A rare case of hyperparathyroidism presenting as brown tumor of the maxilla

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INTRODUCTION

Brown tumors also known as central giant cell granuloma (CGCG) might be mistaken as a tumor but it is not a neoplasia, rather it’s a reparative cellular process. Jaffe, in the year of 1953, described it as a benign intraosseous lesion composed of cellular fibrous tissue with multiple foci of hemorrhage and aggregations of multinucleated giant cells with occasional trabeculae of woven bone.[1] The condition can affect any part of skeleton, involvement of ribs, clavicle, and pelvis being most common. Among facial skeleton, mandible is seen to be affected in 4.5% of patients and maxilla usually is less likely to be affected.[2]

The condition may represent a very late stage of primary or secondary hyperparathyroidism with 4.5% of patients presenting with primary hyperparathyroidism and the same to affect with secondary disease in 1.5–1.7% of patients but 0.1% is the overall reported prevalence of brown tumor.[2] The condition can be a component of number of metabolic bone diseases such as osteitis fibrosa, cystica generalisata, or Recklinghausen’s disease of bone.[3] The proposed pathogenesis for the condition is a persistent increase in the level of parathyroid hormone for a longer period of time results in the initiation of both the

Case Report

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INTRODUCTION

Brown tumor is an intraosseous benign lesion consisting of cellular fibrous tissue with multiple foci of hemorrhage and aggregations of multinucleated giant cells with occasional trabeculae of woven bone and can affect any bone of body. Among facial skeleton, it is rare to find maxilla being affected by it and the condition may represent a late stage of primary or secondary hyperparathyroidism. The name brown tumor is due to the typical brown color of hemorrhage and hemosiderin present in the lesion on histopathology. Case Report: A 22-year-old female presented with a gradually progressive swelling on the left side of face. The swelling was bony hard swelling in consistency with CT scan showing multiloculated lucent lesion measuring 6.8 × 4.8 × 4.4 cm with enhancing soft-tissue component involving the left maxillary and ethmoid sinus. The histopathology report was suggestive of brown tumor like feature. Biochemical analysis showed increased value of serum alkaline phosphatase and parathyroid hormone. Discussion: The proposed pathogenesis for this condition is persistent increase level of PTH causes an imbalance in osteoclastic and osteoblastic homeostasis as well as calcium-phosphorus regulation and resulting in rare presentation of central giant cell granuloma and this presents as a bony swelling. Conclusion: In patients presenting with bony swelling of facial bones, metabolic disorder of calcium should always be considered in the differential diagnosis and a detailed evaluation for its causation should be made.

KEY WORDS: Alkaline phosphatase, brown tumor, hyperparathyroidism, osteoblast, osteoclast, serum calcium

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fibrous and osteoclastic reactions in the skeleton system, thereby causing an imbalance in the activities of osteoclastic along with osteoblastic cells, thereby resulting in replacement of osseous component with fibrous tissue in the marrow along with thinning of the cortex. They usually manifest as focal lesions in the areas of bone resorption.

The name brown tumor is due to the typical brown color of hemorrhage and hemosiderin present in the lesion. Histologically, the tissue consists of spindle cell connective tissue stroma consisting of multinucleated giant osteoclastic cells along with hemorrhage and hemosiderin laden macrophages. The condition also shows features of invasiveness in some instances but as it does not carry any malignant potential so it is differentiated from true giant cell tumors of bone which is important.

The condition resulting from hyperparathyroidism results in alteration of biochemical profile related to calcium metabolism. The condition may result increase or decrease of serum calcium level, this depends on the calcium reserve as well as the duration of the condition. Increase in level of serum parathyroid hormone is seen, thereby stimulating the bone metabolism resulting in increase in the level of serum alkaline phosphatase and lower level of phosphorus with or without deficiency of Vitamin D.

There are certain radiological changes seen in hyperparathyroidism as a result of increase in osteoclastic and osteoblastic cells, some of the changes seen on X-ray are multiple osteolytic lesions with mottled appearance in the calvarium region and it presents as salt and pepper pattern in X-ray skull, whereas telescoping of phalanges seen in X-ray wrist.

Patients with brown tumor have set of proven clinical manifestations along with certain radiological findings and changes in biochemical analysis. A combination of all these findings helps in coming out with the diagnosis of brown tumor as similar lesion can also be a presentation in cases of reparative granuloma which needs to be ruled out with the absence of elevated level of parathyroid hormone.

Although the disease has been reported in many age groups, mostly it is seen in patients with age >50 years with a female preponderance.

The present case report describes a rare case of brown tumor of maxilla, an uncommon location in a young female.

