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Case Report

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UNUSUAL PRESENTATION OF PRIMARY HYPERPARATHYROIDISM: IMAGING FEATURES.

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ABSTRACT

Hyperparathyroidism is an endocrine disorder characterized by increased level of circulating parathyroid hormone (PTH), in excess of the amount required by the body.Parathyroid adenomas are benign tumors of the parathyroid glands and are the most common cause of primary hyperparathyroidism.Less than half of the patients with hyperparathyroidism manifest skeletal lesions. The classical findings of advanced hyperparathyroid skeletal disease are rarely encountered Today in western countries but are still seen in developing countries. We report a rare case of Primary hyperparathyroidism presenting as an exophytic mandibular mass.

KEYWORDS: Brown tumor, Mandible, Osteosclerosis, Osteitis Fibrosa Cystica, Primary Hyperparathyroidism, Parathyroid adenoma.

INTRODUCTION

The term primary hyperparathyroidism (PHPT) refers to the inappropriate or unregulated overproduction of the parathyroid hormone (PTH). It leads to abnormal calcium homeostasis. High levels of PTH lead to increased renal resorption of calcium, phosphaturia, and increased synthesis of 1,25-dihydroxyvitamin D3, which increase interstitial calcium resorption and increased resorption of the bone.[1]

Primary hyperparathyroidism[PHPT] is usually due to a benign tumor (adenoma) of one of the four parathyroid glands that secretes excessive PTH. The PHPT occurs two to three times

more commonly in women than in men, and mainly in those of 30 to 60 years of age.[2]

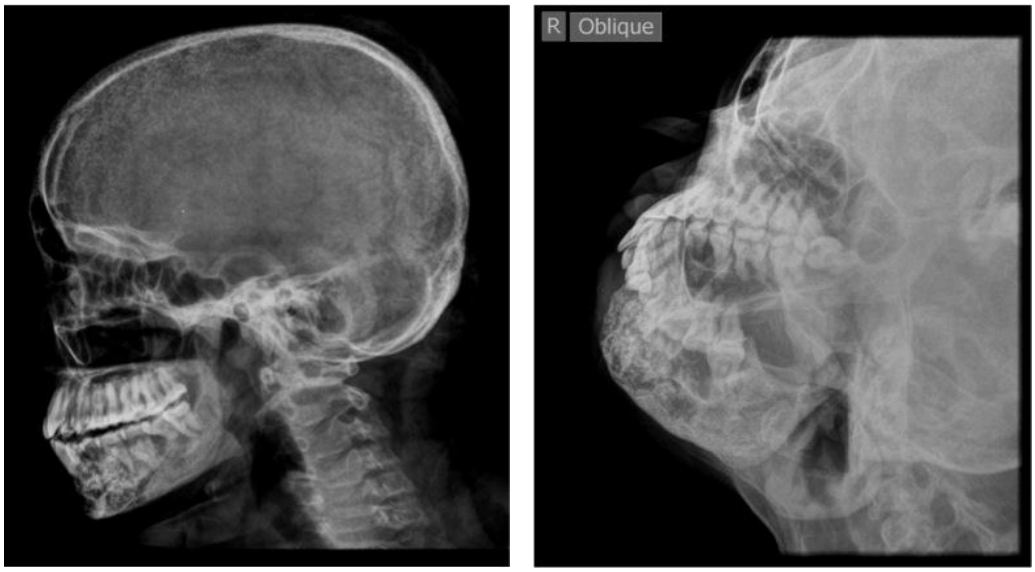
The most common complaints of these patients are weakness, anorexia, nausea, vomiting, constipation, abdominal pains, muscular and joint pains, polyuria, polydipsia, and emotional instability. Furthermore, a variety of osseous changes may be present that include metastatic calcification, subperiosteal erosion, brown giant cell lesion, and rarely osteosclerosis.[3]

Brown tumors are rarely the first symptom of hyperparathyroidism and can occasionally be mistaken for malignancy. Considering the rarity of Brown tumor in PHPT, we report this case with Brown tumor in the mandible. A thorough diagnostic work-up emphasizing on biochemical and various imaging modalities were discussed. Patient was also investigated from the perspective of Multiple Endocrine Neoplasia (MEN) syndrome.

CASE REPORT

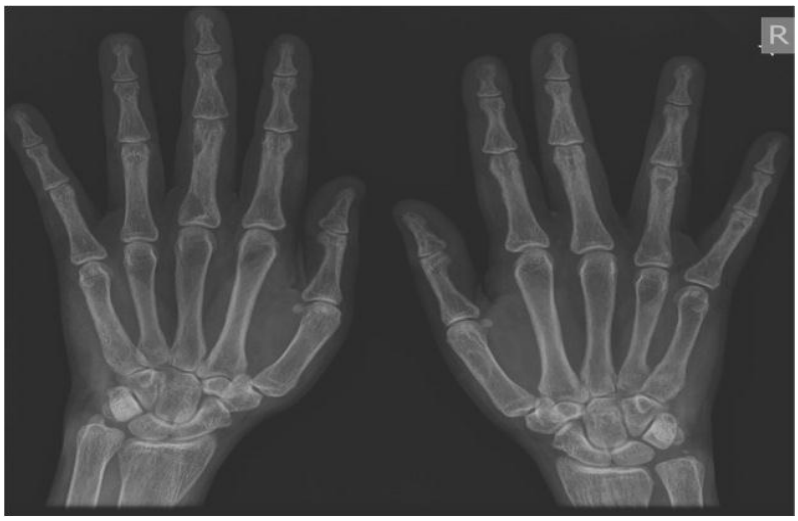
Here, we reporta case of 33 year-old women referred for evaluation of a painless swelling in the right mandible since 2 years, increased in size in the last 5-6 months.The patient also complained of lower limb edema, weakness, anorexia and weight loss for which symptomatic treatment was taken, in various centers prior to admission in our center.

