Case Report

Coexistence of hyperparathyroidism and peripheral giant cell granuloma of the jaw: A rare case report

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Abstract

Peripheral giant cell granuloma (PGCG) known as "giant cell epulis" is a benign, reactive exophytic gingival lesion that accounts for less than 10% of all gingival lesions. PGCG affects females more than males with middle age predilection. Till now the etiology of PGCG remains unclear but various factors that can cause PGCG include poor oral hygiene, food impaction, following an extraction, dry mouth, hormonal disturbance, and hyperparathyroidism. The reported recurrence rate of the lesion is 5.0%–70.6%. The present case report describes the rare case of PGCG with primary hyperparathyroidism in a male patient with a history of swelling in the mandibular anterior region.

Keywords: Giant cell, hyperparathyroidism, peripheral giant cell granuloma

Introduction

Peripheral giant cell granuloma (PGCG) is a common benign, reactive exophytic lesion of the oral mucosa. It can arise from periodontal ligament or periosteum of the alveolar bone.[1] There are various etiological factors for PGCG such as poor oral hygiene, food impaction, following the extraction, xerostomia, hormonal imbalance, and hyperparathyroidism (HPT).[2,3] The recurrence rate of the lesion is 5.0%–70.6%.[4] In the case of recurrence of any lesion, multiple etiologies should be considered. PGCG is considered to be a reactive lesion occurring due to chronic irritation and shares an identical morphology with central giant cell granuloma. The genetic etiology includes activating mutations in the MAP-kinase signaling pathway, *KRAS*, and *FGFR1* mutations.[5]

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In giant cell lesions, patients should be evaluated for HPT to rule out a brown tumor.[6] HPT was first found by Von Recklinghausen in 1891. It is of 3 types: primary, secondary, and tertiary.[7] The prevalence of primary hyperparathyroidism (PHPT) associated with giant cell lesions is 5.9%.[7] PHPT results in hypercalcemia and affects many organs like bone, kidney, soft tissues, and central nervous system. The odontogenic tissues and jawbones are also affected as a systemic manifestation of PHPT.[8] The occurrence of both PGCG and PHPT is more in females.[9] The ratio of female and male for PGCC is 2:1 and for PHPT is 3:1.[10,11] Hereby, we are presenting a rare case of PGCG with PHPT in a male patient.

Case Report

A 40-year-old male patient with a chief complaint of swollen gums in the anterior region of the mandible reported to the Department of Periodontics and Implantology of Hi-Tech Dental College and Hospital, Bhubaneswar. The patient had the same history of swollen gums 2 years back which was excised.

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Following that after a year, there was a small swelling developed in relation to #32, #33. The swelling grew rapidly and attained a size of 5 × 4 cm [Figure 1] extending from #32 to #33. The swelling was well-defined solitary, oval in size with a pedunculated base. The surface was smooth and shiny with surface ulcerations. The etiology of the present lesion was found to be trauma; thus, the diagnosis was more toward pyogenic granuloma. Further on palpation, the swelling was found to be soft and nontender and there was profuse bleeding on probing. The oral hygiene status of the patient was fair with mild calculus present around the anterior mandibular teeth. Although there was no other abnormality detected on the extraoral examination, the patient looked weak and emaciated. Also, he complained of occasional fatigue and tiredness. A provisional diagnosis of pyogenic granuloma was made. Following that, a routine lab investigation was carried out, which revealed high serum calcium (10.9 mg/dl) and PTH level (72 pg/ml). A diagnosis of PHPT was made based on the findings. The patient was referred to the endocrinologist for further treatment. Further intraoral investigation radiographic investigation showed mild crestal bone loss in relation to # 32, #33. Written informed consent was obtained from the patient along with the ethical clearance from the institutional ethical committee (E/C3456). Complete surgical excision of the swelling was performed after scaling and root planning [Figure 2]. The periodontal dressing was placed over the surgical site [Figure 3]. The patient was prescribed with antibiotics and analgesics and oral hygiene instructions were given. The histopathology report confirmed the diagnosis of peripheral giant cell granuloma. The H and E section showed para keratinized stratified squamous epithelium covering underlying granulomatous stroma composed of numerous proliferating multinucleated giant cells, fibroblasts, proliferating vessels, and chronic inflammatory cells [Figure 4 a and b]. A 6-month and 1-year follow-up showed no further swelling in the oral cavity [Figures 4 and 5].

