

## Peripheral giant cell granuloma recurring as an exclusively intra-osseous lesion: An unusual clinical presentation

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### Abstract

Giant cell lesions of the jaws represent distinctive clinico-pathological spectrum. They manifest as peripheral and central lesions, occurring as solitary growths to involving multiple regions of the jaw. The present report presents a unique case of giant cell lesions of the jaws, wherein a peripheral giant cell granuloma recurred exclusively as a central giant cell lesion in a young patient. The recurrence was noted after a time-span of 3 years since the diagnosis and surgical excision of the peripheral lesion. Biochemical investigations were advised to rule out the possibility of hyperparathyroidism. Following a confirmed diagnosis of central giant cell granuloma, not associated with any other systemic conditions, an apt treatment plan was devised for an early rehabilitation of the patient.

### Introduction

Gingival lesions constitute a noteworthy figure of clinical differential diagnosis in the paediatric population. One of such common lesion, which manifests as a solitary, exophytic growth, is the peripheral giant cell granuloma (PGCG). It is a reactive, proliferative, extra-osseous lesion which is commonly located on the mandible, involving the gingival or the

alveolar mucosa in dentate and edentulous patients respectively.<sup>1,2</sup> PGCG is reported to have a wide recurrence rate, varying from 5% to 70.6% of cases, probably attributed to the surgical technique used to excise the lesion.<sup>3</sup>

A relatively lesser common lesion with an identical histopathological picture as that of PGCG, but with a distinct clinical course and intra-osseous occurrence, is the central giant cell granuloma (CGCG). It is considered as a benign lesion of the jaws with an unknown etiology.<sup>4</sup> Since both of these lesions share an alike microscopic appearance, few authors have suggested that PGCG might be the soft tissue counterpart of the central lesion. Nevertheless, it is still uncertain, whether the entities are discrete or comparable.<sup>5,6</sup> In context to the previous statement, the present case report elicits an ambiguous presentation of PGCG in a young patient, recurring as an exclusively intra-osseous lesion, involving the same location in the jaw.

A web-based literature search was performed via PubMed database, with keywords central, peripheral, giant cell granuloma and recurrent peripheral giant cell granuloma. The literature search revealed various published original studies, case series and review articles, but none describing recurrence of PGCG as a central lesion. Hence, to best of our knowledge, the existing case is the first report on PGCG recurring as a CGCG.

Thus, the present case report describes the unique presentation of the giant cell lesions of the jaw with a special emphasis on their origin, similarities and differences, along with their clinical significance.

### Case Report

An 8-year old male patient reported to the department with gingival overgrowth on the lingual side of mandibular premolar region since 8 to 10 months. Preliminary inquisition revealed insignificant medical history. On inspection, a solitary growth was noted, 3×3 cm in size, extending from permanent right mandibular lateral incisor to distal surface of second premolar. The lesion was pedunculated, irregular in shape, with overlying surface erythematous and ulcerated. On palpation, the lesion was soft and tender, with tendency to bleed. Orthopantomographic examination revealed soft tissue shadow of the lesion in the right premolar region (Figure 1A). These clinical and radiographic findings indicated a benign lesion, and the following differential diagnoses were considered: pyogenic granuloma, peripheral ossifying

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fibroma, PGCG, and peripheral odontogenic fibroma. The patient was scheduled for surgical excision. Following which, under local anaesthesia, the lesion was excised down to the periosteum. There was no evidence of bone involvement during surgical excision. After complete excision of the lesion, the exposed surface was cauterized to control the bleeding and the entire specimen submitted for histopathologic examination. Microscopic examination revealed multinucleated giant cells within a background of spindle-shaped and ovoid mesenchymal cells in the deeper connective tissue stroma of oral mucosa (Figure 1B). Areas of hemorrhage and inflammatory cells, both acute and chronic, were frequently present. A zone of dense fibrous connective tissue separated the giant cell proliferation from the surface epithelium (Figure 1B). Based on the histopathology, a diagnosis of PGCG was confirmed.

After 3 years, the same patient reported with a chief complain of swelling in the mandibular posterior region, since 3 to 4 months. Extra-oral examination revealed a diffuse swelling of approximately 3×3 cm over the left mandibular body (Figure 2A). The surface of the swelling was smooth with no evidence of sinus opening or pus discharge. On palpation, the swelling was non-tender with bony hard consistency. There was no significant regional lymphadenopathy. Intra-orally, a swelling of approximately 3×4 cm was evident, extending from the distal aspect of right canine till

