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Surgical management of hyperparathyroid jaw tumour syndrome: A case report

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Abstract

Parathyroid hormone plays an important role in calcium regulation, it causes resorption in bones, increased calcium absorption from Gastrointestinal tract, calcium tubular reabsorption in kidneys and aids in synthesis of 1,25 dihydroxy Vitamin D. The extra cellular calcium level serves as a negative feedback mechanism to control the parathyroid hormone level. Hyperparathyroidism is an endocrine disorder in which there is increased secretion of parathyroid hormone. It occurs commonly in female and clinically manifests as poor muscle tone, excitability, back pain and gastric irritation. In long bones hyperparathyroidism causes osteolytic lesion Osteitis Fibrosa Cystica otherwise called as brown's tumour. Brown's tumour usually affects the femur, mandible and maxilla. Hyperparathyroidism usually manifests as Osteitis Fibrosa Cystica (brown's tumour) in jaws but can also associated with hereditary hyperparathyroidism syndromes like hyperparathyroid jaw tumour syndrome. Here we report a case of Hyperparathyroid jaw tumour syndrome and its management with relevant review of literature.

Keywords: Hyperparathyroidism, Cemento ossifying fibroma, alkaline phosphatase, curettage, iliac bone graft

Introduction

Case Report

A 22year old female reported to the department of Oral and Maxillofacial surgery with the complaints of swelling in the right lower back tooth region of jaw for the past one year. The swelling was of gradual onset, slow growing and asymptomatic. Patient had a history of similar bony swelling in the left side of the jaw for which she underwent surgical excision under local anesthesia 8 years back and patient was unaware of the other specifications of the surgery and thus it was considered to be a benign fibroosseous lesion. Patient had no history of similar swelling in the family.

On examination patient had facial asymmetry with swelling of 2x2 cms in size with well-defined margins and normal skin surface. [Figure 1] Mouth opening was 40mm interincisal and Temporomandibular Joint was normal without any deviation, clicking and tenderness in occlusion, rest and movement. On palpation the bony hard swelling was tender and showed no pulsations. Intra orally the swelling in the right side of mandible extended from the distal region of 44 to the mesial region of 46 [Figure 2] which showed negative aspiration. The IOPA showed mixed radiolucency with radioopaque spicules dispersed along with resorption of distal root of 36 and mesial root of 37. The orthopantomogram showed multilocular radiolucency with radioopaque spicules extending from 45 to 48 region [Figure 3]. The computerised tomography of the lesion showed an expansile multilocular lesion with bicortical expansion from 45 to 46 region [Figure 4]. Our differential diagnosis list included the following fibroosseous lesion cemento ossifying fibroma, florid cement osseous dysplasia, fibrous dysplasia, piagets disease, brown's tumour, and hyperparathyroid jaw tumour syndrome.

The patient had increased serum calcium-14.2mg/dl, decreased serum phosphorus-2mg/dl, increased alkaline phosphatase to 369IU/L and increased serum parathyroid hormone level-135pg/ml. The Fine needle aspiration cytology showed spindle cells and few multinucleated giant cells. And incisional biopsy revealed bony trabeculae in rich fibroblastic stroma with cementoid and osteoid substances with few giant cells.

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Ultrasound of neck showed hypoechoic mass on left posterior thyroid gland suggestive of parathyroid adenoma. From the biochemical investigations and ultrasonogram of the neck the swelling was suspected to be a fibroosseous lesion probably Osteitis fibrosa cystica (brown's tumour) occurring in hyperparathyroid patient.



