once it's normal indicate successful treatment. Bone scan is not useful to monitor therapy because it remains positive during repair healing phase. Figure 4 is a bone and gallium scan of a 26-year-old female patient presented with swelling on the left side of the lower jaw two weeks after tooth extraction. Bone and gallium scan ordered to rule out osteomyelitis.

Osteonecrosis of the jaw (ONJ): Osteonecrosis of the jaw, commonly called ONJ, occurs when blood supply to the jaw bone is interrupted and bone is exposed. Most cases of osteonecrosis of the jaw happen after a dental extraction. Other causes includes: Trauma, infection, steroid therapy, bisphosphonate used to treat osteoporosis and cancer therapy.

Diagnosis of ONJ is done when exposed, necrotic bone is present in the maxilla or mandible for at least 8 weeks. It may be asymptomatic for long period of time. When symptoms develop pain usually precedes other signs. In more advanced stage ONJ manifests with purulent discharge and pain from the exposed bone in the mandible and less likely from the maxilla. Imaging will help in confirming the diagnosis and monitor therapy. Plain radiograph may be diagnostic but more advanced imaging techniques may be ordered and include: cone beam CT, MRI, bone scan, and PET CT [13].

Figure 5 is a bone scan of a 68-year-old Saudi female patient with osteoporosis who developed pain in anterior right mandible two months after bisphosphonate therapy. Bone scan requested to rule out osteonecrosis of the jaw.

Fibrous dysplasia: Fibrous Dysplasia (FD) is a bone disorder in which normal bone and bone marrow are replaced by fibrous tissue [14]. There are three types of FD: monostotic, polyostotic, and polyostotic associated with endocrine disorders [15]. FD usually affect long bones, craniofacial bones, ribs, and pelvis [16]. Monostotic FD is less serious than polyostotic type however and because of high frequency in the jaws it is of greater concern to the dentist [17]. The diagnosis of FD is based on clinical examination and radiological examination (Panorama x-ray, cone beam CT, MRI, bone scan) and diagnosis confirmed by histopathologic examination. The general dentist can be the first to detect this disease in daily practice using panoramic radiography. Therefore, it is important for the dentist and oral surgeon to have good knowledge of FD in order to make the proper diagnosis and avoid complications of the disease. Bone scan shows marked increased uptake in the affected areas. Figure 6 is a bone scan of a 25-year-old female patient who presented to the dental clinic reporting a slow, painless increase in size of her right mandible over the last 6 years leading to facial deformity. A panoramic X-ray showed alteration in the pattern of the cancellous bone. Bone scan requested to assess extent and disease activity.

Hyperparathyroidism (HPT): HPT is a disorder characterized by increased Parathyroid Hormone (PTH) production by parathyroid glands. It can be primary HPT (parathyroid adenoma) or secondary HPT (due chronic renal failure). The PTH regulates serum calcium concentration and bone metabolism.

HPT affects women more than men in their fifth decade of life. Osteitis fibrosa cystica is the skeletal manifestation of primary HPT and can affect any bone including the jaws.

Diagnosis of HPT is mainly based on clinical and biochemical examination (Elevated serum PTH and hypercalcemia) and radiological examination including parathyroid nuclear scan and bone scan. The dentist and oral surgeon may suspect the diagnosis on panoramic radiograph or cone beam CT [18,19]. Bone scan will show the extent of the disease in whole the skeleton in general and facial bones in particular showing diffuse increased tracer uptake of the affected bones. Figure 7 is a bone scan of a 50-year-old female patient presented with progressive enlarging, painless swelling of the jaw with speech difficulty. The patient was diagnosed with primary hyperparathyroidism. Bone scan requested to assess extent and disease activity.

Paget's disease (PD): Paget's disease is a chronic progressive bone disease involving one bone (monostotic) or multiple bones (polyostotic) of the skeleton. It is characterized by rapid resorption and deposition of the affected bone, resulting in increased local vascularity and fibrous tissue in the marrow [20]. PD is a disease affecting both elderly male and female with age more than 50 year with male predominance and 3:2 ratio [21].