the right first molar posteriorly with obliteration of buccal vestibule (Figure 2B). The surface was covered with normal mucosa with no evidence of ulcerations. On palpation, the swelling was hard in consistency, non-tender with expansion of bucco-lingual cortices. On aspiration few drops of blood was obtained. Orthopantomogram revealed a well-defined multilocular radiolucent lesion surrounded by a thin corticated scalloped margin extending from the distal aspect of canine till the distal aspect of mandibular first molar with thinning of inferior cortical border of mandible (Figure 2C). Laboratory investigations such as routine hemogram, serum calcium, phosphorous, and parathyroid hormone assay were within the normal range. Incisional biopsy was performed and histopathology revealed a fibro-vascular connective tissue stroma with irregularly distributed foreign body type of giant cells, located mainly at the periphery of extravasated blood, suggestive of CGCG (Figure 2D). Microscopic examination also showed presence of cannibalistic giant cells, which is the marker of aggressive behavior of giant cell lesions (Figure 2D black arrow).

## Discussion

PGCG has a frequency of 24.4% among young population.<sup>7</sup> CGCG is reported to comprise of approximately 7% of all the benign lesions of the jaw.<sup>8,9</sup> The prevalence of CGCG reported by several authors include 0.15%, 0.17% and 0.37%.<sup>10</sup> However, till date a case of PGCG recurring exclusively as CGCG has not been reported in the literature.

PGCG frequently occurs in the third to fourth decade of life and exhibits a female predilection.<sup>1,11</sup> CGCG is commonly reported before the age of 30 years and similar to PGCG shows a female preponderance.<sup>9,10-12</sup> In the present case the patient was a young male. Concerning the age and clinical progression, the present case findings were consistent with the published literature, *viz.*, both PGCG and CGCG in young patients tend to run an aggressive course, affecting the adjacent anatomic structures and have multiple recurrences.<sup>2,4,13</sup>

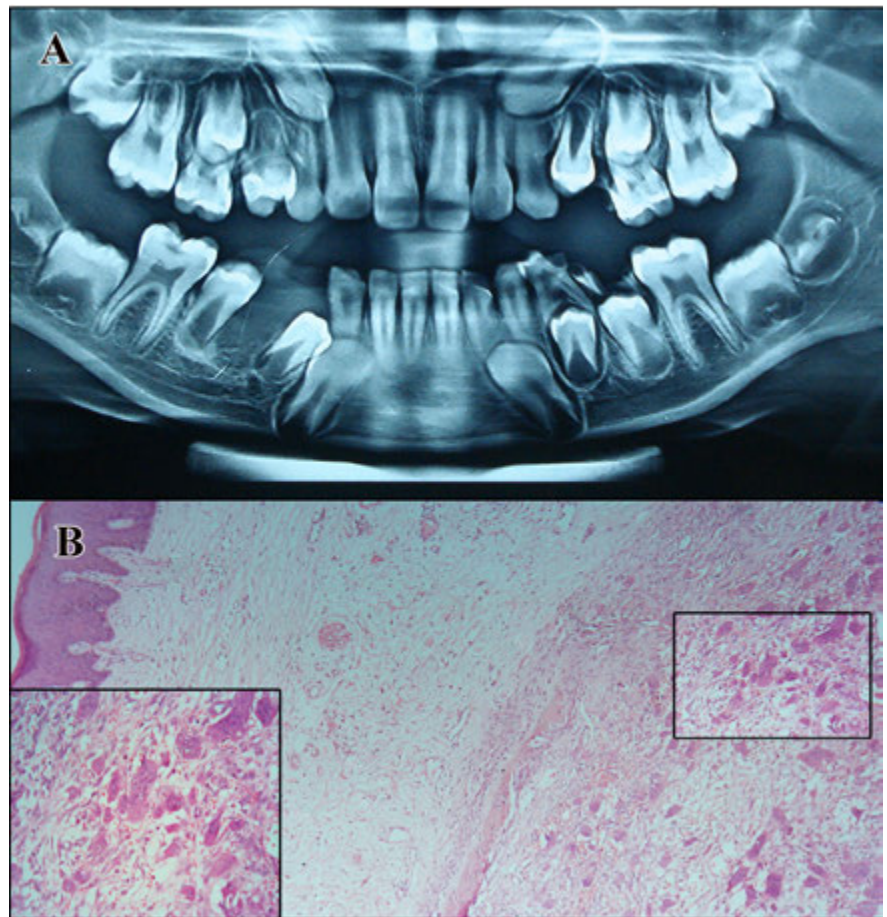
PGCG is postulated to arise from the periosteum or the periodontal ligament. The etiology is suggested to be local irritating factors and chronic trauma. The factors include bacterial plaque, calculus, food debris retention, traumatic extractions, defective dental restorations, ill-fitting prosthesis, dental implants, chronic infections and trauma from malocclusion.<sup>1,6,7,11</sup> In addition the role of xerostomia and hor-

mones have also been suggested.<sup>8</sup> Rare occurrence of PGCG in cases with hyperparathyroidism has also been reported by several authors.<sup>8,14,15</sup>