Fig 1: swelling in the lower right side of the face



Fig 2: obliteration of buccal vestibule



Fig 3: Orthopantomogram showing multilocular radiolucency

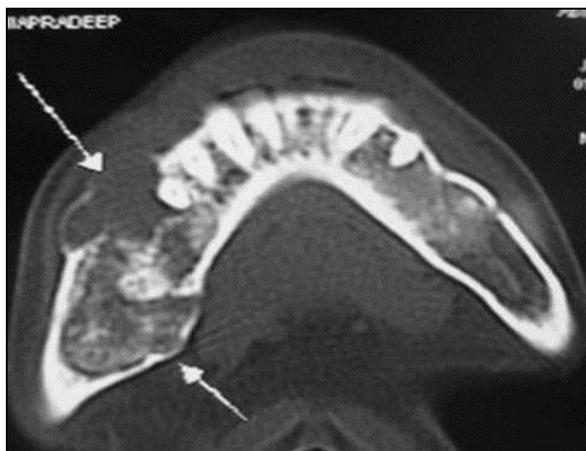


Fig 4: Axial Computerised tomography showing buccal perforation



Fig 5: Post parathyroidectomy swelling increased in size



Fig 6: post parathyroidectomy axial Computerised Tomogram showing buccal and lingual perforation

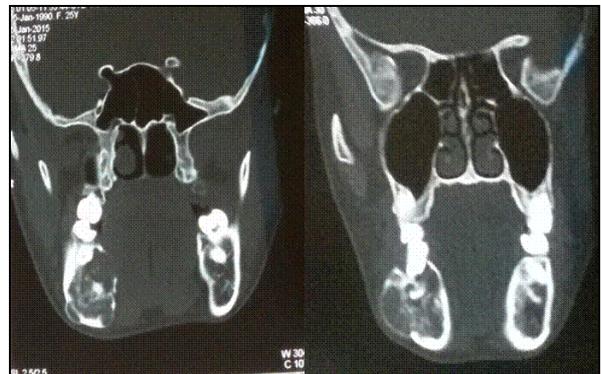


Fig 7: Post parathyroidectomy coronal computerised tomogram



Fig 8: tumour encompassing inferior alveolar nerve

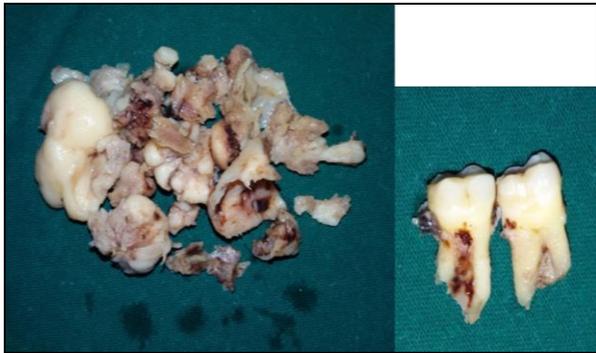


Fig 9: enucleated specimen along with extracted 46, 47.



Fig 13: post-operative showing no facial asymmetry



Fig 10: Post enucleation defect



Fig 14: one year post-operative orthopantomogram showing good bone fill



Fig 11: iliac corticocancellous graft



Fig 12: iliac graft fixed into the defect

The patient was referred to a general surgery centre for the left inferior parathyroidectomy. After parathyroidectomy, a year later presented with the swelling which increased in size of 4x5 cm extending from the mesial aspect of 44 to distal aspect of 47 [Figure 5]. The CT showed mixed radio lucent lesion extending from the mesial aspect of 44 with involvement the infra alveolar nerve to the ascending ramus with the dimensions of 6.5 x 4cms [Figure 6, 7]. Re incisional biopsy was done in relation to 44 region showed bony trabeculae dispersed in rich fibroblastic stroma with cementoid and osteoid substances suggesting of cement-ossifying fibroma. Thus on correlating the history of hyperparathyroidism with the histopathological diagnosis of Cemento Ossifying Fibroma the diagnosis of Hyperparathyroid Jaw tumour Syndrome was made and the treatment plan of conservative surgical excision along with curettage with iliac corticocancellous block reconstruction of the defect under general anaesthesia was proposed.