At early stage of the disease the patient may be asymptomatic. In more advanced stage the patient presents with pain and deformity of the affected bone. When the cranio-facial bones are involved (in particular the maxilla and/ or the mandible) facial deformity develops and the patient may complain of hearing and speaking difficulties [22].

The diagnosis of PD is based on clinical findings, radiological examinations including bone scan and elevated serum alkaline phosphatase. Whole body bone scan demonstrates disease extent with marked increased uptake in the affected areas in addition to its use for follow up and therapy monitoring.

Figure 8 is a bone scan of a 74-year-old male patient presented to the dentist reporting progressive swelling of the maxilla over the past few years. Panoramic x-ray showed cortical thickening of the body of the maxilla with teeth displacement**.** Bone scan requested to assess extent and disease activity.

PET CT: Squamous cell carcinoma (SCC) of the left maxilla

SCC of the oral cavity is a neoplastic process with certain risk factors mainly smoking and alcohol consumption. It can involve any part of the oral cavity. Usually it presents as a non-healing ulcer. In the early stages and patients will present with localized maxillary pain and teeth mobility.

Evaluation of mandibular and maxillary invasion in SCC is a major challenge to determine both therapeutic approach and prognosis [23]. Therefore, a reliable assessment is crucial for treatment planning to obtain both radical tumor resection and good functional results.

Different imaging modalities are used to assess mandibular and maxillary invasion by SCC of the oral cavity, including plain radiography, CT, thin cut 3 D mandibular and maxillary CT, MRI, bone scan, SPECT-CT, and PET/CT [24-28].

All of these modalities play certain roles in the evaluation of the mandible and maxilla, however each of them have specific pitfalls and therefore argument still exists about the optimal strategy in its use [26].

The reported sensitivities and specificities of CT, MR, and PET/CT appeared to be similar in the detection of mandibular and maxillary invasion by SCC of the oral cavity. The combined analysis of the 3 modalities yielded improved sensitivity compared with the single use of them without a statistically significant difference [29]. 18 F- PET/CT has the power to assess local extent of SCC, any distant metastases, post-operative and radiation therapy and evaluation for residual or recurrent disease. Figure 9 is a FDG PET/CT of a 40-year-old male patient with SCC of the mandible with jaw pain and limited mouth opening. FDG PET/CT was requested for initial staging and post-operative to assess therapy results.

PET CT: Squamous cell carcinoma of the tongue: SCC of the tongue is one of the most common oral and maxillofacial malignant tumors [30]. Diagnosis is based on clinical, histological and radiological imaging. Studies have showed that CT and MRI provide morphological assessment of tongue cancer and unable to detect lymph node micro-metastasis. However, PET/CT provides both anatomical and metabolic information of tongue cancer and has several applications including staging, radiotherapy planning, treatment revision, response evaluation, and recurrence detection [31-33]. Figure 10 is a pre and postoperative FDG PET/CT of a 48-year-old male patient with SCC of the tongue.

Summary

Oro-facial pain is a common complaint in the dental and maxillofacial field. It can have a variety of causes, including infection, benign and malignant neoplasm, and metabolic diseases. Although oro-facial pain mostly is due to a local process, one should always rule out a systemic cause. This is especially true when no evident local lesion can be found. The diagnosis is usually based on clinical and radiological findings. However, when the treating physician still has some uncertainty in diagnosis or needs additional data, NM is a useful imaging tool offering important diagnostic information complementing the information obtained from other imaging modalities in particular a better understanding of the pathophysiology of the disease and therapy monitoring (Table 1).