Physical examination revealed right sided facial asymmetry due to a Painless firm swelling that involved the body of right mandible.Intra-orally there was a large, smooth, reddish-pink exophytic mass occupying the lower right oral cavity. Neck examination revealed, fullness within the region of the inferior pole of the left lobe of the thyroid gland, chest wall pain at palpation and edema of Lower limbs. Blood picture showed lymphocytosis (55%). RA factor and C-reactive protein were negative. Urine analysis results were unremarkable. The biochemical pictures revealed hypercalcemia, hypophosphatemia and elevated serum alkaline phosphatase .Serum Calcium 11.6 mg/dL (normal range, 8.4–10.3 mg/dL), Serum Phosphorus 1.77 mg/dL (normal range, 2.4–4.2 mg/dL) and Serum Alkaline phosphatase 1260 IU/L (normal range 30–115 IU/L). The serum parathyroid hormone (PTH) levels were markedly increased 878.2 pg/ml (normal range, 10–65 pg/mL). The lateral skull radiograph (Fig.1a) shows granular appearance of the skull with multiple areas of normal bone interspaced between, giving typical "Pepper pot skull" appearance with loss of distinction of inner & outer table. In addition oblique right mandible (Fig1b) shows a mixed osteolytic and sclerotic lesion with cortical thinning and coarse trabeculae suggestive of Osteitis Fibrosa Cystica (Brown tumor).

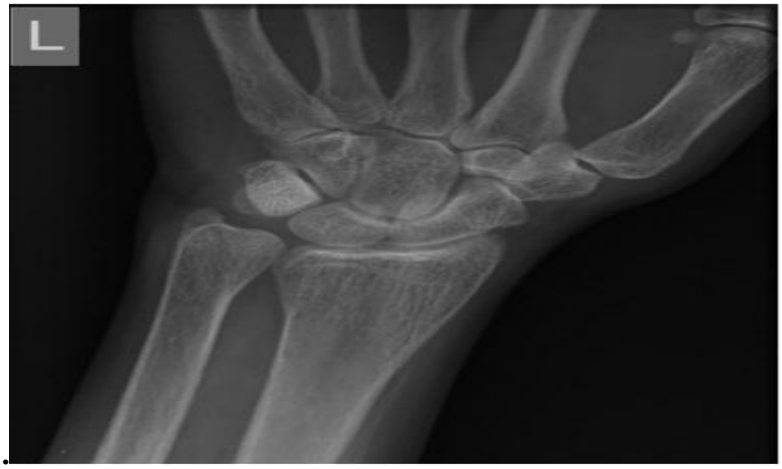


Based on the age, gender and clinical, radiological and haematological findings, differential diagnosis of the lesion included osteogenic osteosarcoma, desmoplastic fibroma of bone, ameloblastoma, metastasis from unknown primary, or brown tumour of hyperparathyroidism. Prior to biopsy/fine needle aspiration cytology (FNAC) from the lesion, the patient was referred for askeletal survey, neck and abdominal ultrasound, and general medical and gynaecological consultation to rule out metastasis from an unknown primary.

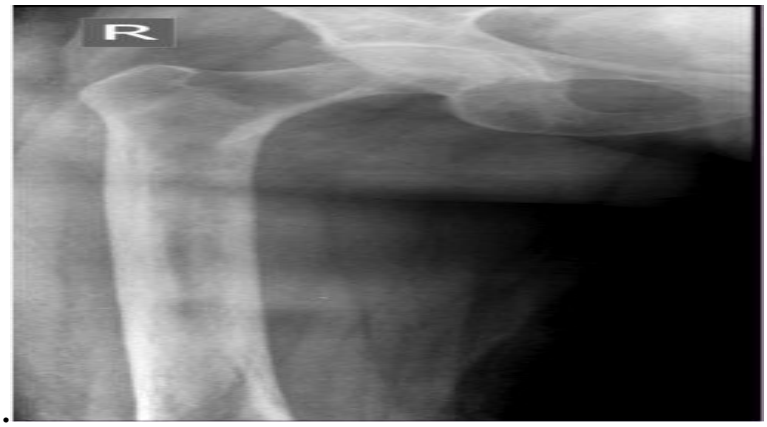
Posterio-anterior radiograph of the hands (Fig. 2) showed osteopenia with subtle acro-osteolysis**,** subperiosteal resorption of the medial aspect of middle phalanges and intracortical tunneling involving the metacarpals,with few lytic lesions in the proximal phalanges.