Under General anaesthesia, with the crevicular incision from 48 to 43 and anterior release incision extending till mucobuccal fold of 32, the tumour was exposed [Figure 8]. Sacrificing the inferior alveolar nerve the tumour was excised anteriorly in toto and posteriorly the extensions into the ascending ramus were curetted. As inferior border was not involved it was retained after enucleation [Figure 9, 10], anterior iliac medial cortico cancellous block graft [Figure 11] was harvested and fixed to the recipient site through reconstruction plate [Figure 12]. During the post-operative period, patient was maintained under Intermaxillary fixation for 2 weeks the healing phase of the graft was uneventful [Figure 13] showing graft acceptance and considerable bone fill in the one year follow up. [Figure 14].

Discussion

Our differential diagnosis list included the following

fibrous lesion cemento ossifying fibroma, florid cement osseous dysplasia, fibrous dysplasia, paget's disease, brown's tumour, and hyperparathyroid jaw tumour syndrome.

Cement osseous dysplasia is the commonest fibrous lesion of tooth bearing segment of the jaw. This manifests as nonexpansile lesion occurring as periapical, focal and florid types commonly associated with female with hormonal imbalance. The cement osseous dysplasia extending than 2cm in size is considered to be florid type, manifesting without an expansile lesion, radiographically mixed radioopacities. Biopsies in florid cement osseous dysplasia leads to acute suppurative osteomyelitis leading to sequestration [1].

Paget's disease is an osseous dysplasia resulting from pagetic osteoclasts causing rapid bone turn over from the mutation of Sequestosome 1 (SQSTM 1) gene [2]. It causes expansile lesion commonly in maxilla with slight male predominance, increase in alkaline phosphatase level and cranial neuropathies. Histologically the trabeculae of bone are irregularly arranged in fibrous stroma resembling jigsaw puzzle pattern. Radiologically showing cotton wool appearance. It progresses in three stages osteoclastic, osteoblastic and burn out stage [3].

Fibrous dysplasia is a benign dysplastic disease of bone resulting in altered osteogenesis from the mutation occurring in GNAS 1 Guanine nucleotide binding protein alpha stimulating activity polypeptide 1 gene affecting male and female equally. This may also involve melanocytes causing McCune Albright syndrome and endocrine cells causing Jaffe Lichtenstein syndrome [4]. Based on the site of mutation and distribution of lesions it is divided in monoosteotic, polyosteotic and craniofacial forms. Clinically it shows expansile lesion increased alkaline phosphatase level radiographically a ground glass pattern without encapsulation and histologically thin osteoid formation in fibroblastic stroma in intermediate stage the osteoid developed is in Chinese letter pattern without osteoblastic lining and in later stages the woven bone is replaced by lamellar bone showing reverse lines. The lesion's growth ceases along with the skeletal growth [5].

Hyperparathyroidism being the third most common endocrine disorder; it can be primary, secondary and tertiary. Primary hyperparathyroidism is due to parathyroid adenoma followed by parathyroid hyperplasia and parathyroid carcinoma [6]. Secondary hyperparathyroidism is due to the hyperfunction of parathyroid gland to compensate the renal loss of calcium in renal failure patients causing renal osteodystrophy [7]. Tertiary hyperparathyroidism is due to the autonomous functioning of parathyroid gland [8]. The hallmark feature of hyperparathyroidism is poor muscle tone and excitability. Hypercalcemia can also be caused by paraneoplastic syndromes associated with renal, gynaecological and bronchogenic carcinoma.

Brown's tumour or Osteitis Fibrosa Cystica is the manifestation of hyperparathyroidism in bones especially of femur, mandible and maxilla. Often this occurs as the first sign of hyperparathyroidism manifesting as cystic cavities with intermingled by new bone formation. Radiologically appears as a mixed radiolucency or ground glass appearance [9]. Histologically it shows fibrous pattern with osteoclast like giant cells interspersed in the fibrous stroma. The diagnosis is through lab investigation hypercalcemia, elevated alkaline phosphatase and decreased phosphorus [10]. The treatment is to correct the hyperparathyroidism, once the hyperparathyroidism is treated the tumour regresses in 6 to 8 months [11]. Osteitis Fibrosa Cystica happened to be our

provisional diagnosis as the mixed radiolucency was expansile, well demarcated and the patient showed elevated calcium, phosphorus, alkaline phosphatase and left inferior parathyroid adenoma with elevated parathormone level.