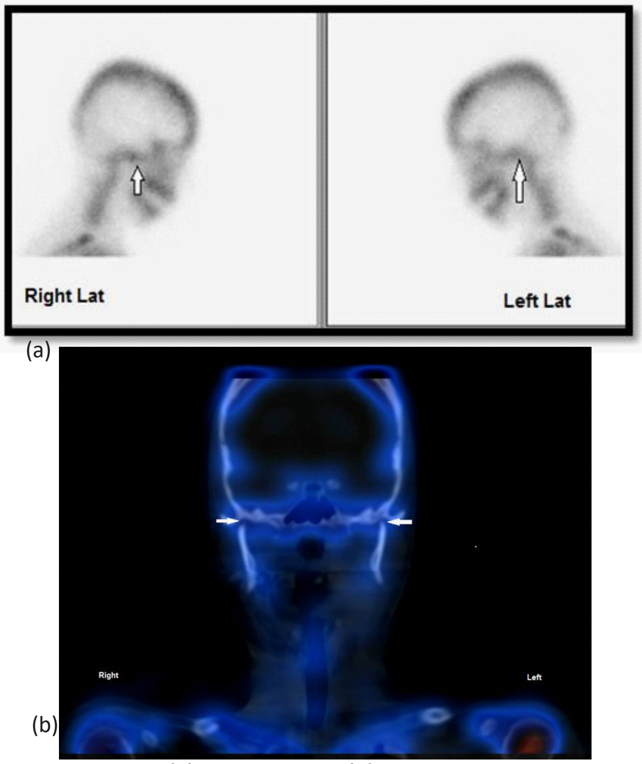

Figure 2: Planar **(a)** and SPECT CT **(b)** bone scan images showed bilateral atrophic condyles with no tracer uptake (Arrows).

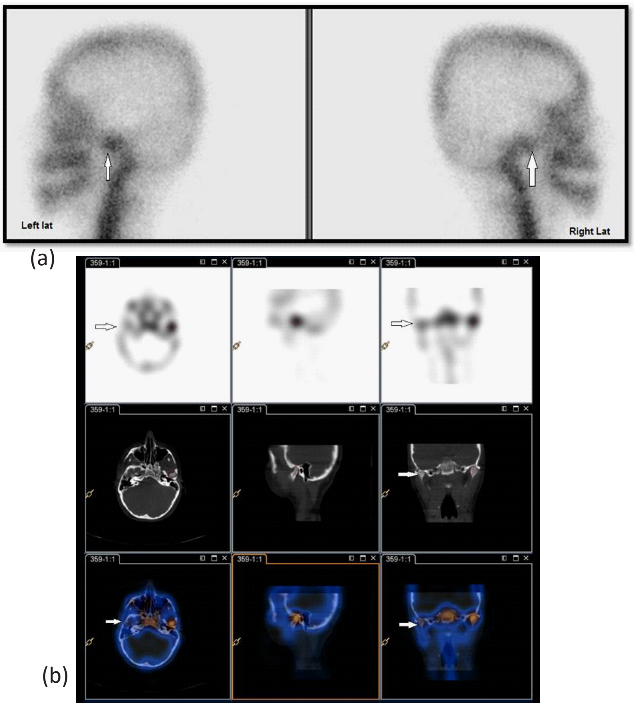

Figure 1: Planar **(a)** and SPECT CT **(b)** bone scan images showed hypoplastic right mandibular condyle with decreased radiotracer counts (underactive) compared to the left side (Arrows).

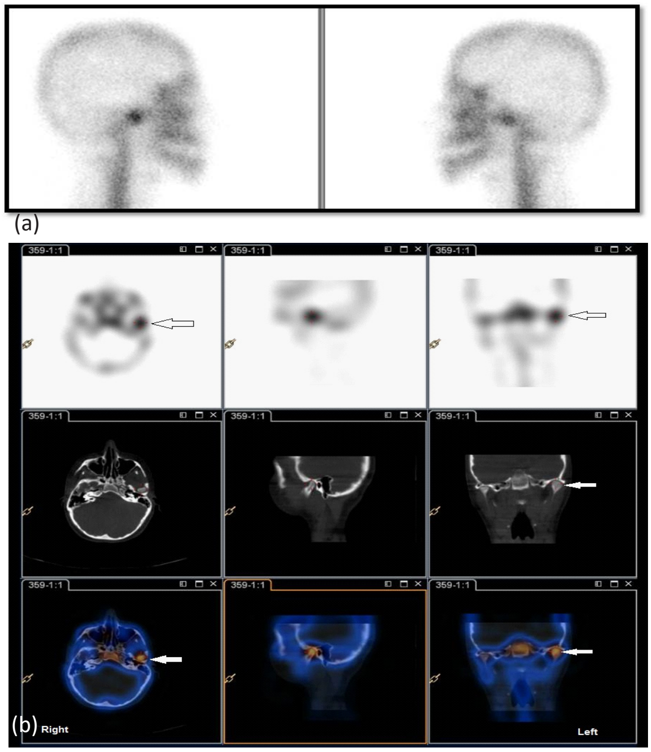

Figure 3: Planar **(a)** and SPECT CT **(b)** bone scan images showed enlarged and increased uptake in left condyle compared to right one consistent with left condylar hyperplasia (Arrows).

