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CASE REPORT

Giant cell peripheral granuloma: post-surgical recurrence. Literature review and clinical case report

Granuloma periférico de células gigantes: recidiva postquirúrgica. Revisión de la literatura y reporte de un caso clínico

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ABSTRACT

Giant cell peripheral granuloma is defined as a non-neoplastic soft-tissue lesion caused by a hyperplastic reaction resulting from trauma or local inflammation. Clinically it can be observed as an asymptomatic nodule, generally exhibiting a reddish-bluish hue and variable diameter. It frequently affects marginal gingival tissue. Histologically, it is characterized by the proliferation of mononucleated and multi-nucleated giant cells. In general, treatment consists of surgical extirpation and curettage of affected bone walls. Recurrence is a distinct possibility. In the present paper, a scientific literature review is presented along with the presentation of a clinical case of a 14 year old patient diagnosed with Giant cell peripheral granuloma: the lesion was surgically removed using an electric scalpel. The lesion recurred 4 weeks after surgery. Epidemiology of the case was reviewed, along with its clinical, radiographic and histological characteristics. Available therapeutic options and protocols were equally reviewed as well as issues related to differential diagnosis of hyperplastic reactive lesions of the periodontal complex. Priority was given to the causes of the lesion's recurrence.

RESUMEN

El granuloma periférico de células gigantes se define como una lesión de tejidos blandos no neoplásica, ocasionada por una reacción hiperplásica como consecuencia de un traumatismo o inflamación local. Clínicamente se observa como un nódulo asintomático, generalmente de coloración rojiza azulada de diámetro variable y que afecta frecuentemente la encía marginal. Histológicamente se caracteriza por la proliferación de células gigantes mononucleadas y multinucleadas. En general, su tratamiento consiste en la exéresis quirúrgica más legrado de las paredes óseas afectadas, pudiendo existir la posibilidad de recidiva. A continuación se presenta una revisión de la literatura, y se describe un caso clínico diagnosticado como granuloma periférico de células gigantes en un paciente de 14 años, cuya lesión fue removida quirúrgicamente utilizando electrobisturí, evidenciando posterior recidiva. Se discute la epidemiología, características clínicas, radiográficas e histológicas de dicha patología, así como las posibles opciones terapéuticas y protocolos. Además, se comentan brevemente los aspectos relacionados al diagnóstico diferencial de las lesiones reactivas hiperplásicas del complejo periodontal, priorizando las posibles causas de la recidiva.

Key words: Giant cell peripheral granuloma, giant cell epulis, gingival overgrowth, giant cell granuloma.
Palabras clave: Granuloma periférico de células gigantes, épulis de células gigantes, sobrecrecimiento gingival, granuloma de células gigantes.

INTRODUCTION

Giant cell peripheral granuloma (GCPG) is the most frequent lesion of this histological profile found in the jaws.[1] It is an infrequent lesion. It is considered a reactive, extra-osseous, exophytic and non-neoplastic lesion, originating from the periostium or periodontal ligament. It mainly appears in marginal gums and alveolar mucosa of totally or partially dentate patients. It is also known as giant cell epulis, osteoclastoma, repair cell granuloma or giant cell hyperplasia. It is important

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to differentiate it from giant cell central granuloma (GCCG), which is an intra-osseous, destructive, aggressive lesion found in the anterior section of the jaws, and is also composed of mono-nucleated giant cells.[2] Nevertheless, greater prevalence of GCPG over GCCP has been observed (3:1).[3]

Drs. Lipa and Dan[4] mentioned several possible etiologies for GCPG. Nevertheless, the etiology of GCPG still remains uncertain. Among the possible GCPG causes, the following can be mentioned among many others: dental extraction procedures, periodontal surgery, presence of local irritant agents, (dental biofilm and dental calculus), overflowing restorations, indiscriminate use of toothpicks, chronic infection, foodstuff impaction and fractured teeth.[3-13] Wolfson & al,[14] reported in 1989 a GCPG case in a patient initiating orthodontic treatment. Other authors[15-17] reported this alteration in patients with hormonal unbalance associated to hyperparathyroidism.

