Primary Hyperparathyroidism Presenting As A Maxillary Mass - Brief Review And A Case Report Of Brown Tumor

Vipul Garg[1], Swati Roy[1], Abhiney Puri[2], Rakhi Gupta[3]

Abstract

Background: Primary hyperparathyroidism is usually identified as hypercalcemia and hypophosphatemia; however in a scenario especially in developing countries, the disease is often recognised in its overt phase. **Design:** Report of a 36 year old male patient who presented with a mid face and palatal swelling and was later diagnosed as a case of hyperparathyroidism after complete serological and histopathological examination. **Result:** Hyperparathyroidism should be considered in the list of differential diagnosis for mid face swelling. Routine blood examination coupled with histopathological report is considered to be the gold standard for arriving to a diagnosis of brown tumor.

Keywords: Primary Hyperparathyroidism; Biochemical Serum Examination; Histopathology

INTRODUCTION

Primary hyperparathyroidism (HPT) is characterized by hypersecretion of parathormone (PTH), which is caused by adenomas in 85% of all cases. Most cases of primary HPT are identified by hypercalcemia and hypophosphatemia on routine multipanel serum testing. Less than 5% of cases are recognized by the presence of brown tumors.[1] Routine biochemical screening has resulted in earlier diagnosis of primary hyperparathyroidism (PHPT) at an asymptomatic or minimally symptomatic stage. This has led to a changing pattern of clinical presentation of PHPT from an overt disease with predominantly skeletal manifestations of the 1970s to a more subtle disease of the 1990s. However, although this is true for the Western population, in the Indian subcontinent, with a vitamin D-deficient population, PHPT still has a predominant skeletal presentation.[1] Vitamin D deficiency may become more common because of widespread use of protective sunscreens that block UV light and, with it; PHPT may again become a more symptomatic disease. Therefore, the oral and maxillofacial surgeon must remain aware of these lesions and their association with PHPT.[2,3]

Brown tumors develop in bones, most commonly in jaws, presenting as well-demarcated, circumscribed, osteolytic lesions.

Corresponding Author : Dr. Vipul Garg, Department of Oral and Maxillofacial Surgery, Himachal institute of dental sciences, Paonta Sahib. **E-mail:** vips.saggy@gmail.com **(M)** +91-9882042753

1 Senior lecturer, Department of Oral and Maxillofacial Surgery, Himachal institute of dental sciences, Paonta Sahib.
2 Professor & HOD, Department of Oral and Maxillofacial Pathology, Himachal institute of dental sciences, Paonta Sahib.
3 Reader, Department of Oral and Maxillofacial Pathology, Himachal institute of dental sciences, Paonta Sahib.

Their histological picture is characterized by masses of soft tissue composed of giant cells in a fibrovascular stroma with cyst like spaces lined by connective tissue, foci of haemorrhage, all simulating changes that may be related to microfractures undergoing organization with the release of hemosiderin. These areas appear as a friable red-brown mass, hence the term brown tumors.[1,4]

While most authors agree that the initial treatment of PHPT is surgical excision of the diseased parathyroid gland thereby causing the bony lesions secondary to the disease to regress, others have combined parathyroidectomy with curettage and enucleation of the jaw lesions.[5,6,7]

The following report describes a case of PHPT with a brown tumor of the right maxilla. The case and the review highlights the importance of a thorough diagnostic work-up for all lesions in the maxillofacial region and also serves to add another facet to the myriad of presentations associated with primary hyperparathyroidism.

Case Report

A 36-year-old male patient of Asian Indian descent was referred to the department of oral and maxillofacial surgery, for evaluation of a painless swelling in right maxilla, occupying nearly the entire palate of right side. The initial clinical and radiological evaluation indicated an aggressive odontogenic neoplasm or a metastasis from an unknown primary; the suspicion of a systemic metabolic or endocrine disorder lay low on the list of differential diagnosis.