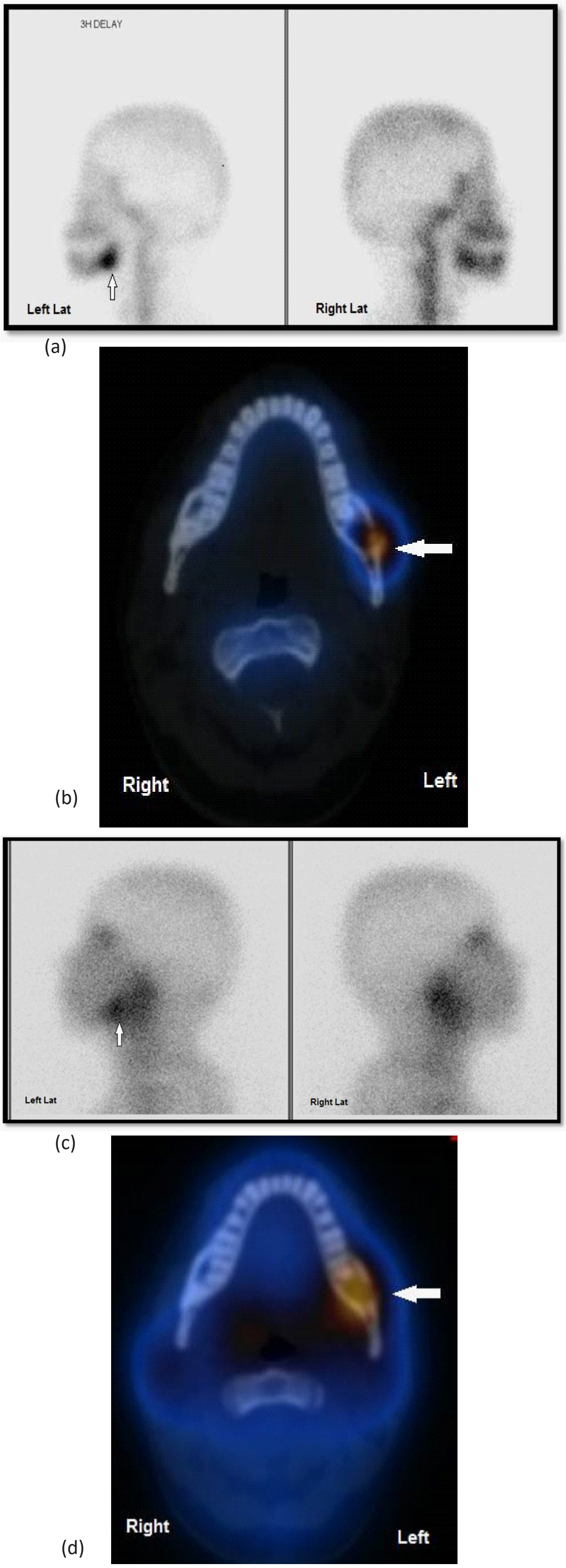

Figure 4: Planar **(a)** and SPECT CT **(b)** bone scan and gallium scan**(c,d)** images showed focal matched increased tracer uptake in both studies in left mandible consistent with active bony infection(osteomyelitis in left mandible).