**CASE REPORT**

A 22-year-old female presented with a gradually progressive swelling on the left side of her face for the past 4 months. There is neither history of trauma nor any history of surgery. There is neither any history of bleeding from nose nor any history of double vision. There was no history of repeated fractures, pain abdomen, increased thirst, and urine frequency. There is no numbness in infraorbital region.

On examination, a single swelling was present on left side of the face over the malar region, it was bony hard, non-tender and non-mobile. Skin over the swelling was freely mobile. It measured 6 × 8 cm in size with poorly defined margins. It extended from the left infraorbital margin superiorly and extending and abutting the alveolar process of maxilla inferiorly, medial extent starts 2 cm away from the ala of the nose, and laterally up to the level of tragus of the ear. There was mild proptosis of the left eye. There were no visible dilated veins nor any visible pulsation seen or heard. Rest of the head-and-neck examination including cervical lymph node did not reveal any positive findings. Nasal examination showed a bulge of bony consistency in the lateral wall of nose [Figure 1].

She underwent radiographic examination in the form of contrast-enhanced computed tomography with 3 mm serial axial sections of the face and it showed a multiloculated lucent lesion measuring 6.8 × 4.8 × 4.4 cm with enhancing soft-tissue component involving the left maxillary, ethmoid sinus [Figure 2a], and left lateral pterygoid plate [Figure 2b] having sclerotic margins with significant bony expansion with epicenter in the left maxillary sinus. No obvious cortical breach was seen in the bone. Maxillary antrum reduced in volume considerably.

Her urine routine and microscopic examination was found to be normal and ultrasound of whole abdomen did not find any calculus in urinary tract and high-resolution ultrasonography of neck did not find any parathyroid lesion. Kidney function test was also normal. Complete blood count as well as platelet count and bleeding time and clotting time (CT) did not show any abnormal value.

![Figure 1: Picture of the patient showing pre-post-operative photograph. (Note the decrease in size of maxillary swelling and improvement in proptosis)](image)

![Figure 2: (a) CT scan showing multiloculated lesion involving the left ethmoid and maxillary sinus. (b) CT scan showing lesion extending to the left pterygoid plates)](image)
Exploration of the swelling was planned with the aim of providing a cosmetically acceptable face. The surgical approach was through sublabial route by doing Caldwell-Luc procedure. On exposing the maxillary sinus, blackish-brown pieces of friable bone were found which was gradually chiseled out and till mid of procedure appreciable bleeding was encountered, whole of the maxillary wall was involved with lesion.

On gross appearance, the mass came out in piece meals and was foul smelling, reddish-brown in color, soft and friable in consistency, and on an aggregate, it measured $3.5 \times 2.0 \times 2.0$ cm. Normal mucosa of maxillary antrum was evident but volume was considerably decreased due to bony lesion. The wound was closed with 3–0 Vicryl suture in the gingivobuccal sulcus and packing was left in the antrum exiting through the intranasal antrostomy and also pressure pack was applied over the left malar region, cold fomentation was started from the 1st post-operative day. The packing was removed on the 2nd post-operative day, on pack removal foul smelling secretion started coming and the patient was stated on nasal wash but complaint of foul smell persisted for many days. A cosmetically acceptable appearance was gained at post-operative day 14 with improvement in proptosis [Figure 1].

The histopathology report was suggestive of brown tumor-like feature with the following.

Microscopic description, multiple sections examined, showed proliferative fibroblastic tissue with admixed numerous osteoclasts such as giant cells and stromal cells. There were interstitial hemorrhage, focal hemosiderin deposition, and fibroblastic tissue appeared vascularized. The provisional diagnosis of giant cell lesion along with brown tumor as one of the manifestations of hyperparathyroidism among the possible causes was made [Figure 3].

Biochemical analysis showed increased value of serum alkaline phosphatase and parathyroid hormone. There was low value of serum phosphorus but a normal value of serum calcium and Vitamin D$_3$ [Table 1].

The patient was given oral calcium in a dose of 500 mg twice a day and Vitamin D supplement and patients did not show any recurrence of swelling and her blood parameters gradually improved.

**DISCUSSION**

Brown tumors are condition sometimes seen in cases with persistent hyperparathyroidism and are mostly of two types, primary and secondary form, and sometimes also a third form called tertiary hyperparathyroidism. The primary form occurs mostly due to the formation of parathyroid adenoma of varying size and results in continuous autonomous secretion of parathyroid hormone and is usually seen in postmenopausal women. Secondary hyperparathyroidism is usually diagnosed when there is hyperplasia with an increased PTH to compensate for prolonged hypocalcemia. In some patients with secondary hyperparathyroidism, continuous parathyroid stimulation may cause adenoma formation and autonomous PTH secretion and the condition is known as tertiary hyperparathyroidism.

