Central Giant Cell Granuloma: First Manifestation of Primary Hyperparathyroidism

Jigna S Shah, Mahalaxmi B Panda

*Professor & Head of Department ** Postgraduate Student, Department Of Oral Medicine & Radiology, Government Dental College & Hospital, Ahmedabad-380016, India

Abstracts: Hyperparathyroidism results in an altered state of osseous metabolism involving bone resorption and tissue change known as osteitis fibrosa cystica, which is the end stage of this disease. It is rare because now-a-days it is usually diagnosed and treated before symptoms develop. Presentation of brown tumor in the jaws is rarely the first sign. Here a case of a 32 year old female patient with previously undiagnosed primary hyperparathyroidism, who presented with a mandibular swelling as initial sign of the disease is reported. Further investigations revealed a diagnosis of parathyroid adenoma. Evaluation of the patient has been reviewed in this case report. [Jigna S NJIRM 2017; 8(5):101-104]

Key Words: Hyperparathyroidism, Central Giant Cell Granuloma, Ultrasonography, Scintigraphy

Author for correspondence: Mahalaxmi Panda, 25/2, Officer's Family Accomodation , New Golibar Maidan, Pune 411001 E-Mail: panda.mahalaxmi@gmail.com M: 9426911768, 9112158518

Introduction: Central giant cell granuloma (CGCG) is a benign lesion of bone which may be locally aggressive or asymptomatic in nature. In 1953, Jaffe described it as reparative granuloma of jaw bones.[1] But the term reparative is obsolete, as CGCG causes the destruction of involved bones. According to WHO, it is an intraosseous lesion consisting of cellular fibrous tissue that contains multiple foci of hemorrhage, aggregations of multinucleated giant cells, and occasional trabeculae of woven bone.[2] Females are predominantly affected with a sex ratio of 2 : 1 and more than 70% of lesions affecting mandible. Clinically, facial swelling, asymmetry, and expansion of cortical plates are seen and radiographically, resorption of roots of teeth with cortical perforation is well appreciated.[3] Patients who present with central giant cell lesion of maxilla or mandible should be screened for hyperparathyroidism (HPT) to differentiate it as brown tumor. Normal levels of parathormone (PTH) ranges between 12 and 70 pg/mL[4,5] and excessive secretion of leads to a metabolic bone disorder known as HPT. Although it is rare, CGCG of facial bones can be its first manifestation.[1-5]

HPT is categorized as primary, secondary, or tertiary. Primary HPT (PHPT) is an endocrinopathic condition characterized by hypersecretion of PTH, which may be caused by an adenoma (solitary/multiple) (80–85%), idiopathic hyperplasia (15-20%), or parathyroid carcinoma (<0.5%). Renal calculi, osteoporosis (10-20%), neuropsychiatric symptoms and peptic ulcerdisease or pancreatitis may be seen rarely.[4] Secondary HPT is caused by hypocalcaemia or vitamin D deficiency acting as a stimulus of excessive PTH production. Chronic renal failure is the main cause of secondary HPT. Tertiary HPT is caused by the development of autonomous parathyroid hyperplasia after long-standing secondary HPT, most often in patients with renal failure.[3,4]

Skeletal involvement in classic PHPT is characterized by a strikingly high rate of osteoclastic bone resorption and is accompanied by a cellular repair process that results in the accumulation of fibrous stroma and connective tissue cells along with multinucleated giant cells.[3-5] Oral radiographic manifestations of primary hyperparathyroidism include unilocular or multilocular osteolytic lesion with generalized loss of lamina dura and an alteration in trabecular pattern.[8] This case highlights the presentation of primary HPT as a large brown tumor in the mandible, an unusual first manifestation as well as unusual location mimicking central giant cell granuloma.