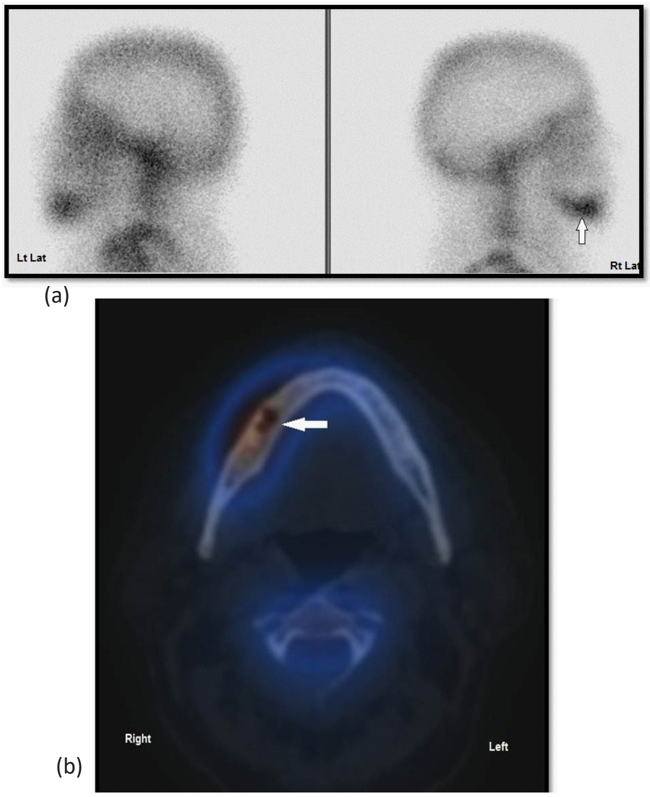

Figure 5: Normal blood flow and blood pool in right mandible (not shown) makes osteomyelitis unlikely. Delayed planar **(a)** and SPECT CT **(b)** bone scan images showed photopenic area (defect) in anterior right mandible surrounded by increased tracer uptake (Arrows) compatible with osteonecrosis with adjacent reactive osteoplastic activity.

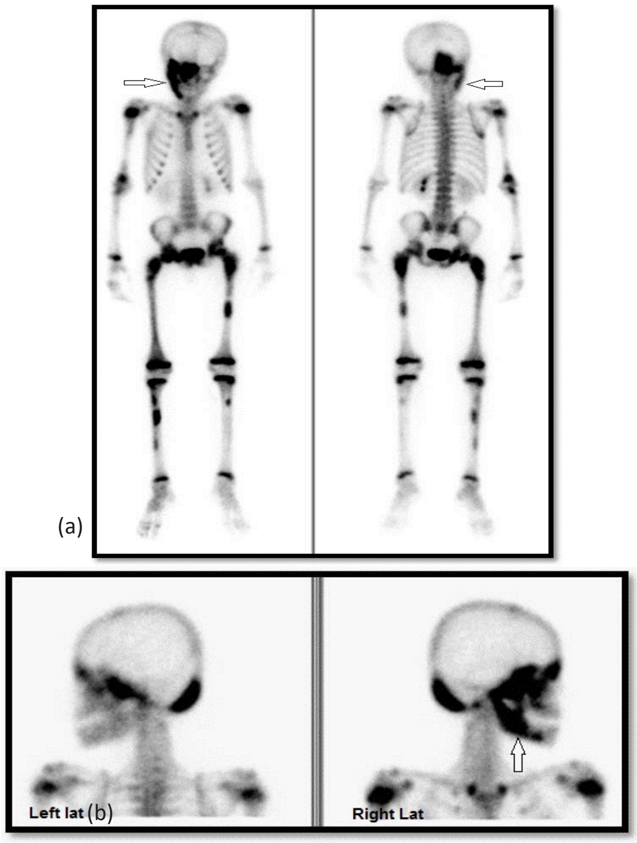

Figure 6: Planar whole body **(a)** and spot lateral skull **(b)** bone scan images showed multiple areas of increased uptake in the skeleton and right mandible (Arrows) consistent with polyostotic fibrous dysplasia.