No ethnic predilection associated to the lesion has so far been described. GCPG can have its onset in patients of all ages, nevertheless it has been mainly found in groups of patients between the third and seventh decade of life. Females exhibited a slightly higher percentage than males (2:1).[1,15,18-22] The reason for this predilection was probably related to the influence of female sex hormones at the onset or during the development of the granuloma. Nevertheless, research results have not achieved to establish a link between both entities, and have yielded inconclusive and confusing results.[23,24] Clinically, the lesion is described as a dome-shaped tumefaction, with a firm, sessile base, of dark-red, bluish-red and / or purplish red hue (areas particularly susceptible to epithelial ulceration).[25] It exhibits a smooth and shiny surface, measures from 0.5 to 2.0 cm in diameter, is of soft or gelatinous consistency, exhibits slow growth around one or more teeth. In some instances, dental mobility or even dental displacement are elicited. GCPG is a painless lesion, which causes symptoms only in cases of ulceration or super-infection. Hemorrhage after meals or dental brushing is a frequent finding. Greater predilection for the mandibular area has been observed, specifically in the pre-molar and molar region.[25] Dr Sapp[2] mentioned the fact that an inter-dental papilla might be involved in the lesion, even though this fact is not considered a pathognomonic sign. According to Dr Flaitz,[26] there could be radiographic signs of bone involvement, such as alveolar bone superficial resorption and slight broadening of the periodontal ligament space at the apical level of affected teeth. In edentulous areas, it has been observed that cortical bone presents a concave resorption zone underneath the lesion (flattening).[15] Radiographic records are important, since, although GCPG is a lesion pertaining to soft tissues, a radiographic image can indicate whether the lesion is a peripheral expression of a central lesion, (GCCG) or whether there is erosion in the underlying cortical bone. The aforementioned is relevant when speaking about differential diagnosis and therapeutic proposals.[15] GCPG treatment consists on the surgical extirpation of the lesion, with curettage of the bony base, and elimination of irritant factors in order to prevent recurrence. This procedure can be undertaken with CO_2 laser or an electrocautery. Nevertheless, some authors recommend the use of a cold scalpel, since this allows surgical curettage of lesions with bone involvement.[1]

CLINICAL CASE PRESENTATION

Fourteen year old female patient. Medical history did not reveal systemic alterations, blood chemistry was non-contributory. The patient attended the clinic seeking removal of a gingival epulis located at the premolar area of quadrant number IV. Clinical examination revealed a sessile-based, shiny, purplish-red, nodular lesion measuring ± 1.5 centimeters. The lesion was present in the marginal gingival tissue, from the vestibular side of

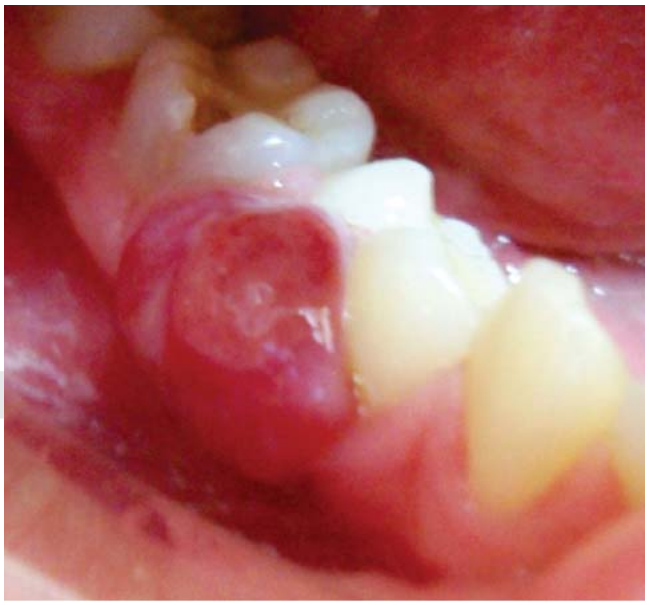


Figure 1. Sessile-based exophytic reddish nodular lesions with smooth surface, present in the marginal gingival tissue from 4-4 to the 4-6 medial portion.