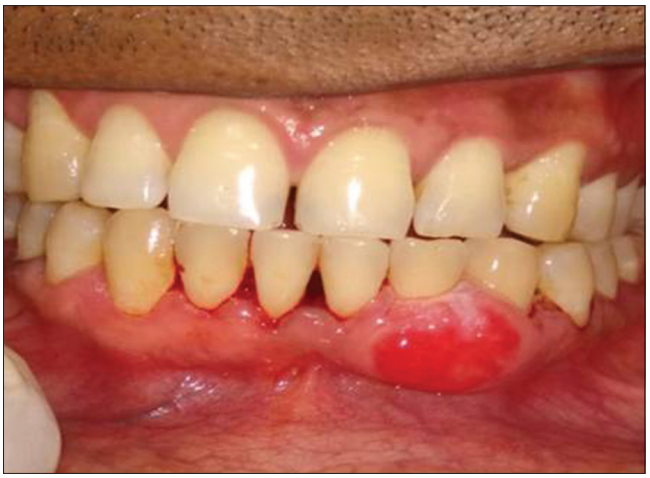

Figure 1: Swelling in relation to # 32 to 33

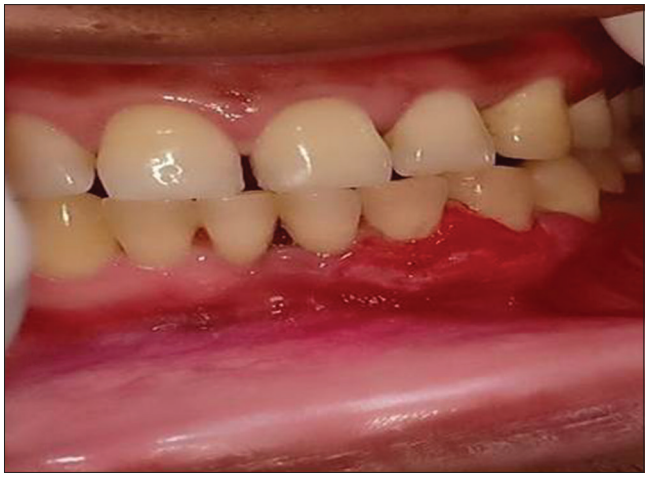

Figure 2: Surgical excision of the lesion

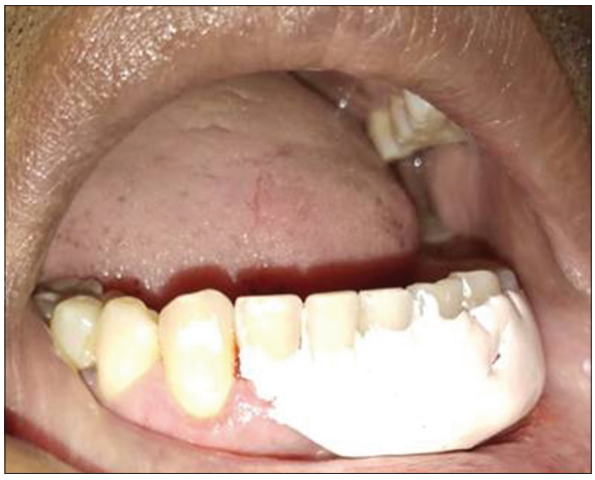

Figure 3: The periodontal dressing (Coe-Pak) was placed over the surgical site

Discussion

This case report represents a case of PGCC with PHPT. PGCG is a benign gingival lesion which reckoned less than 10% of all gingival lesions.[9] Jaffe coined the term giant cell reparative granuloma for PGCG.[9] Further, Bernier and Cahn named it peripheral and central cell reparative granuloma.[12] Subsequently, the giant cell granuloma was divided as central and peripheral by Bhaskar *et al.* in the year 1959.[13] Peripheral giant cell granuloma is a benign, nonodontogenic tumor of the oral cavity.[14] It mostly occurs in the mandible and has female predilection.[15] PGCG is more common in premolar and molar region though its occurrence in incisor and the canine region has been reported.[14,15] Usually, PGCG is well-demarcated, sessile, or pedunculated deep red to bluish red in color similar to the present case.[16]