Case Report: A 32 year old female patient reported to Oral Medicine and Radiology department with chief complaint of pain and swelling in lower right anterior region since a month which is progressively increasing in size, associated with difficulty in mastication. Past dental history revealed extraction of 46 due to pain before three years. Medical history is unremarkable. On eliciting personal history it was revealed that patient was lethargic with generalized musculoskeletal ache, reduced appetite since past few months and increased mood swings. Patient was poorly built, malnourished but calm and cooperative with stable vital signs.

Extraoral examination revealed facial asymmetry with a single, diffuse swelling measuring 3x3 cm diameter in right mandibular parasymphysis region. It was hard in consistency with normal overlying skin. There was

no local rise in temperature. Left submandibular lymph node was enlarged, palpable, measuring 1x1 cm in diameter, firm in consistency, mobile and tender. Intra oral examination revealed a solitary, well-defined swelling of size 3x4cm diameter extending from right mandibular canine region to 1st molar region, obliterating the vestibular depth and expansion of buccal cortical plate. Surface of swelling was smooth, tender, compressible and firm in consistency. Mucosa over the swelling was normal. Grade II mobility of teeth was noted i.r.t 44 45 and vitality test showed delayed response. [Figure 1] History and above clinical findings, were suggestive of bening tumor of right mandible. Differential diagnosis included central giant cell granuloma, ameloblastoma and fibro-osseous lesion.

Radiological examination included intraoral periapical radiographs, orthopantomogram and right lateral oblique radiograph of mandible, showed single ill-defined mixed radiolucent-radiopaque lesion of size 3x4 cm from 43 to 47 region from alveolar crest to lower border of mandible. Multilocularity was noted causing mild root resorption, divergence of roots with effacement of lamina dura. Internal structure showed hazy mixed appearance with randomly oriented faint trabecular pattern. These findings suggested the probable diagnosis of central giant cell granuloma. [Figure 2] Radiographic differentials included ameloblastoma, odontogenic myxoma and fibro-osseous lesion of mandible. It was followed by computed tomography that revealed expansile lytic lesion in right lower alveolus involving root of premolar with multiple internal septations abutting adjacent buccal mucosa confirming the diagnosis of central giant cell granuloma. [Figure 3]

Incisional biopsy was done and histopathological examination showed presence of increased number of giant cells and bundles of fibrous connective tissue with plump fibroblast and presence of woven bone suggestive of central giant cell granuloma. [Figure 4]

Thereafter routine biochemical investigations were done that revealed: Serum calcium: 14.11 mg/dl (normal 8.5-10.5mg/dl), Serum phosphorus: 2mg/dl (2.5-5 mg/dl), serum alkaline phosphatase: 313.00 U/L (28-78U/L), parathormone- 1421.3 pg/ml (11-79 pg/ml). This raised the suspicion of hyperparathyroidism; hence ultrasonography was advised that reported the presence of heterogeneous, hypo-echoic lesion, of size approximately 10x10x24 mm with internal and peripheral vascularity, arising from lower pole of left thyroid gland. [Figure 5] Further investigation of parathyroid technetium scintiscan ($^{99}Tc^{m}$ sestamibi scintigraphy; MIBI methoxy-isobutyl-isonitrile) showed area of increased tracer uptake in the left inferior parathyroid region as well as in right mandibular region suggestive of "Parathyroid adenoma" involving left inferior parathyroid gland. [Figure 6] Radiographs of chest, hands and pelvis showed normal appearance.

Patient underwent complete parathyroidectomy of enlarged left inferior gland and the excised mass was sent for histopathological examination that revealed features of parathyroid adenoma. No treatment was instituted for mandibular central giant cell granuloma. After the surgery, patient was advised antibiotics, calcium supplements and multivitamin tablets. Blood investigations, serum chemistry and the parathyroid assay were carried out postoperatively which showed a serum calcium level as 9.8mg/dl (8.5–10.5mg/dl) and PTH assay of 56.6pg/ml (12–65 pg/ml). Patient was reviewed initially every month followed by 3 monthly examinations for about a year. It was marked that there was progressive decrease in size of the brown tumor of mandible after removal of parathyroids. The postoperative orthopantomogram showed areas of increasing radio opacities replacing multicystic radiolucent areas. [Figure 7] Followup of one year revealed, the patient is healthy with without any complications.