The patient gave history of gradually progressive swelling of the right palatal aspect of maxilla since last 2 years. The size had increased rapidly in the last 5–6 months. He denied any history of renal stone, neuropsychiatric symptoms or gastrointestinal symptoms. The patient also complained of gradual generalized weakness and weight loss along with difficulty in walking and performing routine domestic work.

Extra-oral examination revealed a 5 x 5cm hard, non-tender, non-pulsatile, maxillary swelling with non adherent normal overlying skin. The rest of the physical examination was unremarkable. Grossly the swelling involved the entire right maxilla extending from right infraorbital margin to lateral nasal wall and resulted in gross right sided facial asymmetry which exhibited crepitus in some places.

On palpation, the right submandibular region revealed enlarged, tender and mobile lymph nodes with a firm consistency. On intra oral examination a swelling of size 2 x 2 cm was noted on the right half of the hard palate (Fig 1). Few teeth were clinically seen in the mouth and nearly all of them were mobile (Miller's grade II/III).

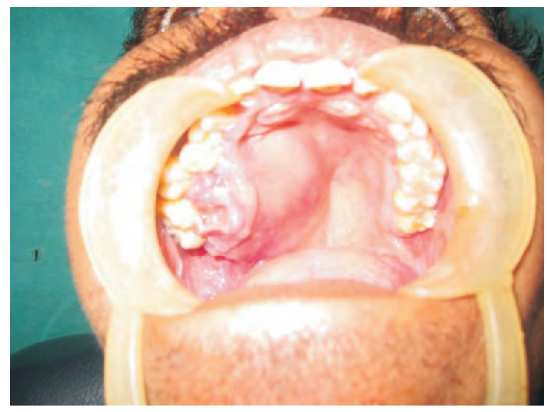

Figure 1: Intraoral: Lesional Mass Causing Swelling Of One Half Of The Palate

Radiographic examination showed radio-opacity of the left maxillary sinus. Computerized tomography (CT) of the maxilla revealed an ill-defined radiolucency extending from the right infraorbital rim till alveolar process including the lateral wall of

nose perforating the cortical plate buccally and palatally (Fig 2). Routine blood investigations showed anaemia with Hb of 9.9 gm/dL. Clotting studies were normal. Serum chemistry results were within normal range.

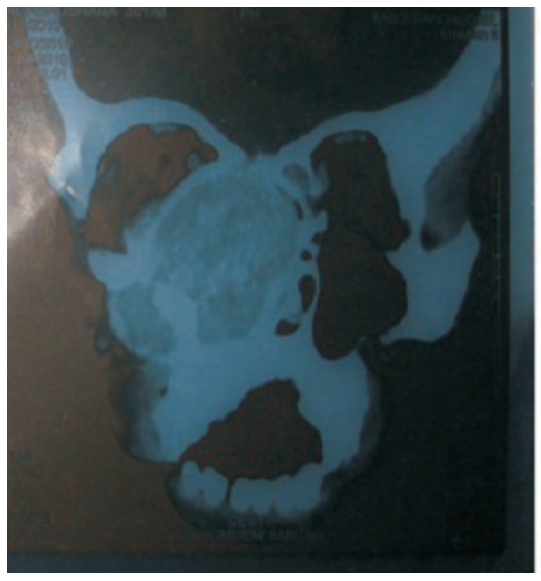

Figure 2: Computed Tomographic Image Showing The Extent Of The Lesion

Based on the age, gender, 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.

Incisional biopsy was performed under local anaesthesia. The histopathology report revealed a giant cell granuloma. Microscopically, the lesion was composed of multinucleated giant cells scattered in a loose fibrillar matrix with many ovoid or spindle-shaped mononuclear cells (Fig 3). These giant cells varied in both size and shape, contained multiple nuclei, and were unevenly distributed throughout the lesion (Fig 4). Areas of haemorrhage, newly formed osteoid, and bone tissue were also observed.