Subramanian *et al.* reported a case of peripheral giant cell granuloma in a 38-year-old male that represented as a localized painless, lobulated, purplish-red overgrowth of gingiva localized to the region of 14 and 15, extending from the interdental papilla on the buccal aspect to the palatal aspect.[17]

The differential diagnosis of PGCG includes pyogenic granuloma, hemangioma, metastatic carcinoma, and peripheral ossifying fibroma, which are proliferative gingival lesions that can show very similar characteristics but have a difference in

histology and recurrence rate.[18,19] Another condition could also be considered such as peripheral odontogenic fibroma that represents clinically a dome-shaped or nodular,fibrotic growth in gingiva like PGCG. However, histologically it consists of fibrous or fibromyxomatous stroma containing varying numbers of islands of odontogenic epithelium, which are distinguishable from PGCG.[20] The striking histopathological features of PGCG are the presence of numerous proliferating fibroblasts, vascularized fibro cellular stroma with numerous capillaries, and numerous multinucleated giant cells.[21,22] The distinctive feature of PGCG is mainly due to the excess number of giant cells that are clustered in the connective tissue stroma [Figure 6]. The exact origin of giant cells is uncertain but it has been suggested that cells like osteoblasts, macrophages, endothelial cells, and spindle cells can give rise to these multinucleated giant cells.[23]

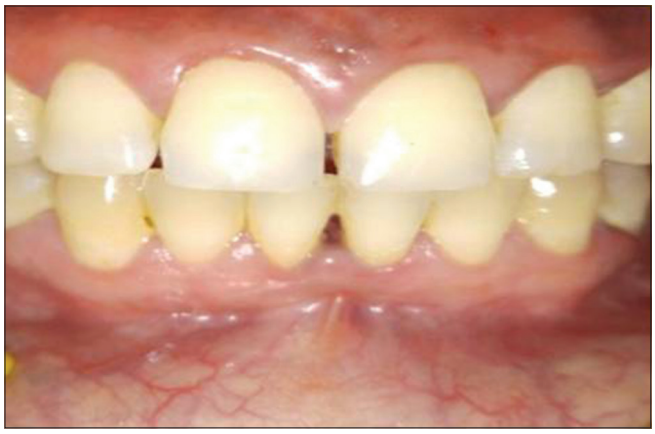

Figure 4: One-year postoperative follow-up. a: Histopathological picture showing para keratinized epithelium overlying the connective tissue stroma. b: Giant cells in the stroma