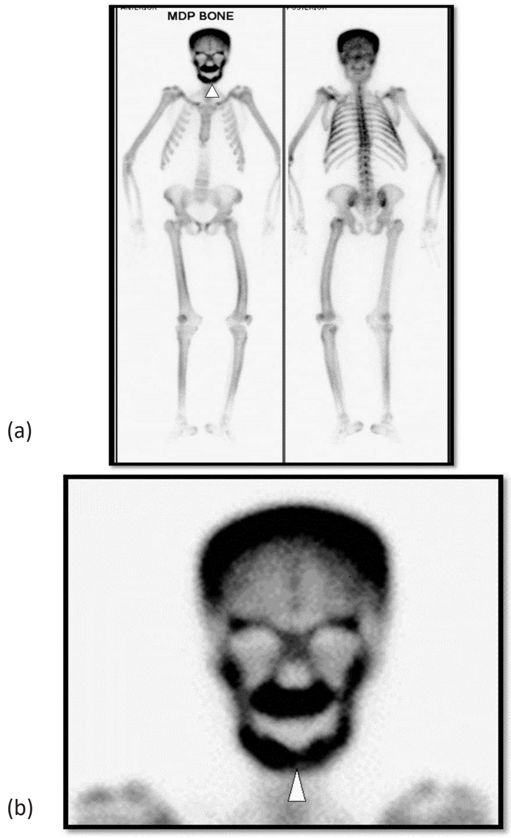

Figure 7: Planar whole body **(a)** and spot lateral skull **(b)** bone scan images showed multiple areas of increased uptake in the skeleton and mandible (Arrows) consistent with hyperparathyroidism.

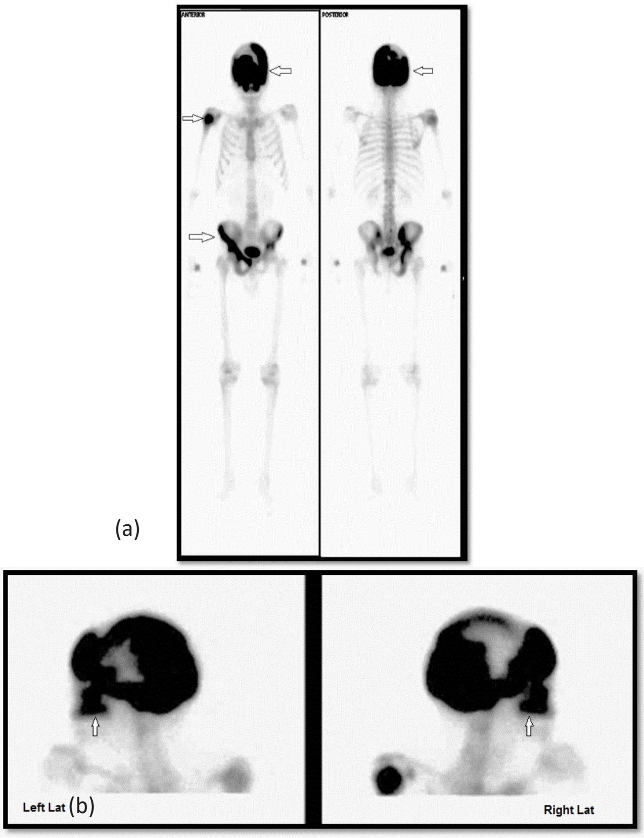

Figure 8: Planar whole body **(a)** and spot lateral skull **(b)** bone scan images showed multiple areas of increased uptake in the skeleton and maxilla (Arrows) consistent with polyostotic Paget's disease.