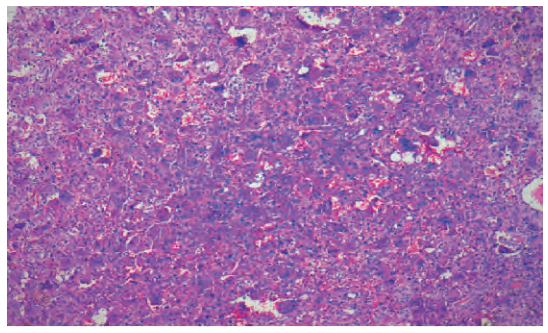

Figure 3: Hematoxylin And Eosin Image- 10x Magnification- Cluster Of Giant Cells And Extravasated Red Blood Cells And Delicate Fibrillar Stroma

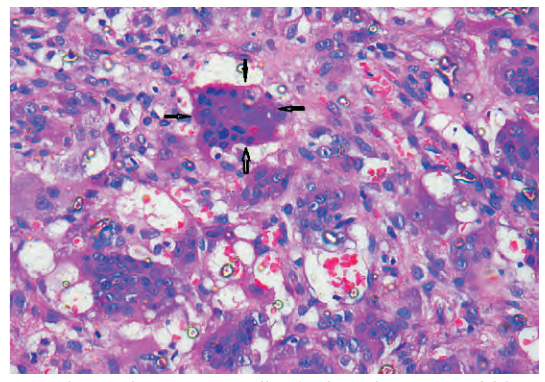

Figure 4: Hematoxylin And Eosin Image- 200x Magnification-multinucleated Giant Cell With Variable Number Of Nuclei

Subsequent blood analysis revealed an elevated parathyroid hormone level (314 pg/ml: normal, 12–72 pg/ml), while serum calcium levels were normal. This led to a possibility of brown tumor secondary to PHPT.

The neck ultrasound revealed a well-defined 2 x 2 cm hypoechoic mass posterior to the right lobe of the thyroid, which showed internal flow on Doppler suggestive of a parathyroid neoplasm.

Finally, ultrasound guided FNAC of the parathyroid was conducted. The parathryroid smears were moderately cellular, and the cells had round nuclei and scanty cytoplasm arranged singly in clusters, suggestive of a parathyroid adenoma.

Based on the above clinical, radiological,

biochemical and cytopathological findings, a final diagnosis of normocalcaemic primary hyperparathyroidism presenting as a massive maxillary brown tumour was made.

DISCUSSION

HPT is a disease of excess PTH secretion and can be sub classified into four types. Primary HPT is the unregulated overproduction of PTH caused by either a single adenoma in a parathyroid gland or diffuse hyperplasia of one or more glands. The overproduction of PTH can also be secondary to a chronic, abnormal stimulus for its production, such as low serum calcium associated with renal failure or vitamin D deficiency. Most patients who receive dialysis for renal failure have high level of HPT. The tertiary form is characterized by autonomous hypersecretion of PTH and develops after renal transplantation in patients with chronic, secondary HPT. The fourth type occurs due to ectopic parathyroid hormone produced by hormone secreting malignant tumors .[8,9]

Primary hyperparathyroidism is most commonly caused by adenoma (81%) followed by hyperplasia (15%), with carcinoma accounting for only 0.5%-4%.[5,10] It may also be inherited as an autosomal dominant condition in patients with hyperparathyroidism jaw tumor syndrome (HPT-JT syndrome) and multiple endocrine neoplasia syndrome (MEN syndrome).[5,11]

Most of the patients with primary hyperparathyroidism are above 60 years and women are affected two to four times more commonly. Patients with a classic triad of signs and symptoms of hyperparathyroidism are described as having “stones, bones and abdominal groans”. Stones refer to the fact that the patients have a marked tendency to develop renal stones (nephrolithiasis) because of elevated serum calcium levels. Metastatic calcifications are also seen. Bones refer to the variety of osseous changes that may occur in conjunction with hyperparathyroidism. Abdominal groans refers to the tendency for the development of duodenal ulcers.[12]

