



Clinical case

Hybrid lesion: management of an unusual pathology

Lesión híbrida: manejo de una patología inusual

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ABSTRACT

Hybrid lesions are considered a rare pathology that present elements of different entities, each of which have a tumor category. There are currently less than ten reported cases of hybrid lesions showing association of a central giant cell lesion and an ossifying fibroma. Since a treatment protocol for this type of pathologies is not well established in the literature, we present a case of integral management, including rehabilitation, based on the review of the literature. This is a 31-year-old female patient with an initial diagnosis of central giant cell lesion in the left mandibular body, who was treated with intralesional triamcinolone, finding no response after six weeks of treatment, so we decided to do a block resection of the lesion and simultaneous reconstruction with a free anterior iliac crest graft, obtaining a definitive histopathological result of a hybrid lesion (central giant cell lesion plus ossifying fibroma), later implant-supported prosthetic rehabilitation was performed. In cases of hybrid lesions, we consider that surgical management is adequate, given the particular behavior of said entity that does not respond adequately to pharmacological management, we recommend avoiding the use of antiresorptive medications since it would prejudice

RESUMEN

Las lesiones híbridas se consideran una patología rara que presenta elementos de diferentes entidades, cada una de las cuales tiene una categoría tumoral. En la actualidad hay menos de diez casos notificados de lesiones híbridas que muestran la asociación de una lesión central de células gigantes y un fibroma osificante. Dado que un protocolo de tratamiento para este tipo de patologías no está bien establecido en la literatura, presentamos un caso de manejo integral, incluyendo la rehabilitación, basado en la revisión de la literatura. Se trata de una paciente de 31 años con un diagnóstico inicial de lesión central de células gigantes en el cuerpo mandibular izquierdo, que fue tratada con triamcinolona intralesional, sin encontrar respuesta tras seis semanas de tratamiento, por lo que decidimos realizar una resección en bloque de la lesión y la reconstrucción simultánea con un injerto libre de cresta ilíaca anterior, obteniendo un resultado histopatológico definitivo de lesión híbrida (lesión central de células gigantes más fibroma osificante), posteriormente se realizó una rehabilitación protésica implantosoportada. En los casos de lesiones híbridas, consideramos que el manejo quirúrgico es adecuado, dado el comportamiento particular de dicha entidad que no responde adecuadamente al manejo farmacológico, recomendamos evitar el uso de

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the result of a subsequent surgical and reconstructive treatment.

Keywords: Central giant cell lesion, hybrid lesion, anterior iliac crest free graft, implant-supported rehabilitation.

medicamentos antirresortivos ya que perjudicaría el resultado de un tratamiento quirúrgico y reconstructivo posterior.

Palabras clave: Lesión central de células gigantes, lesión híbrida, injerto libre de cresta ilíaca anterior, rehabilitación con implantes.

INTRODUCTION

Hybrid lesions are extraordinarily rare entities that present elements of different pathologies, each of which have a tumor category.^{1,2} There are currently less than ten cases reported of hybrid lesions showing association of a central giant cell lesion (CGCL) and a ossifying fibroma (OF). The World Health Organization in 2017 defines CGCL as a benign osteolytic proliferation, but sometimes locally aggressive, consisting of giant multinucleated osteoclast-type cells in a fibrous tissue stroma with hemorrhagic deposits and hemosiderin.³ OF is defined as a benign bone neoplasm that affects the facial skeleton,³ it has been divided into conventional OF, also called cement-ossifying fibroma and juvenile OF, which is subdivided into trabecular and psammomatoid (*Figure 1*).⁴ Within the possible pathogenesis of hybrid lesions involving giant cells, it is suggested that CGCL associated with fibrous lesions may be the product of a secondary reaction in response to changes in the original stroma of the lesion, where theoretically there is an activation of the osteoclasts as well as their successive transformation in to multinucleated giant cells all this mediated by paracrine mechanisms.⁵ Objective: management of these injuries have not been established to the present day, since cases reported in the literature are scarce,^{1,2,5,6} therefore, the objective of this article is to present a case and it's integral treatment of this pathology, based on the review of the literature.