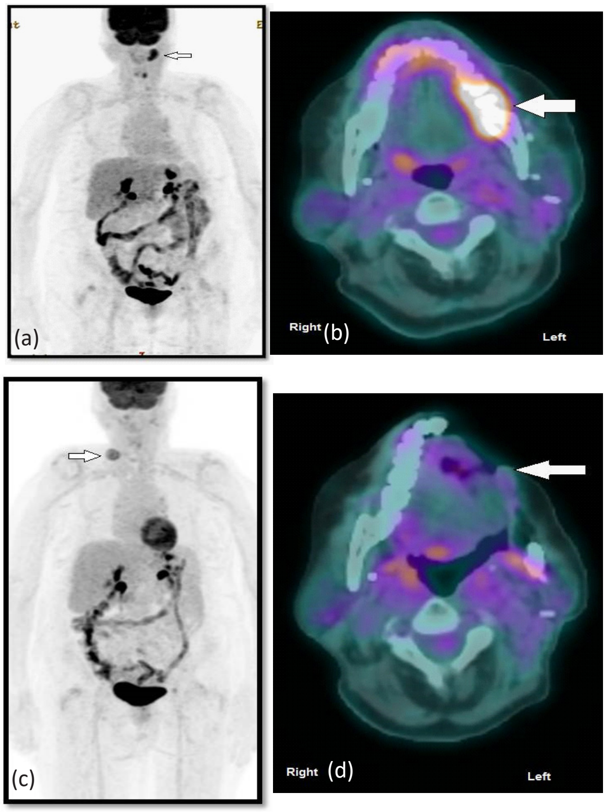

Figure 9: 18F FDG PET CT and maximum intensity projection (MIP): Preoperative study showed FDG avid left mandible lesion with no suspicious local lymph nodes or distant metastases **(a, b)**. Post- operative study showed no residual disease activity in left mandible and suspicious FDG avid lymph node metastases (arrow) in right lower neck **(c,d)**.

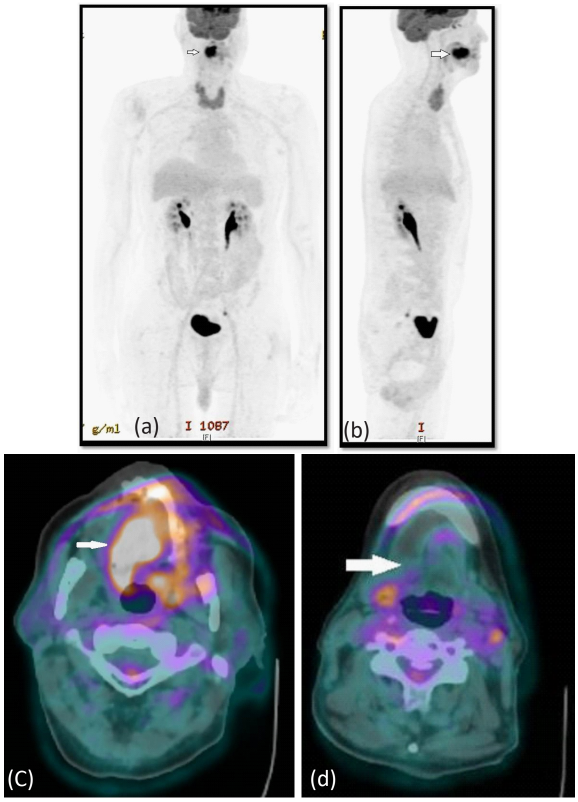

Figure 10: 18F FDG PET CT and maximum intensity projection (MIP): Preoperative study showed FDG avid right hemi-tongue lesion coupled with suspicious multiple small FDG avid bilateral cervical lymph nodes **(a,b,c)**. No suspicious FDG avid distant metastases. Post- operative study showed no residual disease activity in the tongue **(d)**.

Table 1: 18F FDG PET CT and maximum intensity projection (MIP): Preoperative study showed FDG avid right hemi-tongue lesion coupled with suspicious multiple small FDG avid bilateral cervical lymph nodes **(a,b,c)**. No suspicious FDG avid distant metastases. Post- operative study showed no residual disease activity in the tongue **(d)**.

Teaching Points:

Planar and SPECT /CT bone scan in condylar hyperplasia/Hypoplasia:

- Assess condylar metabolic activity at initial diagnosis and on post -operative follow up.

Planar and SPECT /CT bone and gallium scan in mandibular and maxillary osteomyelitis:

- Matched bone and gallium uptake indicate active osteomyelitis at initial diagnosis.
- Gallium scan is used to monitor therapy and once it's normal indicate successful treatment.
- Bone scan is not useful to monitor therapy because remains positive during repair healing phase.

Planar and SPECT /CT bone scan in mandibular osteonecrosis:

- Bone viability at initial diagnosis and monitoring response to antibiotic therapy.

Planar and SPECT /CT bone scan in mandibular fibrous dysplasia/HPT/Paget's disease:

- Assess disease metabolic activity at initial diagnosis.
- Monitoring metabolic activity on conservative or post -operative follow up

Planar and PET /CT in SCC of oral cavity:

- Assess disease extent and distal metastases at initial diagnosis (Staging).
- Post-operative assessment for residual/recurrent disease.
- Follow up for re-staging.

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