Brown tumors represent the terminal stage of HPT. This lesion is a well documented feature of this endocrinopathy. In the past, bone lesions were recognized in 80% to 90% of patients with primary or secondary HPT. In the last few years, these rates have declined to 10% to 15%. This is because of early diagnosis (new and more objective PTH radioimmunoassay techniques) and successful treatment of the disease. [1,13] The bones most commonly involved by brown tumor of HPT are the ribs, clavicles, pelvic girdle, and mandible. Maxillary involvement is quiet rare.[14-16] This makes this case unique.

Intraorally, brown tumors present as painful, hard, clearly visible, and palpable swelling.[1,14] Radiographically, they appear as well-demarcated monolocular or multilocular osteolytic lesions. In the mandible, the cortical bone is expanded and thinned. Brown tumors of the jaws occasionally result in root resorption and loss of the lamina dura and may present as a space-occupying mass in the sinus.[1]

Rosenburg and Guralnick reported that loss of the lamina dura was common radiographic feature in 40% of the patients in their study. Silverman et al found that in 55 patients, none showed complete loss of lamina dura and only 6% exhibited partial loss. Bras et al have suggested that radiographic changes of the jaws may be a late finding in HPT and their interpretations may be complicated by periodontal disease.[1] Other skeletal radiographic findings include subperiosteal

resorption of bone, typically of the medial aspect of the middle phalanges and erosion of distal digital tufts and margins of some joints .The skull radiograph characteristically shows a salt and pepper effect.[1,2]

Jaw lesions of HPT exhibit a picture that is similar to that of central giant cell tumors. A proliferation of spindle cells with extravasated blood and haphazardly arranged, variably sized, multinucleated giant cells is seen. These are osteoclasts, and the action of which is influenced by PTH. Osteoid formation may also occur. All types of PTH present similar histological findings. Histological features alone cannot establish a certain diagnosis, because of many giant cell lesions of the bone (giant cell granuloma, aneurysmal bone cyst, cherubism) show similar histological picture. A certain diagnosis is suggested by clinical history and confirmed by the endocrinologic status of the patient.[17]

At present, the most common method of diagnosis is the incidental detection of hypercalcemia in an asymptomatic patient.[5] This may be attributed to the inclusion of serum calcium levels to the routine blood investigations, which has resulted in early diagnosis and treatment. Increased levels of serum calcium and parathyroid hormones and reduced levels of serum phosphate as well as increased urinary levels of phosphates and calcium are sufficient to diagnose PHPT. Ultrasound, CT scan, or technetium scan techniques can be used to detect the diseased parathyroid gland.[5]

There is general consensus that the most logical approach to the treatment of primary hyperparathyroidism is parathyroidectomy. Opinions are divided on the course of management of the bony lesions once parathyroidectomy has been done. Most authors believe that the bone lesions regress with time after parathyroidectomy with rapid conversion of the bony lesions to normal bone.[1, 2, 5] But according to few authors, surgical intervention should be performed after parathyroidectomy for adenoma because spontaneous regression may take longer than 5 years. Knevezic et al in their study suggested that the patient's age was a relevant factor in the duration of the healing. This is supported by Silverman et al who reported a case of primary hyperparathyroidism in a 15-year-old patient which resolved in 6 months after parathyroidectomy. However, some lesions do not regress but extend beyond the normal anatomy and calcify, and interfere with function and/or esthetics.[5,] Therefore considering the varying school of thought, the final treatment decision lies in the hand of the surgeon.

In the present case the patient underwent parathyroidectomy and is under regular follow up and reports a decrease in the size of maxillary mass.