tooth 44 up to the mesial portion of tooth 46 *(Figure 1)* without compromising the alveolar mucosa located in that area. The lesion was interfering with the chewing process, as well as with the patient´s aesthetics. Multiple carious lesions were equally found as well as no history of previous orthodontic devices. Radiographic examination of compromised teeth revealed absence of bone involvement, root resorption or increase of periodontal ligament space *(Figure 2)*. Next to the gingival lesion, it was observed that tooth 46 presented grade 4 mesio-occlusal caries, with painful symptoms and irreversible pulpitis diagnosis. Epulis treatment consisted of lesion extirpation; the procedure was achieved with electrocautery, having previously infiltrated the area with 2% lidocaine with 1: 80,000 epinephrine *(Figure 3)*. The procedure was completed uneventfully, harvested tissue was sent to be histo-pathologically analyzed *(Figure 4)*. This latter analysis revealed ulceration of the gingival mucosa, proliferation of giant cells with hemosiderin pigmentation in macrophages as well as fibrous stroma. All the aforementioned characteristics were consistent with diagnosis of giant cell peripheral granuloma *(Figure 5)*. Twenty one days after the surgical procedure, tooth 46 was extracted according to the patient´s instructions. The patient reached this decision due to financial reasons. Four months after the surgical removal of the soft tissue lesion, the patient attended the clinic exhibiting gum enlargement, with similar characteristics to the initial lesion. This suggested recurrence of the lesion. The patient is presently under regular control *(Figure 6)*.

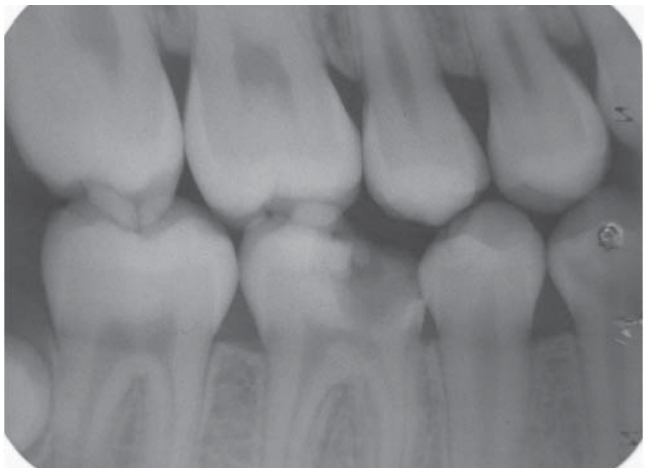


Figure 2. Radiographic image showing uncompromised underlying bone.

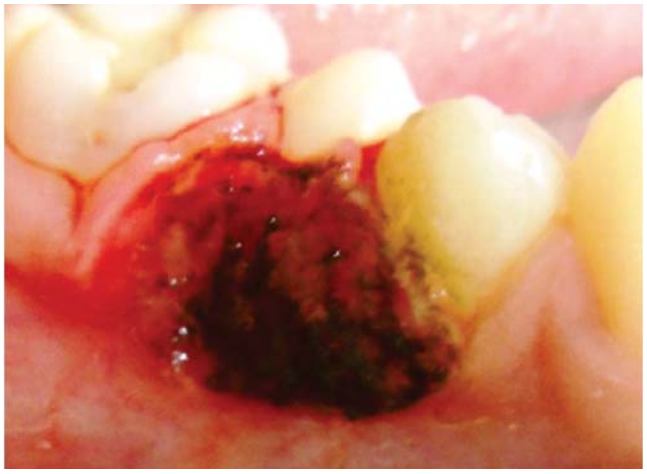
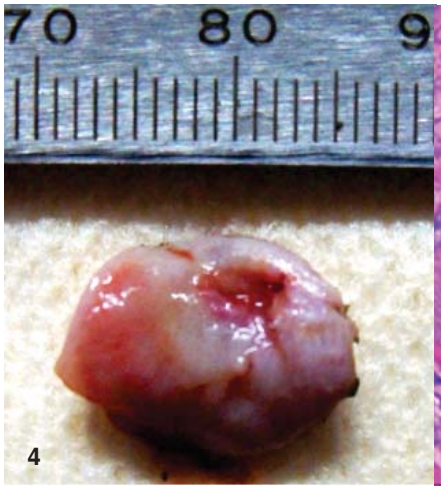
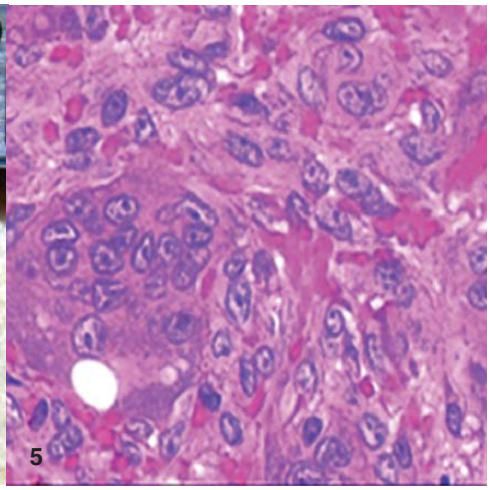


Figure 3. Gingival epulis removal with an electrical scalpel.