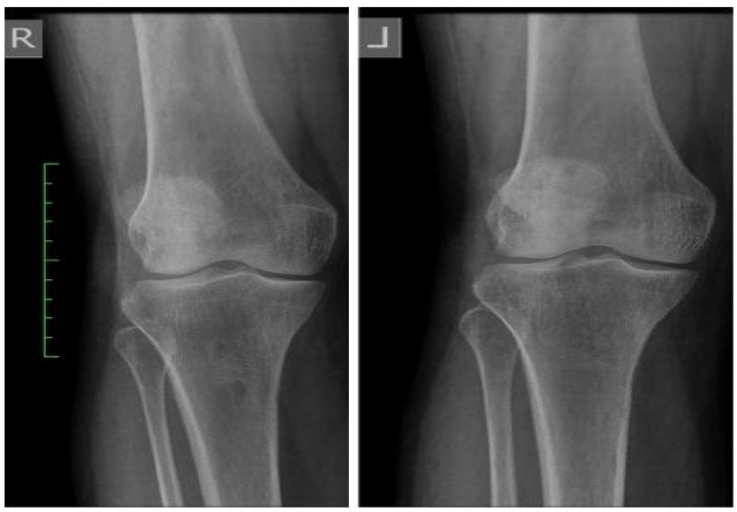
Posterio-anterior radiograph of the wrist (Fig.3) showed erosions at the radial and ulnar styloid processes.



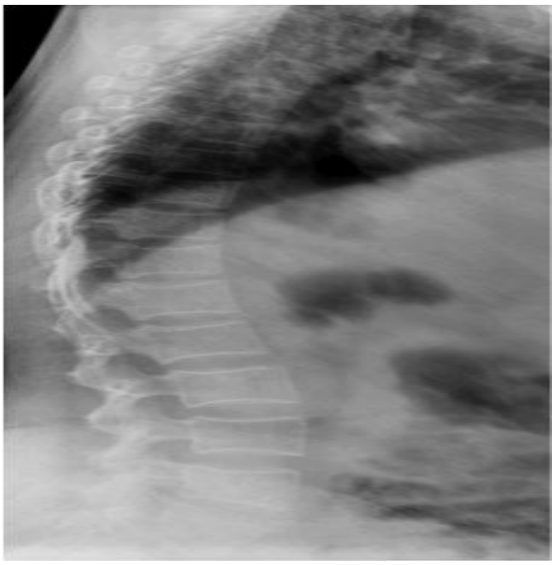
Anterio-posterior Radiograph of right hip joint & proximal femur (Fig.4) shows small radiolucent lytic lesions in the ilium & proximal shaft of femur.



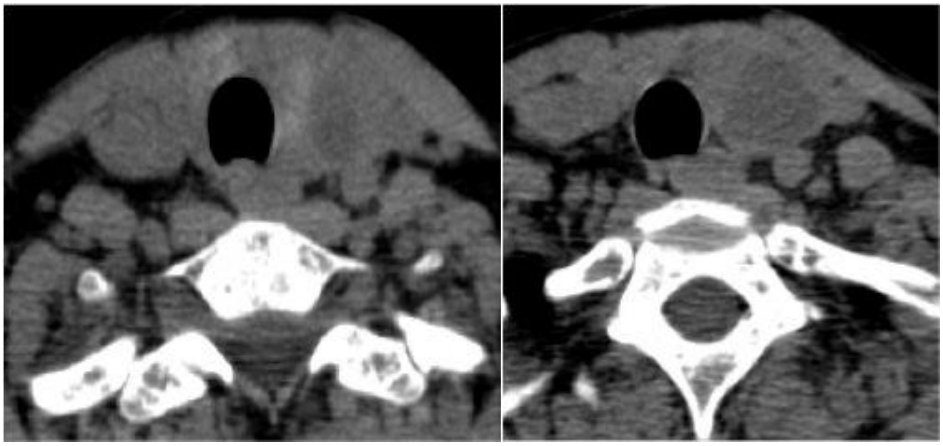
Anterio-posterior Radiograph of both knee (Fig.5) showed small radiolucent lytic lesions in the proximal metaphyseal ends of tibia and distal metaphyseal ends of femur.

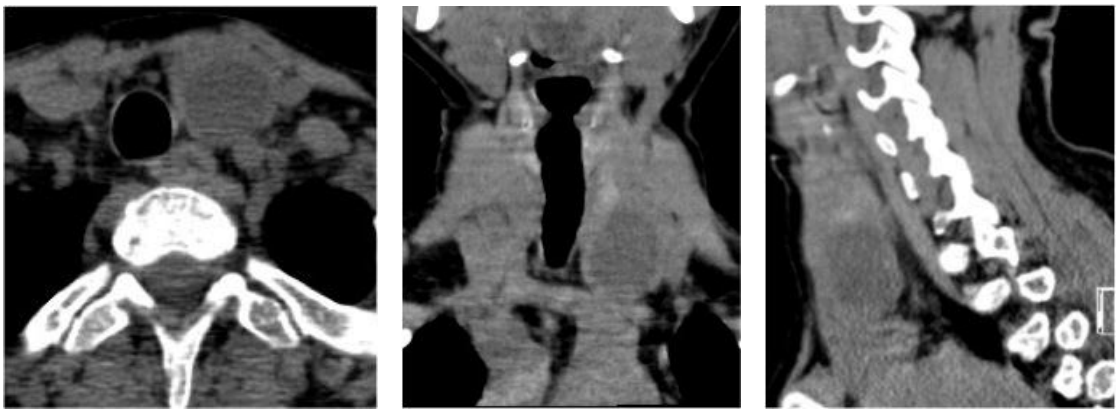


Lateral Radiograph of Dorso-lumbar spine (Fig.6) showed diffuse osteopenia.