CONCLUSION

Brown tumors of the jaw may commonly involve the mandible and rarely involve the maxilla in association with primary hyperparathyroidism. The presence of underlying primary hyperparathyroidism should be sought in all unexplained mandibular and maxillary lesions. A majority of these lesions may disappear with the removal of the parathyroid pathology. This case report emphasizes the importance of recognizing the clinical presentation of this disease entity, a condition that is remediable by surgical and medical treatment.

REFERENCES

1. Triantafillidou K, Zouloumis L, Karakinaris G, Kalimeras E, Iordanidis F.

Brown tumors of the jaws associated with primary or secondary hyperparathyroidism. A clinical study and review of the literature. American Journal of Otolaryngology 2006;27:281–286.

2. Kar DK, Gupta SK, Agarwal A, Mishra S. Brown tumor of the palate and mandible in association with primary hyperparathyroidism. J Oral Maxillofac Surg 2001;59:1352-1354.
3. Harinarayan DV, Gupta N, Kochupillai N. Vitamin D status in primary hyperparathyroidism in India. Clin Endocrinol 1995;43:351-356.
4. Parisien M, Silverberg SJ, Shane E, Dempster DW, Bilezikian JP. Bone diseases in primary hyperparathyroidism. Endocrinol Metab Clin North Am 1990;19:18-34.
5. Spencer J, Daniels M. Primary hyperparathyroidism presenting as a palatal brown tumor. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;98:409-13.
6. Smith AC, Bradley JC. Non-surgical management of hyperparathyroidism of the jaws. J Oral Maxillofac Surg 1987;45:176-81.
7. Yamazaki H, Ota Y, Aoki T, Karakida K. Brown tumor of the maxilla and mandible: Progressive mandibular brown tumor after removal of parathyroid adenoma. J Oral Maxillofac Surg 2003;61:719-22.
8. Allerheiligen DA, Schoeber J, Houston RE, et al: Hyperparathyroidism. Am Fam Physician 1998; 57:1795.
9. Choi C, Terzian E, Schneider R, Trochesset DA. Peripheral giant cell granuloma associated with hyperparathyroidism secondary to end-stage renal disease: A Case Report. J Oral Maxillofac Surg 2008;66:1063-1066.
10. Masson EA, Macfarlane IA, Bodmer CW, Vaughan ED. Parathyroid carcinoma presenting with a brown tumour of mandible in a young man. Br J Oral Maxillofac Surg 1993;31:117-19.
11. Hobbs MR, Pole AR, Pidwirny GN, Rosen IB, Zarbo RJ, Coon H, Heath H, Leppert M, Jackson CE. Hyperparathyroidism jaw tumor syndrome: the HRPT2 locus is within 0.7-cM region on chromosome 1q. Am J Human Genet 1999;64:518-25.
12. Neville BW, Damm DD, Allen CM, Bouquot JE. Oral and maxillofacial pathology. Second edition; 451,724.
13. Auclair PL, Arendt DM, Hellstein JW, et al. Giant cell lesions of the jaws In Oral and Maxillofacial Surgery. Clinics of North America 1997;9:655-80.
14. Guney E, Yigibasi OG, Bayram F, Ozer V, Canoz O. Brown tumor of the maxilla associated with primary hyperparathyroidism. Auris Nasus Larynx 2001;28:369-72.
15. Merz MN, Massich DP, Marsh W, et al. Hyperparathyroidism presenting as brown tumor of the maxilla. Am J Otolaryngol 2002;23:173-76.
16. Martinez-Gavidia EM, Began JV, Milian-Masanet MA, et al. Highly aggressive brown tumor of the maxilla as first manifestation of primary hyperparathyroidism. Int J Oral Maxillofac Surg 2000;29:447-49.
17. Cicconeti A, Matteini C, Piro FR. Differential diagnosis in a case of brown tumor caused by primary hyperparathyroidism. Minerva Stomatol 1999;11:553-58.