Cemento ossifying fibroma is benign lesion of odontogenic origin from pluripotent periodontal blast cells. It occurs in female of 3-4th decade in mandibular premolar and molar region [12]. Histologically it consists of bone trabeculae in cell rich fibrous stroma with osteoid and cementoid matrix. Radiologically it is unilocular, multilocular and mixed type. As it is encapsulated the recurrence rate is low after surgical excision and curettage [13].

Presence of Ossifying Fibroma in the primary hyperparathyroidism patient is rare entity named as Hyperparathyroid Jaw Tumour Syndrome [14]. This syndrome occurs due to inhibitory mutation of Hereditary Parathyroid Type 2 (HRPT 2) gene in chromosome 1 resulting in parathyroidism, ossifying fibroma of jaw, renal tumours like Wilms tumour, uterine tumour like leiomyoma [15, 16]. Histologically the jaw tumours resemble ossifying fibroma with the presence of giant cells [17]. Hyperparathyroid Jaw Tumour Syndrome was first reported by Jackson *et al.* in 1958 [18]. This syndrome occurs in commonly in late adolescent and adults of a family with Autosomal dominant inheritance [19]. The mutated gene is HRPT-2, with 17 exons located in 1q25 position [20]. According to Howell *et al.* this mutation also occurs in parathyroid carcinomas and familial hyperparathyroidism [21], thus 15% of the patients with hyperparathyroid jaw tumour syndrome likely develop parathyroid carcinoma [22]. 30% of the syndrome patient's manifest with jaw tumour, 40% have uterine tumour and other renal manifestations like Wilms's tumour, adenocarcinoma and polycystic kidney disease [23]. Approximately 10% of the patients with HRPT2 mutation are silent carriers [24]. Hyperparathyroid jaw tumour syndrome may also accompany MEN 1, MEN 2A, Familial Isolated Hyperparathyroidism [25]. MEN 1 comprises Pituitary, Parathyroid and Pancreatic tumour characterised by multiglandular enlargement with hypercalcaemia, nephrolithiasis and Zollinger Ellison syndrome. MEN2A comprises of familial Medullary carcinoma thyroid, pheochromocytoma, parathyroid adenoma characterised with hypercalcaemia and nephrolithiasis. MEN 4 comprises of bilateral pheochromocytoma, bilateral medullary carcinoma thyroid and bilateral parathyroid, pituitary adenoma. Familial hypocalcaemic hypercalcaemia comprises uni or multiglandular parathyroid hyperplasia with any other gland involvement [26]. The treatment of parathyroid hyperplasia involves parathyroidectomy of the involved gland [27], and calcimimetics [28] are used when there is contraindication for surgery.

In 1971, Kennett and Pollock described in detail the occurrence of jaw lesions in familial hyperparathyroidism, in which jaw lesion manifested first other than manifestations of hypercalcaemia like gastric irritation, back pain, osteoporosis, poor muscle tone and excitability [29]. A Cemento Ossifying fibroma is a well demarcated benign neoplasm found in jaws composed of rich fibrocellular tissue with osteoid matrix may often contain few giant cells with centrifugal growth pattern [30]. Radiographically nonsyndromic Ossifying fibroma is well demarcated mixed radiolucencies/radioopacities with smooth sclerotic margins [31], but in syndromic cases it appears mostly as radiolucencies with very less radioopacities [32].