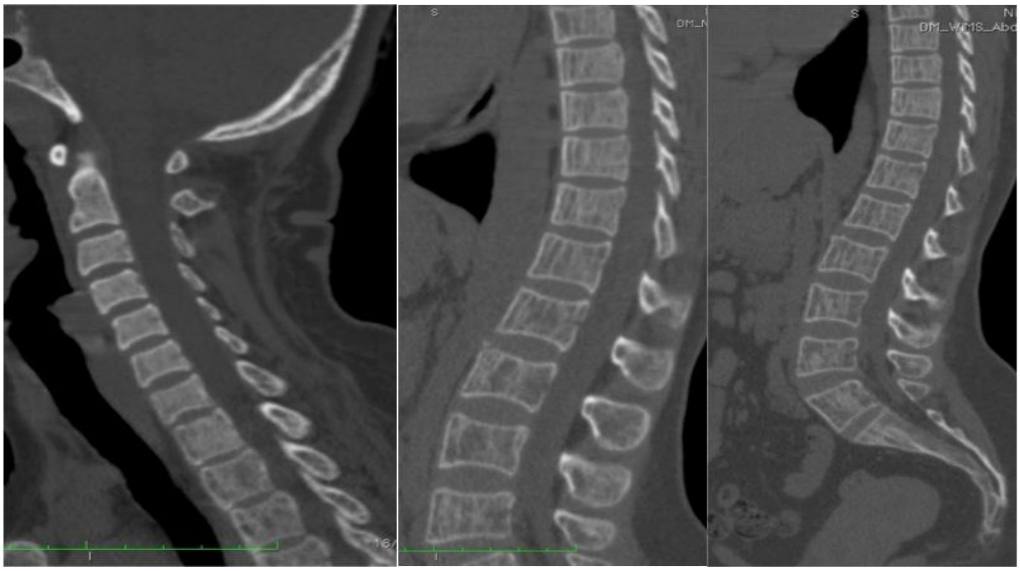


Plain CT of Neck (Fig.7 a-e) Axial, reformatted Coronal & Sagittal images reveal hypodense nodule inferio-lateral to left lobe of thyroid.

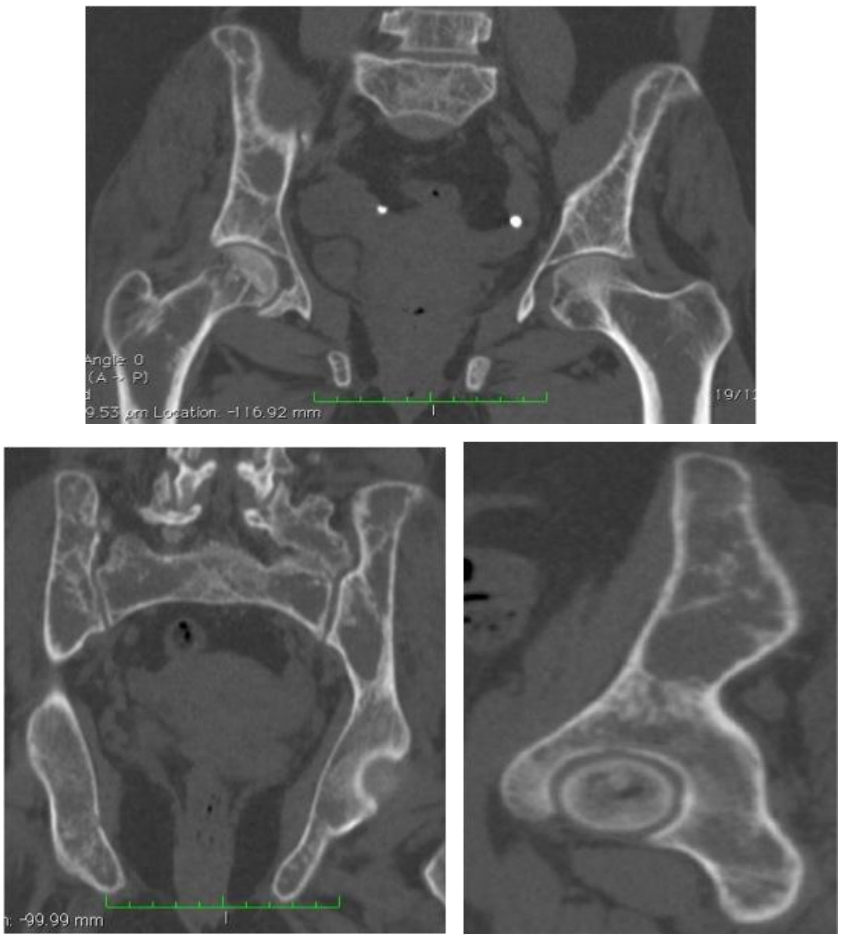




Plain CT (Fig.8a-c) Sagittal &Coronal reformatted images of Cervico-dorsal & Dorso-lumbar spine show generalized osteopenia , Coarse trabeculae & sclerosis (Rugger jersey spine).