Discussion: PHPT occurs in 0.2% to 0.5% of the population. Most common symptoms include fatigue, musculoskeletal aches and pains, back pain, weakness, dyspepsia, polydipsia, polyuria, nocturia, constipation, anorexia, pruritis, nausea, depression and memory loss.[2,5] Our patient presented with complaint of anorexia and lethargy and increased irritation, mood swings and body ache. This disease has evolved from one presenting with the classic triad "painful bones, kidney stones, and abdominal groans" to one where the symptoms are subtle and detection commonly occurs because of documented hypercalcemia on routine biochemical testing which was also seen in presented case.[5-7]

Increased circulating levels of PTH initiates fibrous and osteoclastic reaction in the skeleton. An imbalance of osteoclastic and osteoblastic activity causes bone resorption with fibrous replacement of marrow with

thinning of cortex leading to condition called Osteitis fibrosa cystica (OFC) and brown tumors or osteoclastoma are localized form of OFC.[2,5,10]

Maxillofacial brown tumors are rare; when they occur in this region, they usually involve the mandible. The name is derived from the color of the tissue specimen, which tends to be dark reddish-brown secondary to the abundant hemorrhage and hemosiderin within the lesion. It can manifest at any age but is more common in persons above 50 years with female preponderance. They usually represent the terminal stage of HPT.[1,3,7,8,10] Our patient was 32 year old female, and the diagnosis of brown tumor resulted from finding high levels of PTH mimicking central giant cell lesion in the mandible. It is uncommon to find a brown tumor as the first manifestation of PHPT as seen in our case.

Oral radiographic manifestations of include unilocular or multilocular osteolytic lesion with generalized loss of lamina dura and root resorption (40% cases) loss of cortication around the inferior alveolar canal or maxillary sinus, and an alteration in trabecular pattern i.e. decrease in trabecular density and "blurring" or "ground-glass" appearance of trabeculae.[8-11] Our case had a large multilocular mixed lesion with loss of lamina dura and mild root resorption in lesional area. CT scans were highly valuable for determining exact borders and size of the lesion. Ultrasound and parathyroid scintigraphy were helpful for localizing abnormalities in the bones and parathyroid glands.

Histologically, these tumors have a relatively vascular fibroblast-rich stroma with irregularly distributed clusters of characteristic osteoclastic giant cells. Woven bone can also be seen with thin, bony trabeculae that are irregularly shaped, sized, and oriented. All these features were found in present case. Histopathological features alone cannot establish diagnosis because many other giant cell lesion of bone shows identical features like central giant cell granulomas, cherubism, aneurysmal bone cyst, paget's disease. Clinical features and endocrine status of the patient like increased calcium levels, alkaline phosphatase and parathormone levels confirm the diagnosis as seen in presented case. The only distinguishing characteristic is the presence of hyperparathyroidism in patients with brown tumors.[5,6,9,10] Thus, its mandatory to exclude HPT in all patients with histologically proven giant cell lesion in maxillofacial region. Our patient was investigated for HPT and hypercalcemia only after histopathological findings.

Treatment of brown tumor consists of the reversal of hypercalcemia, which is achieved by parathyroidectomy. After treatment of the underlying metabolic disorder, brown tumors frequently became sclerotic and showed regression as seen in our case. Time required to achieve regression varied widely; mean time was 10 months (range, 1–20 months).[7-11] It is similar to the study by Silverman et al and Suarez-Cunqueiro et al.[2,3,8] We have found in our patient that focal areas of demineralization have regressed, revealing bone regeneration several months after removal of parathyroid adenoma. Patient age appears to be an important factor for predicting the period of time brown tumors require for regression. Daniel described that the length of time for bony regeneration varies from several months in young patients to several years in older patients.[7-9] As the patient reported here was young female in 4th decade, rapid improvement was noted postoperatively followed by regression and total resolution of tumor within span of one year. In case of large tumor, recontouring may be necessary after partial resoulution to improve appearance and function. This can be done by curettage or local excision. If lesion requires a long time period for regression even after normalization of serum calcium and intact parathyroid hormone, corticosteroids may be utilized to reduce tumor size.[4-7]