Cemento ossifying Fibroma of the jaw can be treated by conservative excision, or surgical resection. The jaw lesions

of ostietis fibrosa cystic regress after the surgery but the jaw lesions of hyperparathyroid jaw tumour syndrome require surgical excision. The conventional Cemento ossifying fibroma separates easily from the bone and the chance of recurrence is of 0-30%, usually the reason for recurrence is the regrowth of the remaining lesion in the bone or the inability to distinguish cemento ossifying fibroma with its psammomatoid and juvenile types^[33]. Surgical curettage of the lesion is curative for managing Ossifying fibroma occurring in Hyperparathyroid jaw tumour syndrome^[34].

Conclusion

To summarise, many benign fibrous lesions of the jaw have similar microscopic features and for the process of their diagnosis require clinical and radiological correlation. The brown tumour occurring in jaw as a result of hyperparathyroidism does not require any treatment once the parathyroid levels are corrected and it regresses in a duration of 6-8 months but in hyperparathyroid jaw tumour syndrome the cemento ossifying fibroma requires a surgical excision. And our findings show that the conservative excision of cemento ossifying fibroma syndrome appears to be a versatile, secure, and satisfactory treatment option.

Reference

- Melrose R. The clinico-pathologic spectrum of cemento-osseous dysplasia. *Oral Maxillofac Surg Clin North Am.* 1997; 9:643-54.
- Monfort J, Sala DRE, Romero A. Epidemiological, clinical, biochemical, and imaging characteristics of monostotic and polyostotic Paget's disease. *Bone.* 1999; 24:13S-14S.
- Rebel A, Malkani K, Basle M. Ultrastructural characteristics of osteoclasts in Paget's disease. *Rev Rhum Mal Osteoartic.* 1974; 41:767-71.
- Di Caprio MR, Enneking WF. Fibrous dysplasia. *J Bone Joint Surg Am.* 2005; 87:1848-64.
- Marie PJ. Cellular and molecular basis of fibrous dysplasia. *Histol Histopathol.* 2001; 16:981-8.
- Ramasamy I. Recent advances in physiological calcium homeostasis. *Clin Chem Lab Med.* 2006; 44:237-73.
- 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. *Am J Otolaryngol.* 2006; 27:281-6.
- Selvi F, Cakar S, Tanakol R, Guler SD, Keskin C. Brown tumour of the maxilla and mandible: a rare complication of tertiary hyperparathyroidism. *Dentomaxillofac Radiol.* 2009; 38:53-8.
- Waldron CA. Fibro-osseous lesions of the jaw. *J Oral Maxillofac Surg.* 1993; 51:828-835.
- Neville BW, Damm DD, Allen CM, Banquet JE. *Oral and Maxillofacial Pathology.* Philadelphia: WB Saunders, 1995, 468-470.
- Kramer IRH, Pindborg JJ, Shear M. *Histologic typing of odontogenic tumours.* 2nd edn. Berlin: Springer-Verlag, 1992, 27- 28.
- Keyser J, Postma G. Brown Tumor of the Mandible. *American Journal of Otolaryngology.* 1996; 17:407-10.
- Martin-Granizo R, Sanchez-Cuellar LA, Falahat F. Cemento-ossifying fibroma of the upper gingivae. *Otolaryngol Head Neck Surg.* 2000; 122:775.
- Iacobone M, Masi G, Barzon L, Porzionato A, Macchi V, Ciarleglio FA *et al.* Hyperparathyroidism-jaw tumor syndrome: a report of three large kindred. *Langenbecks Arch Surg.* 2009; 394:817-25.
- Rekik N, Ben Naceur B, Mnif M, Mnif F, Mnif H, Boudawara T *et al.* Hyperparathyroidism-jaw tumor syndrome: a case report. *Ann Endocrinol.* 2010; 71:121-6.
- Agarwal S, Simonds W, Marx SJ. The parafibromin tumor suppressor protein interacts with actin-binding proteins actinin-2 and actinin-6. *Mol Cancer.* 2008; 7:65.