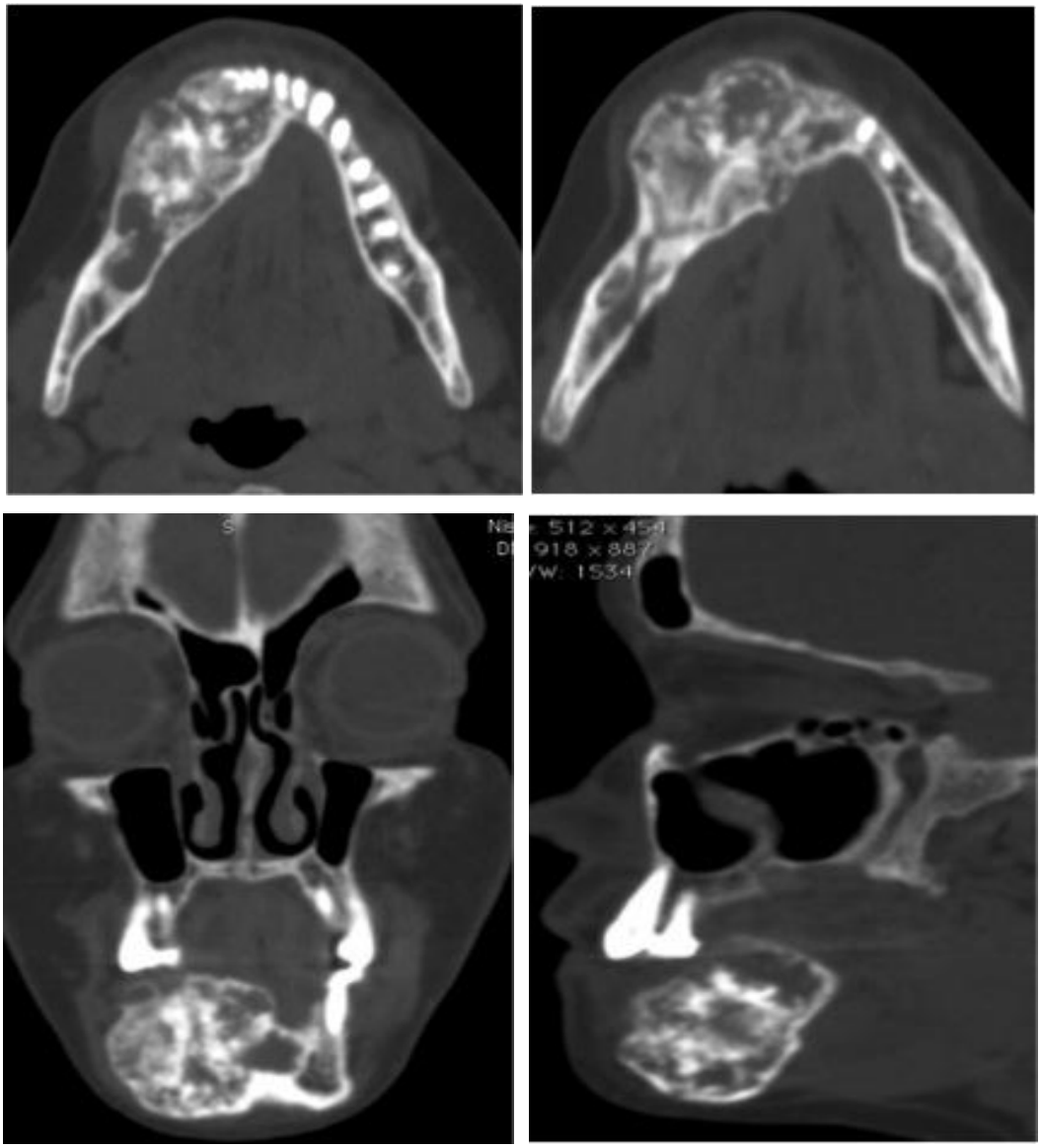


Plain CT Coronal & Sagittal reformatted images of Pelvis (Fig.9 a-c) show generalised osteopenia, coarse trabeculae & osteolytic lesions (Brown tumors).