Conclusion: To conclude HPT is a metabolic bone disorder that might occur either due to hypertrophy/adenoma of the parathyroid gland, manifesting intraorally as a central giant cell granuloma. Timely diagnosis with treatment of the parathyroid lesion, results in complete regression of the intraoral lesion on its own and further progression to osteoporosis and pathological fractures can be prevented. Therefore if any case of CGCG involving the jaw bones is reported, it is mandatory to rule out hyperparathyroidism.

References:

1. Deepanshu Gulati, Vishal Bansal, PrajeshDubey, Sanjay Pandey, and AbhinavAgrawalCentral Giant Cell Granuloma of Posterior Maxilla: First Expression of Primary Hyperparathyroidism-Case

Report.Hindawi Publishing Corporation Case Reports in Endocrinology.Volume 2015
2. Nalini Aswath, Pravda Chidambaranathan. Pimary hyperparathyroidism as central giant cell granuloma of the jaws: Preand posttreatment pattern of clinical and radiographic presentation. IJCRI 201 2;3(8):51 –56.
3. Ruibin Huang, RuyaoZhuang, Yuan Liu, Tianti Li and Jiexiong Huang. Unusual presentation of primary hyperparathyroidism: report of three cases BMC Medical Imaging (2015) 15:23
4. MunaAlhusban, Zaid H. Baqain. Mandibular brown tumor as the first manifestation of primary hyperparathyroidism: A case reportThe Saudi Dental Journal (2011) 23, 107–109
5. Monica S. Eigelberger, W. KeatCheah, Philip H. G. Ituarte, Leanne Streja, Quan-Yang Duh and Orlo H. Clark. The NIH Criteria for Parathyroidectomy in Asymptomatic Primary Hyperparathyroidism. Are They Too Limited? Annals of Surgery • Volume 239, Number 4, April 2004
6. L.-O. Farnebo. Primary hyperparathyroidism. Update on Pathophysiology, clinical presentation and surgical treatment. Scandinavian Journal of Surgery 93: 282–287, 2004
7. Jaime Alonso Rese´ndiz-Colosia, Sergio Arturo Rodrı´guez-Cuevas, Rutilio Flores-Dı´az,Martı´nHerna´ndez-San Juan, Jose´ Francisco Gallegos-Herna´ndez,Sinhue´ Barroso-Bravo, Fernando Go´mez-Acosta,Evolution of maxillofacial brown tumors after parathyroidectomy in primary hyperparathyroidism, Maxillofacial Brown Tumors after Parathyroidectomy HEAD & NECK—DOI 10.1002/hed November 2008
8. Shanmugam K.T,Masthan K.M.K,AravindhaBabu N,Balachander N,Parthiban J,Sharma S.Hyperparathyroidism (Brown Tumor) -A Case ReportInt. Journal of Contemporary Dentistry AUGUST, 2011 • 2(4)
9. Roy Phitayakorn, Christopher R McHenryJaw Tumor: An Uncommon Presenting Manifestation of Primary Hyperparathyroidism World Journal of Endocrine Surgery, January-April 2010;2(1):45-50
10. K.Karunakaran, Kiran Kumar et al. Mandibular brown tumor in association with primary hyperparathyroidism. JIDAS Vol 1. Issue 2. April-June-2010
11. F.Selvi, S,Cakarer et al. brown tumoir of maxilla and mandible: a rare complication of tertiary hyperparathyroidism. Dentomaxillofacial Radiology 2009.

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