Brown tumors are rare focal giant-cell lesions that arise as a direct result of the effect of parathyroid hormone (PTH) on bone tissue in some patients with hyperparathyroidism. Browns tumor is a syndrome associated with an increase in PTH levels by parathyroid glands resulting in hypercalcemia. In the present case report, a 44-year-old female patient presented with a rare case of brown tumor with multiple lesions in the head-and-neck region. The recent advance in various diagnostic and biochemical tests helps in early diagnosis of hyperparathyroidism cases. The dentist should be aware of oral manifestations associated with this type of systemic disease.

**Keywords:** Central giant cell lesion, osteitis fibrosa cystica, osteoclastoma

**INTRODUCTION**

Browns tumor is a syndrome associated with an increase in parathyroid hormone (PTH) levels by parathyroid glands resulting in hypercalcemia. Parathyroid glands monitor the serum calcium concentration. In the nonpathologic state, PTH secretion increases in response to low serum calcium concentrations, thereby enhancing calcium reabsorption and osteoclastic bone resorption. When parathyroid glands become abnormal, there is abnormal increase in PTH secretion result in increased reabsorption of calcium and increased bone resorption.

In the present case report, a 44-year-old female from Visakhapatnam reported to the outpatient department with a chief complaint of swelling in the lower left back tooth region for 5 months. On past dental history, the patient gives the history of enucleation and extraction in relation to 35. It was diagnosed as dentigerous cyst on histopathological examination.

On extraoral examination, swelling was observed on lower one-third of the face on the left side which extending from the left corner of the mouth to tragus anteroposteriorly were as superoinferiorly from alatragal line to 0.5 cm below the lower border of the mandible. Advised radiological investigations. On cone-beam computed tomography (CBCT), shocking multiple hypodense areas with aggressive bone resorption were observed and on blood investigations observed elevated serum parathormone levels: 890 ng/mL.

**CASE REPORT**

A 44-year-old female reported outpatient clinic of GITAM Dental College and Hospital with a chief complaint of swelling in the lower left back tooth region for 5 months. On past dental history, the patient gives the history of enucleation and extraction in relation to 35. It was diagnosed as dentigerous cyst on histopathological examination.

On extraoral examination Swelling was observed on lower one-third of the face on the left side which extending from the left corner of the mouth to tragus anteroposteriorly were as superoinferiorly from alatragal line to 0.5 cm below the lower border of the mandible.
mandible. On intraoral examination, ill-defined swelling with obliteration of buccal vestibule was observed in relation to 34, 36 teeth.

Based on clinical features, a provisionally diagnosed as odontogenic cyst was given. On aspiration, blood-tinged fluid was aspirated.

**Radiological investigations**

On panoramic radiography, a well-defined radiolucent lesion was observed in relation to 46, 47 and right parasymphyseal region and left posterior mandible and on ascending ramus region [Figure 1]. On the occlusal radiograph, bicortical plate expansion on the left side. CBCT revealed an ill-defined bone with hypodense areas involving alveolus of 17 (right maxilla), right body of mandible, left ramus of mandible and right frontal sinus noted. Bilateral temporomandibular joints (TMJs) showed mild degenerative changes [Figure 2]. On hand and wrist radiograph, subperiosteal bone resorption and metastatic calcium deposition were observed. Posteroanterior skull view: multiple punched out radiolucent areas were observed. Based on the above radiological features, the lesion was diagnosed as multiple osteolytic lesions (multiple myeloma, osteodystrophic lesion, Noonan-like multiple giant cell lesion syndrome, hyperparathyroidism).

The blood reports as shown were serum alkaline phosphatase: 358 U/L, serum calcium: 14.0 mg/dl and serum parathormone levels: 890 ng/ml.

**On histopathological examination**

The hematoxylin and eosin-stained soft tissue section exhibited loosely arranged stroma with small capillaries and proliferating fibroblasts. The collagen fiber bundles were arranged in whorl pattern. There were abundant multinucleated giant cells present throughout the tissue. These giant cells consisted of 10–15 nuclei and many of them being prominent, thus showing features of active division. These giant cells were distributed near areas of hemorrhage, extravagated blood [Figures 3-5]. Based on the radiographical, histopathological features and blood investigations, it was diagnosed as brown tumor.