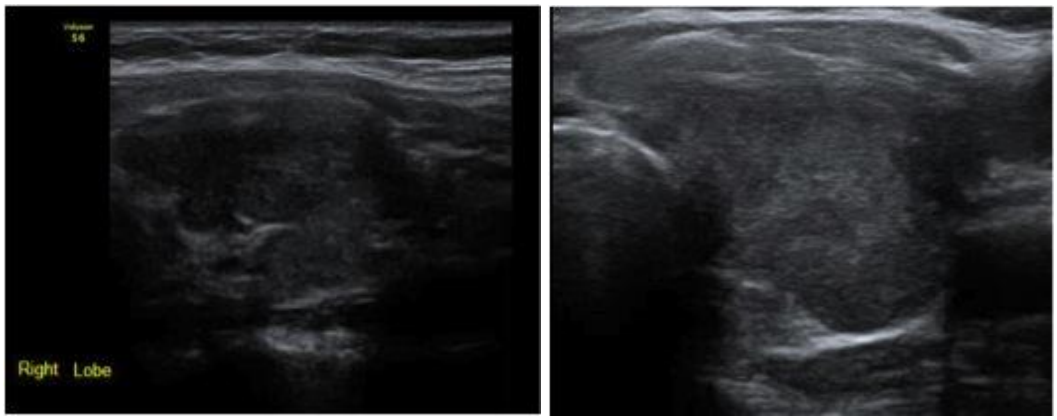


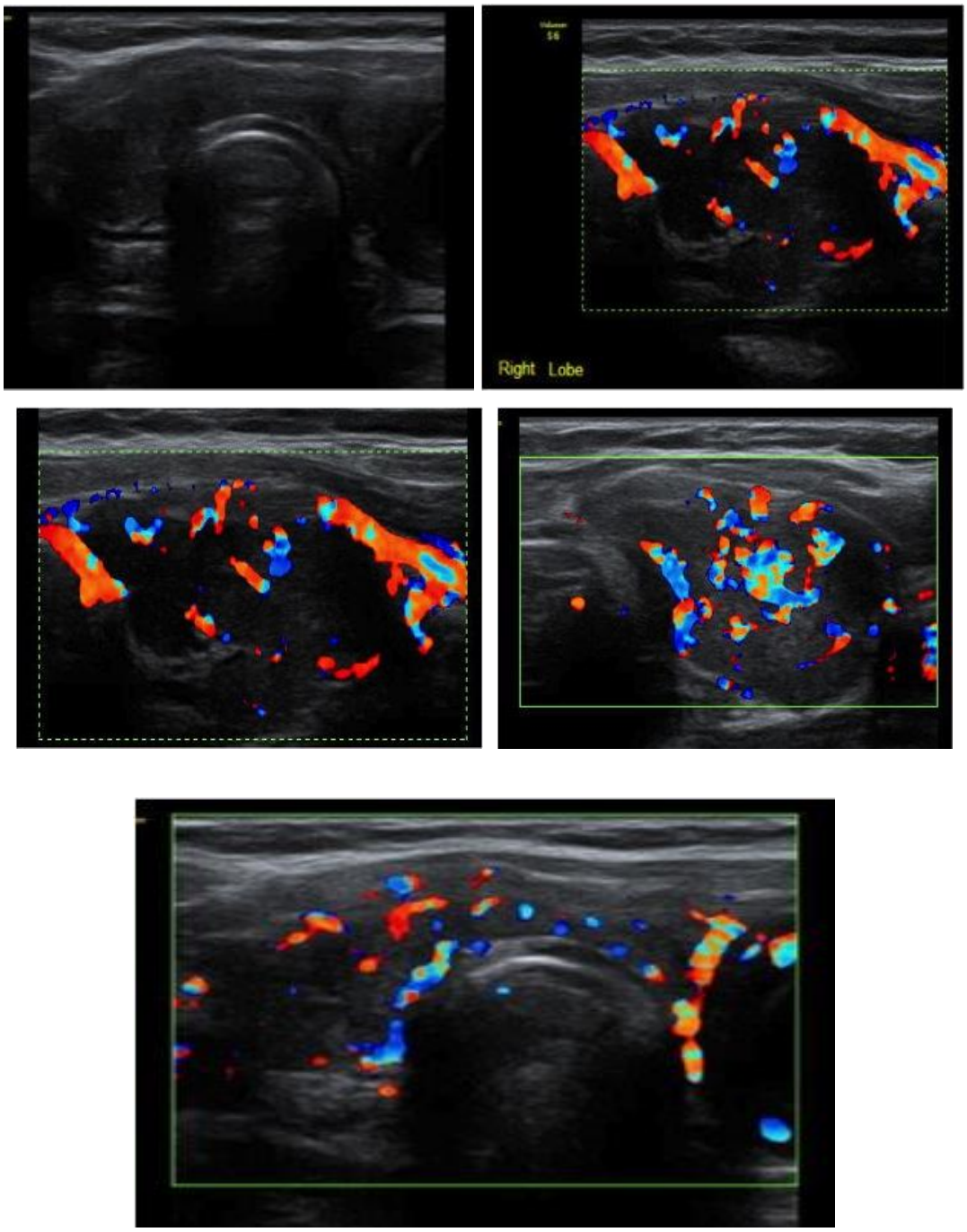
CT Axial, reformatted Coronal & Sagittal images of Mandible (Fig.10 a-d) revealed mixed osteolytic & sclerotic lesion in body of right mandible with Cortical thinning &

coarse trabeculae suggestive of Osteitis Fibrosa Cystica (Brown tumor).