Figures 4 and 5.

Histological and macroscopic aspect of the lesion. Giant cell proliferation with pigmentation of hemosiderine in macrophages and fibrous stroma (HE x 250) can be observed.

DISCUSSION

Scientific literature widely associates GCPG to chronic inflammatory processes which affect a specific area within the oral cavity. Dr Rosember et al.[25] presented the study of 220 patients who had been diagnosed with hyperparathyroidism; in this sample, 4.5% of patients (n = 10) presented GCPG. Dr Falashini[27] mentioned the case of a 25-year-old man with poor oral hygiene. The patient was remitted to the clinic for extraction of tooth 15. One week after the procedure, the patient exhibited an exophytic lesion in the treated area. Histological examination revealed diagnosis of GCPG. The dental-medical history of the patient described in our case, did not present clear evidence of the chronic inflammatory process which triggered the primary apparition of the lesion. Likewise, no history was found of any type of endocrine alteration which might have supported the outstart of the lesion. Ozcan-Cengiz[28] reported the first case of GCPG at the head of the articular condyle. He described it as a painful, pre-auricular mass with a two years evolution. This finding was relevant since it eliminated the exclusive association of GCPG with the oral cavity as well as with the lack of symptoms associated with this lesion, as it was, during decades, previously described in scientific literature.[15] From the clinical perspective, the average size of a GCPG lesion is about two centimeters. Lesions of greater size are generally associated to deficient levels of oral hygiene as well as presence of xerostomy. The potential size of untreated GCPG lesions is as yet unknown, since these lesions are removed before reaching their maximum growth level.[4]

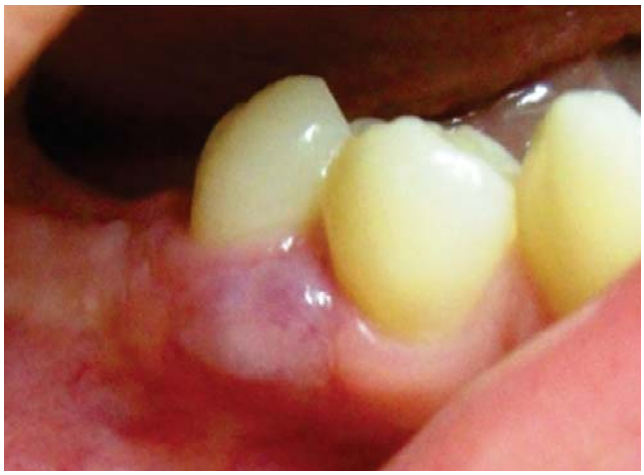


Figure 6. Onset of recurrence of lesion at vestibular gingival margin and papillary gum between 1-4 and 1-5

Drs. Robbins & Cotran[29] defined this type of granuloma as a focus of chronic inflammation consisting of microscopic aggregation of macrophages which transform into epithelial-like cells, surrounded by a rim of mononuclear leucocytes, mainly lymphocytes, as well as occasionally plasmatic cells. It is also mentioned that epithelioid cells fuse to form giant cells in the granuloma periphery or center. Dr. Liu et al.[30] based on immune-histochemical and enzyme-histochemical tests, described that GCPG multi-nucleated giant cells possessed cellular characteristics which were compatible with osteoclasts, cells responsible for bone resorption and remodeling of the human skeletal system. In this respect, this osteoclastic cellular pattern could justify the presence of bone resorption observed in edentulous ridges associated with GCPG (erosion of alveolar bone) as was described by some authors.[15,25] Nevertheless, Dr Arzole[35] presented the hypothesis that GCPG possessed low bone destruction capacity, since they presented fewer and smaller-sized giant cells when compared to GCCG.

Table I. Chronological review of GCPG recurrence after surgical removal as reported in scientific literature.