In 1953, Jaffe categorized the CGCG of jaws as separate entity distinguishing it from the giant cell tumour of extra-gnathic sites.<sup>4,11</sup> Contrary to the above, few authors consider CGCG and giant cell tumours of extra-gnathic locations to be rather different expressions of the same disease process.<sup>16</sup> Presently, CGCG of the jaws has been classified as a non-neoplastic bone lesion by the WHO.<sup>12</sup> Conversely, few authors suggest that CGCG constitutes a benign tumour.<sup>6</sup> Among the systemic causes, it has been found to be associated with neurofibromatosis type I, Noonan syndrome, Ramon syndrome, Jaffe-Campanacci syndrome, cherubism, pregnancy and hyperparathyroidism. Based on its association with the former mentioned syndromes, a genetic etiology has also been postulated. Mutations in gene SH3BP2 (exon 4) has been studied by Teixeira et al. and found to be associated with CGCG.<sup>6,12</sup>

In the present case there were no significant contributing local factors nor signs of chronic trauma. The possibility of hyperparathyroidism was ruled out *via* biochemical tests. Conversely, the syndromic association could not be commented upon as the genetic analyses were not conducted. Further, the excision technique was steered precisely to annul the chances of recurrence. Since a definitive causative factor could not be established for the recurrence, it is indeed intriguing to speculate whether the peripheral and the central lesion share a common origin. Lastly, the possibility that it was a mere chance occurrence of two distinct lesions sharing the same anatomic location can be anticipated as well as.

The present case was reported in the mandibular premolar-molar region. According to the literature PGCG and CGCG exhibit a predilection for mandible. Both lesions frequently occur in the anterior region of the jaw with CGCG often crossing the midline.<sup>1,6,9-11,14</sup> Most cases of PGCG are found to occur around teeth, followed by edentulous areas and around dental



**Figure 1.** A) Orthopantomograph showing soft tissue shadow of the lesion at the right mandibular premolar region. B) Photomicrograph showing surface epithelium and giant cells present in the deeper fibro-cellular connective tissue stroma (hematoxylin and eosin stain, total magnification X40 [Inset X400]).



implants.<sup>11,14</sup> In addition, uncommon location of CGCG such as the mandibular condyle, has been reported by few authors.<sup>12</sup>

PGCG presents as pink to red pedunculated or sessile growth with a smooth or ulcerated surface.<sup>1,14</sup> Smaller lesions usually present as lobulated painless masses whereas larger lesions may interfere with normal functioning of the dentition. However, in children PGCG might show a rapid growth as well as aggressive and recurrent behavior.<sup>2</sup> The recurrence rate of PGCG varies from 5% to 70.6% and published data indicates that recurrent lesions present as extra-osseous lesions.<sup>3</sup> Nevertheless, present case is first of its kind where PGCG has recurred exclusively as CGCG.

Chuong *et al.* were the first to categorize CGCG into aggressive and non-aggressive forms.<sup>9</sup> The aggressive form is rapid in onset, presents with pain, paraesthesia, tooth displacement, extension into soft tissues and swelling causing facial asymmetry. Whereas, the non-aggressive type presents

as a slow growing, asymptomatic swelling, occasionally revealed through radiographic examination.<sup>6,10,11,17</sup> Based on the early onset, clinical presentation and recurrent nature, the present case was categorized into aggressive type of CGCG.

PGCG seldom affects the underlying bone, although it may cause superficial erosion or cupping of the alveolar bone.<sup>11,13</sup> In accordance with the literature, present case did not show any significant involvement of bone on radiological examination, which was later confirmed during the intra-operative procedure. CGCG has varied presentation, ranging from completely radiolucent to mixed radio-opaque–radiolucent form. It may be unilocular to multilocular in appearance with scalloped or ill-defined margins.<sup>6,9,18</sup> Associated findings include displacement of teeth, tooth germs and mandibular canal; root resorption, loss of lamina dura, expansion and perforation of the cortical bone.<sup>17,18</sup> In the present case CGCG presented as a multilocular radiolucent lesion with displacement of roots of