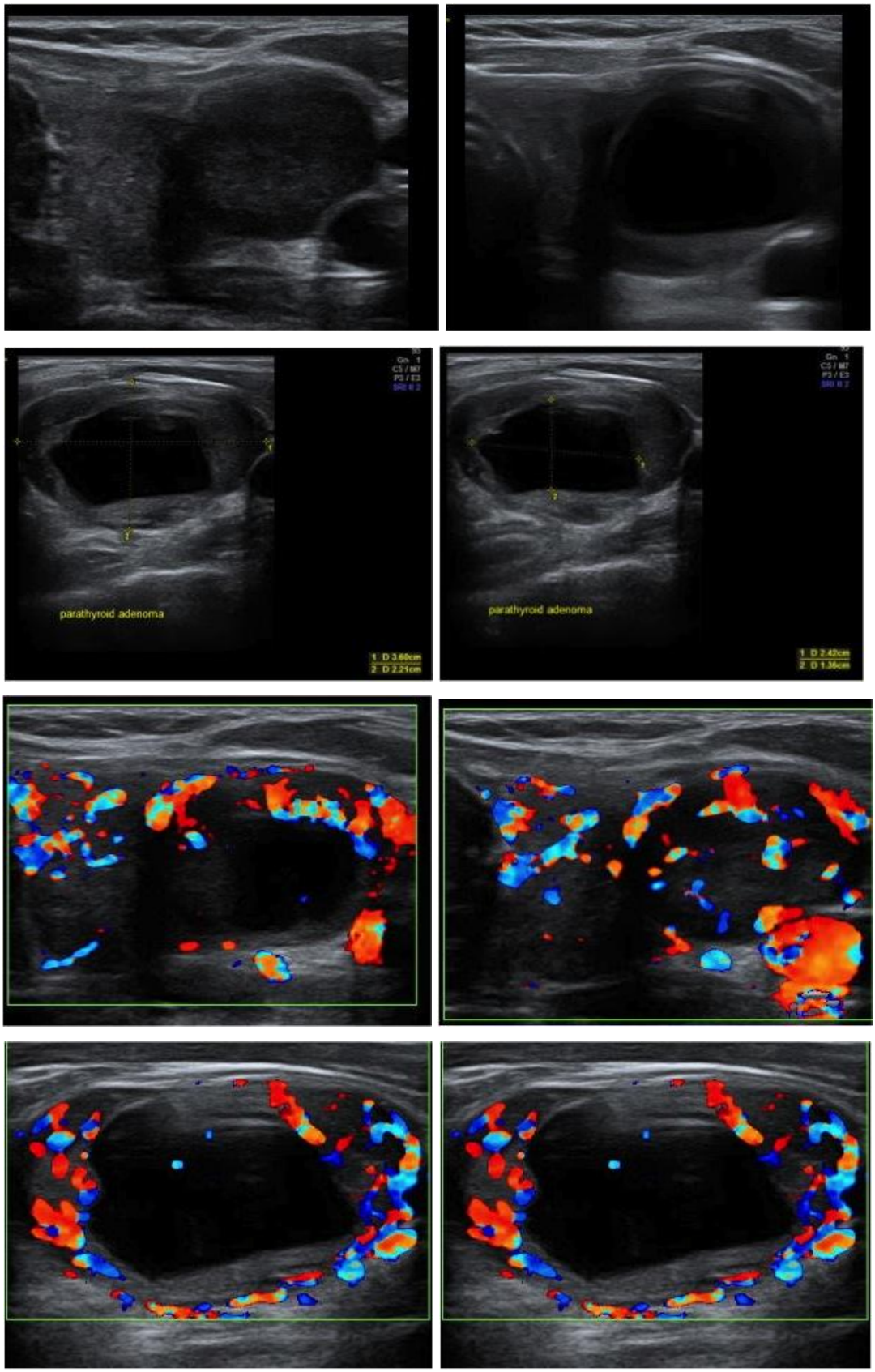


Ultrasound (USG) with colour doppler of thyroid (Fig.11 a-d & e-h) showed diffusely enlarged Hypoechoic thyroid with increased vascularity suggestive of thyroiditis.





Colour Doppler USG of neck (Fig 12a-d & e-h) also showed a well defined hypoechoic nodule (36x21mm) with central cystic area (24x13mm), inferio-lateral to left lobe of thyroid and increased peripheral rim of vascularity suggestive of left parathyroid adenoma.



USG guided Fine Needle Aspiration Cytology of the hypoechoic nodule confirmed parathyroid adenoma.

An ultrasound examination of the Abdomen revealed no abnormality.

DISCUSSION

A product of the chief cells of the four parathyroid glands, parathyroid hormone (PTH) is a key modulator of calcium homeostasis. Complex in its metabolic function, PTH helps maintain the serum calcium level by mobilizing calcium at the bone surface, stimulating osteoclast-mediated bone resorption.[4]

PTH also promotes renal hydroxylation of 25-hydroxy–vitamin D, which,in addition to being instrumental in intestinal absorptionof calcium, binds to intranuclear receptors within bone, producing mediators of calcium mobilization and mineralization of organic matrix.[5] Other effects of PTH include promotion of renal tubular reabsorption of calcium and lowering of serum phosphate level by inducing phosphaturia.[6] Excessive production of PTH, termed Hyperparathyroidismis classified as primary, secondary, or tertiary in form. Primary hyperparathyroidism, due to autonomous hypersecretion of PTH, usually occurs in the setting of a parathyroid adenoma(80%) but can also be seen with parathyroid gland hyperplasia (15%–20%) or carcinoma (0.5%).[7]

Secondary hyperparathyroidism results from stimulation of the parathyroid glands as a response to hypocalcemia or due to apparent insensitivity of the parathyroid glands to elevated serum calcium levels and dysregulation of the normal negative feedback loop(pseudohypoparathyroidism).The most common cause of secondary hyperparathyroidism is renal failure, which results in phosphate retention, hypocalcemia, and 1,25(OH)2D3 deficiency, leading to a compensatory increase in the production of PTH.[6]

Tertiary hyperparathyroidism is seen in cases of secondary hyperparathyroidism, in which the parathyroid glands continue to function autonomously despite correction of the initial cause, resulting in hypersecretion of PTH in the setting of normal calcium levels.[8]

Hereditary hyperparathyroidism is seen in Multiple Endocrine NeoplasiaType -1(MEN-1) syndrome with tumors of the anterior pituitary gland and pancreas. In Multiple Endocrine Neoplasia Type -2a (MEN-2a) parathyroid disease occurs in conjunction with medullary cancer of the thyroid & pheochromocytoma. Another rare syndrome called Jaw Tumor Syndrome (JTS) is associated with hyperparathyroidism in which there are fibrous jaw tumors with parathyroid adenomas, thyroid cancer, renal cysts and Wilms tumors.[9] Although most patients with primary hyperparathyroidism (PHPT),today are asymptomatic due to the widespread availability of laboratory screening for hypercalcemia and earlier detection, the

clinical presentation is variable.[10]

Previously encountered overt symptoms including dementia, depression, peptic ulcer disease, pancreatitis, constipation, renal calculi, and diffuse bone and joint pain are no longer common. Patients now often complain of mild subjective symptoms such as weakness and easy fatigability.[11]

The classic imaging features of advanced primary hyperparathyroidism (PHPT), are also less frequently seen today.Generalized osteopenia is the most common imaging finding in PHPT. Subperiosteal bone resorption is a common finding of advanced hyperparathyroidism, most often seen involving the hands and the feet. Although classically most pronounced at the radial aspects of the second and third middle phalanges, subperiosteal resorption can also be seen involving the medial aspects of the metaphyses of the long bones as well as the ribs and lamina dura of the teeth.