**DISCUSSION**

The parathyroid glands are situated in the thyroid gland, which is not regulated by the pituitary gland, but directly under the control of serum ionized calcium concentrations.[1,2] Hyperparathyroidism occurs in three significant forms as primary, secondary and tertiary [Table 1].[3]

The classic symptoms of the disease are bones, stones, abdominal groans and psychic moans.[4] In developed nations, it is seen in elderly females with mild to moderate hypercalcemia and very few with classic symptoms.[5]

**Normal parathyroid**

Physiology parathyroid glands constantly monitor serum calcium concentration.[6] This involves a complex calcium-ion sensing receptor mechanism in the parathyroid cells that respond to changes in serum calcium concentration. This mechanism occurs in all normal parathyroid glands to maintain the normal serum calcium levels, i.e., 2.1 and 2.65 mmol/L, which is essential for normal bone metabolism, muscle and nerve physiology.[7,8]

The name “brown tumor” is a misnomer derived from the color, which is caused by the vascularity, hemorrhage and deposits of pigment hemosiderin.[9] It is a nonneoplastic giant cell lesion which is slowing growing and locally destructive. Its vascularity, hemorrhage and hemosiderin impart the characteristic brown color. The PTH has a direct effect on bone.[10-14]
Genetic causes of primary hyperparathyroidism

Germline mutations

Loss of heterozygosity

In the tumor suppressor genes

In MEN1, (menin) and CDC73 (formerly HRPT2)

Combined with a second mutation

Increase the predisposition to parathyroid tumors.[15-17]

The MEN1 gene is located in 11q14 and consists of 10 exons that encode 610 amino acid proteins referred to as menin. This protein is present in on dividing cells.

Differentiating between a brown tumor and other giant cell tumors may be very difficult, even with histology [Table 2].

Cases of giant cells associated with neurofibromatosis (type 1),[18] Noonan-like syndrome or both have been reported. Histologically giant cell lesions are exhibiting rich osteoclast fields which could not be easily distinguished from cherubim and Noonan syndrome.[19]

A reparative granuloma is different from the brown tumor by the absence of hyperparathyroidism. In histological section shows giant cells in the less dense stroma but more vascularized.[20] Patients with giant-cell tumors associated with hyperparathyroidism and hypercalcemia to differentiate this granuloma from brown tumors.

CONCLUSION

Brown tumor most commonly affects mandible rarely maxilla, but in our case, multiple lesions in skull, mandible, maxilla, TMJ. The recent advance in various diagnostic and biochemical tests helps in early diagnosis of hyperparathyroidism cases. The dentist should be aware of oral manifestations associated with this type of systemic disease.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal.
Weakness occurs in 20‑40 years old caused due to chronic secondary hyperparathyroidism. Phosphate levels increased fractures. Muscle aching. 

Renal failure. Giant cells are large, round with many nuclei. Symptoms: Osteoporosis, Excessive urination, Abdominal pain, Weakness, Depression, Bone and joint pain. Calcium levels normal, Associated with renal failure or PTH levels increased. 

Symptoms: Long bones skull commonly affected. Histopathological features: Giant cells are uniformly dispersed, Less hemosiderin deposition. Calcium levels increased, Kidney stones, Renal failure, Fractures. PTH: Parathyroid hormone. 