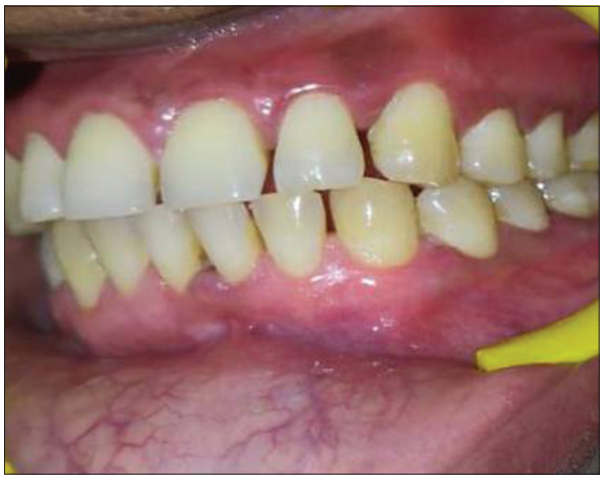

Figure 5: Six-month postoperative follow-up

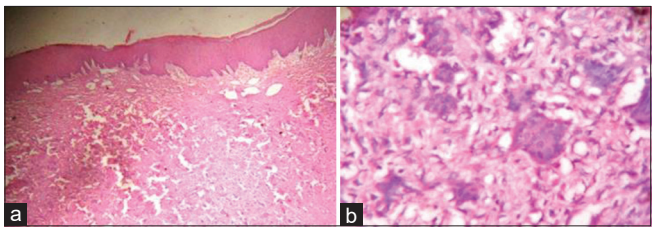

Figure 6: (a) Parakeratinized epithelium. (b) Giant cells in stroma

If there were multiple lesions or if recurrence of the same lesions occurred after surgical removal, then other conditions should also be considered in differential diagnosis such as brown tumor of HPT, cherubism, and aneurysmal bone cyst.[24] Brown tumor can perforate the cervical region of the tooth, and aneurysmal bone cyst is affecting the bone with a more aggressive nature.[25] PHPT is considered as an endocrine disorder that results due to the autonomous overproduction of PTH, usually resulting from parathyroid adenoma (90%), parathyroid hyperplasia (3%), or less commonly an adenocarcinoma (3%), and rarely associated with Noonan type syndrome.[26]

In the present case, as there was a history of multiple excision and recurrence of the lesion, speculation for further lab investigations was carried out to rule out other diseases. Based on clinical findings and histological and lab investigations, a diagnosis of PGCG with PHPT was established. The patient presenting with PGCG may also have other signs and symptoms of PHPT. Generalized weakness, anemia, gastric ulcer, renal stones, and osteoporosis are features of PHPT. In our case, the patient also complained of continuous weakness and his appearance was also very weak and emaciated; thus, systemic involvement needed to be evaluated. Smith *et al.* reported a similar case of PHPT in which the initial clinical presentation was that of an intraoral lesion and PHPT was discovered on routine blood analysis.[27] Also, Burkes reported a case of peripheral giant cell granuloma with the manifestation of PHPT.[28] Parbatani *et al.* presented a case of giant cell epulis as an initial feature of PHPT.[29] Vendrell Marques *et al.*[30] and Matinz-Gavidia *et al.*[31] reported cases of the maxillary brown tumor as an early sign of PHPT. Also, two cases of giant cell lesions were established at the discovery of PHPT by Aoune *et al.*[32] Choi *et al.*[33] found a case of PGCG associated with HPT secondary to end-stage renal diseases. Both PGCG and PHPT have female predilection with female to male ratio; for PGCG, it is 2:1 and for PHPT, it is 3:1.[9-11] However, various cases had been reported affecting the male gender more. Chaparro-Avendano *et al.*[34] reported a study involving three males with PGCG. Bhaskar *et al.*[35], Salum *et al.*[36], Zhang *et al.*[37], and Murat *et al.*[38] showed male predominance in PGCG. Also, Mazeh *et al.*[39] compared the role of gender in PHPT and they concluded that male patients present without symptoms. The positive influence of estrogen and progesterone inclined toward hormonal etiology in our case along with the presence of secondary local factors such as plaque and calculus. There were no classical symptoms of hypercalcemia in our patients, such as bone fractures, renal stones, and abdominal groans. Other symptoms also include paresthesia, headaches, recent fractures, constipation, polyuria, and polydipsia. Mostly the symptoms were asymptomatic and diagnosed while routine laboratory investigations.[40] The treatment of the PGCG is complete excision of the lesion along with the curettage of the

base and borders of the lesion.[41] In the present case, complete excision of the lesion was done along with thorough curettage.

Implications for clinical practice

The pathologist may come across many inflammatory conditions in response to dental plaque like gingivitis and periodontitis. Lesion such as PGCG has greater chances of recurrences and this must be kept in mind while treating such pathologies. The treatment of PGCG comprises complete surgical resection along with the entire base of the lesion. The underlying source of irritation should also be eradicated while treating such lesions to prevent a recurrence.[42,43] Thus, to reach an accurate diagnosis, clinical history, histological, radiological, and laboratory investigations are necessary. The dentist should be aware of the possible association of oral lesions with systemic diseases. The biochemical tests that are diagnostic for such systemic diseases should be recommended to rule out the associated conditions.

Summary and Conclusion

Histopathological examination along with biochemical tests is essential to predict the conclusive diagnosis and treatment planning. The present case confirmed the diagnosis of PGCG with PHPT. Thus, it is necessary that such oral lesions with ambiguous causes should be attributed to a specialist for accurate diagnosis and further treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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