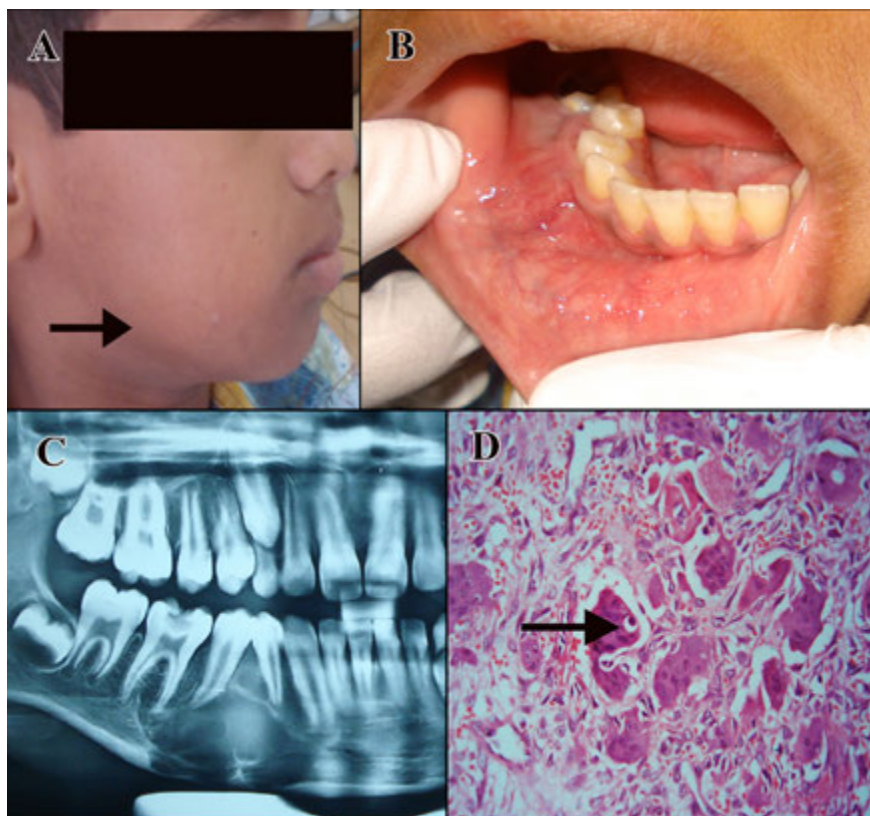
associated teeth.

Microscopically, PGCG comprises of ovoid or fusiform shaped cells, numerous multinucleated giant cells, osseous metaplasia, calcifications, reactive bone and a grenz zone separating the lesional tissue from the superficial epithelium.<sup>1,8,14</sup> Similar to peripheral, CGCG also comprises of two major cell population, *i.e.* the spindle to fusiform shaped cells and prominent multinucleated giant cells dispersed in a fibroblastic stroma. The giant cells are irregularly distributed and often found abundantly near areas of haemorrhage. Other features include macrophages, deposition of hemosiderin, extravasated erythrocytes, osteoid material, dystrophic calcification metaplastic ossification at the periphery and predominantly mononuclear inflammatory infiltrate.<sup>4,6</sup> The aggressive forms show an increased mitotic activity and differences in nuclear variables in multinucleated giant cells.<sup>10</sup> In addition a recent study demonstrated that mean cannibalistic giant cell frequency was greater in aggressive form of CGCG compared to the non-aggressive CGCG.<sup>19,20</sup>

Management of PGCG consists of surgical excision including the base of the lesion as well as elimination of any local contributing factors.<sup>13</sup> Two of the largest case series have reported its recurrence rate to be 10.5% (3 year follow-up) and 17.5%.<sup>1,14</sup> The possible causes of recurrence of PGCG cited in the literature includes persistence of etiological factors and lack of inclusion of the periosteum or entire base of the lesion in the excised specimen.<sup>3,8,11</sup> Treatment of CGCG varies from surgical excision with curettage of the remaining bone to en-bloc resection with reconstruction. The aggressive form may be further managed with other approaches such as radiation, systemic application of calcitonin, intra-lesional injections of corticosteroids, interferon injections and laser therapy.<sup>12</sup> The recurrence rate of CGCG ranges from 11%–49% to 37.5%–70% based on several studies. The aggressive form as well as lesions occurring in young individuals tend to have a higher recurrence rate.<sup>4,6</sup>

## Conclusions

PGCG is a common reactive lesion of the pediatric age group with barely any complications. However, in the present case, the recurrence of PGCG as central lesion was an enthralling phenomena. It is to a great extent debatable, based on the case, as whether PGCG truly represents a peripheral variant of the central lesion or it was merely two separate lesions occurring



**Figure 2.** A) Extra-oral photograph showing diffuse ill-defined swelling at the body of mandible (black arrow). B) Intra-orally, a swelling is seen on the buccal aspect of alveolar mucosa with mild obliteration of muco-buccal fold. C) Orthopantomogram showing well-defined multi-locular radiolucent lesion extending from distal surface of right mandibular canine to the distal root of right mandibular molar. D) Photomicrograph showing numerous giant cells scattered in the fibro-cellular stroma with evidence of cannibalistic giant cell (black arrow).

in the same location of the jaw. To conclude, the present case is an unusual presentation and first case report on PGCG re-occurring as CGCG. It intrigues to further explore the possible histogenesis of the giant cell lesions of the jaws.

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