Reference	Year	Recurrence /total	Recurrence (%)
Giansanti & Waldron[32]	1969	36/720	5.0
Katsikeris et al.[22]	1988	22/224	9.8
Bhaskar et al.[33]	1971	6/50	12.0
Eversole & Rovin[12]	1972	12/63	19.0
Andersen et al.[34]	1973	24/34	70.6
Mighell et al.[25]	1994	14/63	22.2
Total		114/1154	9.9

GCPG treatment, besides surgical extirpation, consists on the suppression of etiological factors.[22,29] Dr Angie[1] mentioned the fact that no differences were found when comparing extirpation with cold scalpel or CO_2 laser. The use of the latter offers advantages like less trans-operative bleeding, wound sterilization, avoidance of the need for sutures, and lesser post-operative discomfort for the patient.[31] Nevertheless, use of electric scalpel as well as cutting laser is limited in lesions that affect adjacent bone; treatment of these lesions requires meticulous surgical curettage.

Even though different authors *(Table I)* have reported variable figures with respect to recurrence, evidence on recurrence causes is limited and inconclusive.

Based on consulted scientific literature, anamnesis and conducted treatment, we can offer five probable causes for GCPG lesion recurrence:

1. Premature extraction of lesion-compromised tooth. Three weeks after primary lesion extirpation, tooth 46 was extracted. This coincides with Falaschini's[27] theory, which clearly associates dental extraction as triggering factor for lesion recurrence.
2. Lack of intra-operative periodontal therapy. In spite of the relative suitable oral hygiene exhibited by the patient, no trans-operative periodontal therapy was conducted (scaling and root planning). This could have triggered a «sequestration» of bacterial plaque remnants which could have remained underneath the lesion during healing process, causing thus a chronic infectious focus which paved the way for a recurrence.[2,15]
3. Insufficient surgical technique. In the present case, electrical scalpel was used as the method to remove epulis. The working area of this instrument is only limited to the supra-periosteal level, and does not reach the bone. The lesion recurrence was probably due to lack of surgical curettage on bone walls.[26]
4. Hormonal alterations. In the present case it would not represent a valid diagnostic option, since the patient in her medical history, referred total absence of endocrine disorders
5. Idiopathic causes.

REFERENCES

1. Angie VCA, Leonardo BA, Cosme GE. Granuloma periférico de células gigantes. A propósito de 5 casos y revisión de la literatura. *Med Ora Patol Oral Cir Bucal*. 2005; 10: 48–57.
2. Sapp JP, Lewis RE, George PW. *Patología oral y maxilofacial*. 2a ed. España: Elsevier; 2004.
3. Junquera LM, Lupi E, Lomabardia E, Fresno MF. Multiple and synchronous peripheral giant cell granulomas of the gums. *Ann Otol Rhinol Laryngol*. 2002; 111: 751-753.
4. Bodner L, Peist M, Gatot A, Fliss DM. Growth potential of peripheral giant cell granuloma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1997; 83: 548-551.
5. Breault LG, Fowler EB, Wolfgang MJ, Lewis DM. Peripheral giant cell granuloma: a case report. *Gen Dent*. 2000; 48: 716-9.
6. Gandara-Rey JM, Pacheco Martins Carneriro JL, Gandara-Vila P, Blanco-Carrion A, Garcia-Garcia A, Madrinan-Grana P, Martin MS. Peripheral giant cell granuloma. Review of 13 cases. *Med Oral*. 2002; 7: 254-259.
7. Pandolfi PJ, Felefli S, Flaitz CM, Johnson JV. An aggressive peripheral giant cell granuloma in a child. *J Clin Pediatr Dent*. 1999; 23: 353-355.
8. Ceballos-Salobreña A, Bermejo-Fenoll A, Aguirre-Urizar JV, Peñarrocha-Diago M. Tumores benignos de la mucosa oral. *Med Oral*. 1995.
9. Bhaskar NS, Cutright DE, Beasley JD, Pérez B. Giant cell reparative granuloma (perihperal): report of 50 cases. *J Oral Surg*. 1971; 29: 110-115.
10. Andersen L, Fejerskov O, Philipsen HP. Oral giant cell granulomas. A clinical and histological study of 129 new cases. *Acta Pathol Microbiol Scand*. 1973; 81: 606-616.
11. Dayan P, Buchner A, Spirer S. Bone formation in peripheral giant cell granuloma. *J Periodontol*. 1990; 61: 444-446.
12. Eversole LF, Rovin S. Reactive lesions of the gingiva. *J Oral Pathol*. 1972; 1: 30-38.
13. Buchner A, Shnaiderman-Shapiro A, Vered M. Relative frequency of localized reactive hyperplastic lesions of the gingiva: a retrospective study of 1675 cases from Israel. *J Oral Pathol Med*. 2010; 39: 631-638.
14. Wolfson L, Tal H. Peripheral giant cell granuloma during orthodontic treatment. *Am J Orthod Dentofac Orthop*. 1989; 96: 519-523.
15. Shafer WG, Levy BM. *Tratado de Patología Bucal*. 4a ed. 1986.
16. Parbatani R, Tinsley GF, Danford MH. Primary hyperparathyroidism presenting as a giant-cell epulis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998; 85: 282-284.
17. Burkes EJ, White RP. A peripheral giant-cell granuloma manifestation of primary hyperparathyroidism: report of two cases. *JADA*. 1989; 118: 62-64.
18. Nedir R, Lombardi T, Samson J. Recurrent peripheral giant cell granuloma associated with cervical resorption. *J Periodontol*. 1997; 68: 381-384.
19. Giansanti JS, Waldron CA. Peripheral giant cell granuloma: review of 720 cases. *J Oral Surg*. 1969; 27: 787-791.
20. Bonetti F, Pelosi G, Martignoni G, Mombello A, Zamboni G, Pea M, Scarpa A, Chilosi M. Peripheral giant cell granuloma: evidence for osteoclastic differentiation. *Oral Surg Oral Med Oral Pathol*. 1990; 70: 471-475.
21. Kfir Y, Buchner A, Hartsen LS. Reactive lesions of the gingiva: a clinicopathological study of 741 cases. *J Periodontol*. 1980; 51: 655-661.
22. Katsikeris N, Kakarantza-Angelopoulou E, Angelopoulos AP. Peripheral giant cell granuloma: clinicopathologic study of 224 new cases and review of 956 reported cases. *Int J Oral Maxillofac Surg*. 1988; 17: 94-99.
23. Littler BO. Central giant cell granuloma of the jaw–a hormonal influence. *Br J Oral Surg*. 1979; 17: 43-46.
24. McGowan DA. Central giant cell granuloma on the mandible occurring in pregnancy. *Br J Oral Surg*. 1969; 7: 131-135.
25. Mighell AJ, Robinson PA, Hume WJ. Peripheral giant cell granuloma: a clinical study of 77 cases from 62 patients, and literature review. *Oral Diseases*. 1995; 1: 12-19.