- Aldred M, Talacko A, Savarirayan R, Murdolo V, Mills A, Radden B *et al.* Dental findings in a family with hyperparathyroidism-jaw tumor syndrome and a novel *HRPT2* gene mutation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006; 102:212-8.
- Jackson CE. 1958 Hereditary hyperparathyroidism associated with recurrent pancreatitis. *Ann Intern Med* 49:829-836.
- Teh BT, Farnebo F, Kristoffersson U. Autosomal dominant primary hyperparathyroidism and jaw tumor syndrome associated with renal hamartomas and cystic kidney disease: linkage to 1q21-q32 and loss of the wild type allele in renal hamartomas. *J Clin Endocrinol Metab.* 1996; 81(12):4204-4211.
- Moon S, Park J, Kim E, Kim J, Han J, Yoo S *et al.* A novel IVS2-1G>A mutation causes aberrant splicing of the *HRPT2* gene in a family with hyperparathyroidism-jaw tumor syndrome. *J Clin Endocrinol Metab.* 2005; 90:878-83.
- Howell VM, Cadinal JW, Richardson AL, Gimm O, Robinson BG, Marsh DJ. Rapid mutation screening for *HRPT2* and *MEN1* mutations associated with familial and sporadic primary hyperparathyroidism. *J Mol Diagn.* 2006; 8:559-66.
- Yamashita Y, Akiyama T, Mizusawa N, Yoshimoto K, Goto M. A case of hyperparathyroidism-jaw syndrome found in the treatment of an ossifying fibroma in the maxillary bone. *Int J Oral Maxillofac Surg.* 2007; 36:365-9.
- DeLellis RA LR, Heitz PU, Heng C. *World Health Organization classification of tumours pathology and genetics: Tumours of endocrine organs.* Lyon (France): IARC Press, 2004.
- Simonds WF, James-Newton LA, Agarwal SK. Familial isolated hyperparathyroidism: Clinical and genetic characteristics of 36 kindreds. *Medicine (Baltimore).* 2002; 81(1):1-26.
- Szabo J, Heath B, Hill VM, Jackson CE, Zarbo RJ, Mallette LE *et al.* Hereditary hyperparathyroidism-jaw tumor syndrome: The endocrine tumor gene *HRPT2* maps to chromosome 1q21-q31. *Am J Hum Genet.* 1995; 56(4):944-50.
- Giusti F, Cavalli L, Cavalli T, Brandy ML. Hereditary Hyperparathyroidism Syndromes. *Journal of Clinical Densitometry: Assessment of Skeletal Health.* 2013; 16(1):69-74.
- Tonelli F, Marcucci T, Fratini G. Is total parathyroidectomy the treatment of choice for hyperparathyroidism in multiple neoplasia type 1? *Ann Surg.* 2007; 246:1075-1082.
- Moyes VJ, Monson JP, Chew SL, Akker SA. Clinical use of cinacalcet in *MEN1* hyperparathyroidism. *Int J Endocrinol,* 2010, 9061-63.
- Fanibunda K, Reed MF. Cemento-ossifying fibroma of the mandible. *Dentomaxillofac Radiol.* 1997; 26:246-248.

30. Sciubba JFJCLB. Tumors and cysts of the jaw. Atlas of tumor pathology. Washington, DC: Armed Forces Institute of Pathology, 2001.
31. Brannon RB, Fowler CB. Benign fibro-osseous lesions: A review of current concepts. *Adv Anat Pathol.* 2001; 8(3):126-43.
32. Aldred M, Talacko A, Savarirayan R, Murdolo V, Mills A, Radden B *et al.* Dental findings in a family with hyperparathyroidism-jaw tumor syndrome and a novel *HRPT2* gene mutation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006; 102:212-8.
33. Knutsen BM, Larheim TA, Johannessen S, Hillestad J, Solheim T, Strumme H *et al.* Recurrent conventional cemento-ossifying fibroma of the mandible. *Dentomaxillofacial Radiology.* 2002; 31:65-68.
34. Odell EW, Morgan PR. Biopsy pathology of the oral tissues. London: Chapman & Hall Medical, 1998, 272-275.