In the present case, raised level of parathyroid hormone secondary to hypocalcemia is the probable cause of the development of bony lesion known as brown tumor. The proposed pathogenesis for this condition is a persistent increase in the level of PTH which causes an imbalance in the osteoclastic and osteoblastic homeostasis along with calcium-phosphorus regulation and resulting in rare presentation of CGCG and this presents as a bony swelling.

Classical skeleton changes are manifested in primary hyperparathyroidism when they are combined with deficiency of Vitamin D and this scenario usually takes time to develop and it do not occur commonly. Brown tumor is not a tumor, but is just a reaction of the bone to above-mentioned conditions. Therefore, surgical resection may not be the primary modality of treatment but is necessary as a biopsy to exclude malignancy and other bone diseases.

The condition needs to be distinguished from other pathology of bone-like giant cell tumor of bone. It can be differentiated by microscopically visualizing the features of invasiveness in certain regions though brown tumor does not carry any malignant potential. Biochemical analysis is a must before coming to a diagnosis of brown tumor. As a result of hyperparathyroidism, there is usually elevation of serum alkaline phosphatase, a biochemical marker of increase bone formation along with parathyroid hormone, serum calcium is found elevated with decrease in the level of serum phosphorus but sometimes, serum levels of calcium may be found normal, the reason for this may be attributed to the deficiency of Vitamin D.
Hence, histopathological examination is not enough for the diagnosis of brown tumor, it needs to be supported with biochemical findings to differentiate between giant cell tumor of the bone and brown tumor of hyperparathyroidism. Histological examination shows a dense fibroblastic stroma with areas of cystic degeneration and hemorrhage, macrophages studded with hemosiderin along with multinucleated giant cells, and similar changes are also seen in other bony pathologies such as fibrous dysplasia, true giant cell tumors, and reparative granulomas and here lie the significance of biochemical analysis.

In reative granuloma, level of parathyroid hormone is not raised. Patients with fibrous dysplasia usually have history of multiple bone fractures in different parts of body with classical radiological finding and can be mono or polyostotic form, parathyroid hormone is generally normal in these cases unless it is also associated with hyperparathyroidism.

A provisional diagnosis of brown tumor is based on classical bony swelling with normal to high blood calcium level along with increase in the level of parathyroid hormone, whereas a definitive diagnosis of browns tumor can only be made on comparing and correlating the clinical, histological, and biochemical analysis.

Among facial bones, mandible is the most common site and accounts for 4% of all cases with hyperparathyroidism, whereas maxillary involvement is extremely rare and few cases are reported in literature. In our case, clinical examination leads us to only suspect some bony tumor, later diagnosis of browns tumor secondary to hyperparathyroidism was confirmed by microscopic findings along with deranged biochemical value except serum calcium which was found normal and the reason for it can be deficiency of Vitamin D, which is a common feature in females from rural area. The problem which was faced in the diagnosis was the rare involvement of maxilla by this pathology.

Proimos et al. also encountered a case with similar presentation and approached. They reported a case of 42-year-old woman who presented with pain and swelling of face with round, radiolucent bony lesion with osteolytic feature in the anterior wall of maxillary sinus of the right side along with extension to floor of orbit, anterior ethmoids, and nasal cavity. They approached the case in similar manner by Caldwell-Luc procedure and then proceeded in the line of brown tumor once it was reported as one of the differential diagnoses on histopathology.

Sia et al. reported a case of maxillary brown tumor in 2012 where the patient presented was an associated case of primary hyperparathyroidism having parathyroid adenoma along with bilateral medullary nephrocalcinosis and maxillary swelling and the case undergone excision of the involved parathyroid adenoma.

Soundarya et al. reported a 60-year male with swelling in the right index finger and left infraorbital and zygomatic region with pain over jaw and they performed excision of the lesion and established the diagnosis based on clinical and laboratory data showing features of hyperparathyroidism along with characteristic histopathological findings.

**CONCLUSION**

In patients presenting with bony swelling of facial bones, metabolic disorder of calcium should always be considered in the differential diagnosis and a detailed evaluation for its causation should be made. In developing nation, vitamin deficiencies are prevalent in every age group. Hence, a complete profile of tests involved in calcium metabolism must be done in patients presenting with bony lesion and histological along with radiological examination helps in coming to a diagnosis. Sometimes, in clinical practice, certain challenges are encountered like rare disease with rare site and rare presentation. Hence, a systematic approach is essential toward diagnosis of any bony lesion.

**REFERENCES**