Terminal tuft resorption can also be seen and hyperparathyroidism should be considered in the differential diagnosis for acro-osteolysis.[5] Other areas of bone resorption are seen at sites of high bone surface area and include subchondral locations, often best appreciated at the sacroiliac, acromio-clavicular, sterno-clavicular, and temporo-mandibular joints, the symphysis pubis, and the patella. Resorption of subligamentous and subtendinous bone occurs most often at the femoral trochanters, the ischial tuberosities, the calcaneal insertions of the plantar aponeurosis and achilles tendon, the inferior margin of the distal clavicle, and the tuberosities of the humerus.[7] Intracortical endosteal and trabecular bone resorption can also be present.

Diffuse or localized osteosclerosis is very rarely encountered in PHPT, and is a more common finding in secondary hyperparathyroidism. When involving the spine, sclerosis can produce a striped appearance, the so-called “rugger jersey” spine.[7]

Brown tumors also known as osteoclastomas,are eccentrically located and often expansile lesions resulting from amassing giant cells and fibrous tissue.Brown tumors are not true neoplasms, but they can be locally aggressive and mimic malignancies.Thus, brown tumors have been described as resulting from an imbalance between osteoclastic and osteoblastic activity, resultant resorption with fibrous replacement ofthe bone and eventual osteitis fibrosa cystica (OFC),which is the end stage of primary hyperparathyroidism.

On radiography and CT, brown tumors are seen as lytic lesions or sclerotic lesions with regular borders and no cortical disruption, periosteal reaction, or inflammatory signs.[12] MRI shows variable intensities on T2-weightedimages and intense enhancement on T1-weighted contrast images.[13]

On USG, parathyroid adenoma appears as a hypoechoic solid mass with echogenicity less than thyroid glandand rarely may contain specks of calcification. About 2% have cystic changes due to degeneration.On CT scan adenoma are seen as hypoattenuating masses with contrast enhancement in 20% cases. On Magnetic Resonance Imaging (MRI) adenoma has variable appearances,intermediate to low signal intensity on T1 weighted images and increased signal intensity or isointense with fat on T2 weighted images. Although directed US examination, CT of the neck, and MRI are useful in the complete evaluation of primary hyperparathyroidism, 99mTc-sestamibi parathyroid Scintigraphy is now considered the best preoperative localizing modality for the detection of parathyroid adenomas.[14]

As parathyroid scintigraphy can be limited by the coexistence of thyroid nodules or other metabolically active tissues such as lymph nodes, diffuse hyperplasia, or metastatic thyroid cancer, it is often correlated with CT results to yield functional and anatomic localization.[8] Patients with PHPT showed high prevalence of thyroid disease, especially in postmenopausal women.[15] Our patient also had associated Thyroiditis. Treatment is parathyroidectomy and at higher centers minimally invasive radioguided parathyroidectomy (MIRP) has become the preferred method of removing parathyroid tumors.[16]

The National Institutes of Health (NIH) criteria for selecting patients for parathyroidectomy include the following.

a) typical parathyroid-related symptoms involving the skeletal, renal, or gastrointestinal systems;
b) a sustained elevation of serum calcium level more than 1–1.6 mg/dL (0.25–0.40 mmol/L) above the upper limits of normal;
c) a substantial decline in bone mass;
d) a decline in renal functionby 30% or more;
e) nephrolithiasis or worsening of calciuria;
f) severe neuromuscular psychological problems;
g) unwillingness ofthe patient to continue under medical supervision.[17]

PHPT presenting in the mandible as aexophytic mass is a rare presentation. A mass involving one or both jaws as the presenting complaint has been reported in 4.5% of the patients with hyperparathyroidism.[18] Although, the cause of PHPT is still poorly understood, surgical parathyroidectomy results in a long-term cure in greater than 95% ofthe cases.[19] Our patient underwent surgery and a left lower parathyroidectomy was performed. After surgery the serum PTH and serum calcium returned to normal.

CONCLUSION

PHPT is now usually detected in the early and asymptomatic phase because of recent improvements in biochemical analytic techniques. Brown tumor of mandible is a benign clinical entity appearing as an extremely rare manifestation of PHPT, which can be difficult to distinguish from other tumors, tumor-like lesions, and metastatic disease. When a middle aged patient, presents with unexplained lytic bone lesions or pathological fractures, surgeons, endocrinologists, and especially radiologists should be reminded of this unusual presentation of PHPT to avoid unnecessary surgical removal. Our case highlights the importance of a thorough diagnostic work-up for PHPT. A definitive diagnosis is only possible upon completion of clinical, radiological, and biochemical analysis.

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