Table 1: Classification of hyperparathyroidism

| Primary hyperparathyroidism | Secondary hyperparathyroidism | Tertiary hyperparathyroidism |
|----------------------------|-------------------------------|-------------------------------|
| PTH levels increased       | Calcium levels normal         | Calcium levels increased      |
| Calcium levels increased  | PTH levels increased          | PTH levels more increased     |
| Phosphate levels decreased | Phosphate levels normal       | Phosphate levels increased    |
| Caused due to MEN1 and MEN2a | Caused by hyperphosphatemia  | Caused due to chronic secondary hyperparathyroidism |
| Symptoms                   | Muscle aching                 | Symptoms                      |
| Osteoporosis               | Weakness                      | Muscle aching                 |
| Excessive urination        | Fractures                     | Kidney stones                 |
| Abdominal pain             | Bone deformities              | Renal failure                 |
| Weakness                   |                               | Fractures                     |
| Depression                 |                               |                               |
| Bone and joint pain        |                               |                               |

The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Arunkumar KV, Kumar S, Deepa D. Brown tumor in mandible as a first sign of vitamin D deficiency: A rare case report and review. Indian J Endocrinol Metab 2012;16:310‑5.

2. Mackenzie‑Feder J, Sirrs S, Anderson D, Sharif J, Khan A. Primary hyperparathyroidism: An overview. Int J Endocrinol 2011;2011:251410.

3. Indumati Rao K, Priya N, Rao K, Ashwin D. Brown tumor of the mandible: A rare complication of tertiary hyperparathyroidism. Dentomaxillofac Radiol 2009;38:53‑8.

4. Rai S, Rattan V, Bhadada SK. Giant cell lesions associated with primary hyperparathyroidism. J Maxillofac Oral Surg 2015;14:930‑4.

5. Maskey R, Panchani R, Varma T, Goyal A. Primary hyperparathyroidism in India: A cocktail of contemporary and classical presentations: Lesson from 47 cases. Indian J Endocrinol Metab 2013;17:S209‑11.

6. Rosenberg EH, Guralnick WC. Hyperparathyroidism, a review of 220 proved cases with special emphasis on findings in the jaws. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;99:464‑70.

7. Haslett C, Chilvers ER, Hunter JA, Boon NA. Davidson’s Principles and Practice of Medicine. 18th ed. USA: Churchill Livingstone; 2000. p. 375‑9.

8. De Lange J, Van den Akker HP. Clinical and radiological features of giant central-cell lesions of the jaw. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;99:464‑70.

9. Teh BT, Kyrtoli S, Farnebo F, Bergman I, Wong FK, Weber G, et al. Mutation analysis of the MEN1 gene in multiple endocrine neoplasia type I, familial acromegaly and familial isolated hyperparathyroidism. J Clin Endocrinol Metab 1998;83:2621‑6.

10. Carpten JD, Robbins CM, Villablanc A, Forsberg I, Presciutti S, Bailey‑Wilson J, et al. HRPT2, encoding parafibromin, is mutated in hyperparathyroidism‑jaw tumor syndrome. Nat Genet 2002;32:676‑80.

11. Thakker RV. Multiple endocrine neoplasia—Syndromes of the twentieth century. J Clin Endocrinol Metab 1998;83:2617‑20.

12. Shattuck TM, Välimäki S, Obara T, Gaz RD, Clark OH, Shoback D, et al. Somatic and germ‑line mutations of the HRPT2 gene in sporadic parathyroid carcinoma. N Engl J Med 2003;349:1722‑9.

13. Howell VM, Haven CJ, Kahnoski K, Khoo SK, Petillo D, Chen J, et al. HRPT2 mutations are associated with malignancy in sporadic parathyroid tumours. J Med Genet 2003;40:657‑63.

14. Ruggieri M, Pavone V, Polizzi A, Albanese S, Magro G, Merino M, et al. Unusual form of recurrent giant cell granuloma of the mandible and lower extremities in a patient with neurofibromatosis type I. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106:422‑8.
19. Idowu BD, Thomas G, Frow R, Diss TC, Flanagan AM. Mutations in SH3BP2, the cherubism gene, were not detected in central or peripheral giant cell tumours of the jaw. Br J Oral Maxillofac Surg 2008;46:229-30.

20. Fernandez-Bustillo AJ, Martino-Gorvea R, Murillo-Cortes J, Garatea-Crelgo J, Palomero-Rodriguez R. Primary hyperparathyroidism. Presenting as brown tumors in the maxilla. Med Oral 2000;5:208-1.