26. Flaitz CM. Peripheral giant cell granuloma: a potentially aggressive lesion in children. *Pediatr Dent*. 2000; 22: 232-233.
27. Falaschini S, Ciavarella D, Mazzanti R, Di Cosola M, Turco M, Escudero N, Bascones A, Lo Muzio L. Granuloma periférico de células gigantes: análisis inmunohistoquímico de la población celular en tres casos clínicos. *Av Odontoestomatol*. 2007; 23 (4): 181-188.
28. Ozcan C, Apaydin FD, Apa DD. Peripheral giant cell granuloma of the mandibular condyle presenting as a preauricular mass. *Eur Arch Otorhinolaryngol*. 2005; 262: 178-181.
29. Kumar V, Abbas AK, Fausto N. *Robbins y Cotran: Patología estructural y funcional*. 7a ed. España: Ed. Elsevier; 2005.
30. Liu B, Yu SF, Li TJ. Multinucleated giant cells in various forms of giant cell containing lesions of the jaws express features of osteoclasts. *J Oral Pathol Med*. 2003; 32: 367-375.
31. España-Tost AJ, Velasco-Vivancos V, Gay-Escoda C, Berini-Aytes L, Arnabat-Dominguez J. Aplicaciones del láser de CO_2 en Odontología. RCOE. Madrid: Ergon; 1995.
32. Giansanti JS, Waldron CA. Peripheral giant cell granuloma: review of 720 cases. *Oral Surg Oral Med Oral Pathol*. 1969; 27: 787-791.
33. Bhaskar SN, Cutright DE, Beasley JD. Giant cell reparative granuloma (peripheral): report of 50 cases. *J Oral Surg*. 1971; 29: 110-115.
34. Andersen L, Fejerskov O, Philipsen HP. Oral giant cell granulomas: a clinical and histological study of 129 cases. *Acta Pathol Microbiol Imminol Scand Sect A*. 1973; 81: 606-616.
35. Arzola-Rober JF. *Comparación citométrica e inmunohistoquímica de los granulomas a células gigantes centrales y periféricos* [Tesis Doctoral]. Santiago, Chile: Universidad de Chile; 2005.

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