CLINICAL CASE

A 31-year-old female attended our office referred by her orthodontist due to a radiographic finding of a unilocular radiolucident image of approximately 3.5 cm with radiopaque areas and a sclerotic halo, located in the region of the left mandibular body. At the physical examination it presents its dental formula complete, oral mucous with adequate coloration and hydration, absence of dental mobility, without volume increase in it's left mandibular region, the patient denies sensory

changes (*Figure 2*). At the presurgical assessment no alterations were observed; exploratory puncture was performed (without obtaining material), incisional biopsy was subsequently carried out, with the histopathological result compatible with CGCL, which is why parathyroid profile, calcium and phosphate were requested, the results were found within normal parameters, ruling out the diagnosis of a brown tumor. We began with a weekly protocol infiltrating 1 cm³ composed of a mixture of triamcinolone and 2% lidocaine with epinephrine 1: 100,000 (in a 50/50 ratio) for every cubic centimeter of lesion. After two months of infiltrative treatment, no changes in it's radiographic characteristics were observed, so we decided to escalate to a surgical management. Under the effects of balanced general anesthesia, marginal mandibular resection of approximately 4.5 cm was performed, with simultaneous application of a free anterior iliac crest graft and reconstruction plate placement (*Figure 3*). The surgical piece was sent for it's histopathological study (*Figure 4*) which reported: a proliferation of a well-vascularized mesenchymal tissue, with the presence of abundant giant cells of foreign body type on a stroma of mononuclear cells, transition areas with a proliferation of cells tapered with bone metaplasia, some with osteoblastic edging and areas with different degrees of basophilia. The definitive diagnosis was: central giant cell lesion (CGCL) with ossifying fibroma (OF). Three weeks after the surgery, the patient presented graft exposure, which was managed with antibiotic therapy, strict oral hygiene, use of chlorhexidine gel and endodontic treatment of the following teeth: central incisor, lateral incisor and second lower left molar, which presented pulp necrosis. The therapeutics used allowed the closure of the exposure by second intention (granulation tissue). After six months of evolution, we observed a loss of 50% in bone volume of the reconstructed area, so we decided to perform guided bone regeneration using lyophilized human graft, platelet-rich plasma and titanium mesh (under local anesthesia); the left lower lateral incisor was removed by grade III mobility; the patient evolved satisfactorily. Subsequently,

a rehabilitation protocol was performed using an implant-supported prosthesis with five implants (DIO, Korea) (Figure 5). Currently, the patient is coursing her third year after surgery with no evidence of recurrence.

DISCUSSION

The CGCL were initially described as an analogous lesions of the ones found in long bones, later Jaffe called them «giant cell reparative granuloma», a term that was used for many years; however, because it show no repair characteristics this term was omitted.⁷ These represent the 7-10% of maxillary lesions, showing a predilection for the female gender and being more prevalent before the age of 30. The most frequent site of appearance is the jaw with balanced distribution between the anterior and posterior region; when they appear in the maxilla they are predominantly located in the anterior region.^{3,8} CGCL have been classified as aggressive and non-aggressive lesions, Chuong described in 1986 the clinical and histopathological characteristics of each of them. Non-aggressive lesions are asymptomatic and are usually diagnosed as a radiological finding, on the other hand, aggressive lesions are associated with pain, increased volume, sensory abnormalities, cortical perforation and root resorption.⁹ For the management of CGCL it is important to consider the possible relationship that they may present with endocrine alterations characterized by the increased of parathormone secretion, defined as hyperparathyroidism.¹⁰ Less than 2% of this pathology cases debuted with bone lesions in the facial skeleton, known as brown tumor,¹¹ however it is pertinent to discard this diagnosis by laboratory

studies prior to the establishment of a surgical or pharmacological treatment. The treatment of CGCL depends on their clinical aggressiveness. Within the therapeutic options we find different types like surgical, pharmacological, radiotherapy and combined treatment. Other surgical management options have been described for mandibular lesions like curettage with or without adjuvant therapy such as cryosurgery, peripheral osteotomy and Carnoy solution,¹² in aggressive cases the resection with 5 mm margins is recommended; since the lesion is not characterized by presenting invasion to the perineural tissue the preservation of the inferior alveolar nerve should be considered, performing skeletonization if necessary.^{13,14} Calcitonin agents (nasal and infiltrated), triamcinolone with different protocols, pegylated and non-pegylated interferon alpha and denosumab¹⁵ have been used as pharmacological agents, with a role in the treatment of aggressive and non-aggressive lesions, limiting their progression in long term follow-up and decreasing the morbidity of surgical treatment.¹⁴ In our case, when obtaining the initial histopathological result of CGCL and given the non-aggressive behavior of the lesion, we initially opted for pharmacological therapy with triamcinolone, since there is evidence in the scientific literature of total remission of lesions in a period of six weeks;¹³ the response to the intralesional steroid has been related to the amount of glucocorticoid receptors present in multinucleated giant cells, with a better response to a greater number of receptors,¹⁶ however there was no remission or reduction in our case, so we decided to perform a surgical treatment obtaining the definitive histopathological result of hybrid lesion. We associate the failure of the initial pharmacological

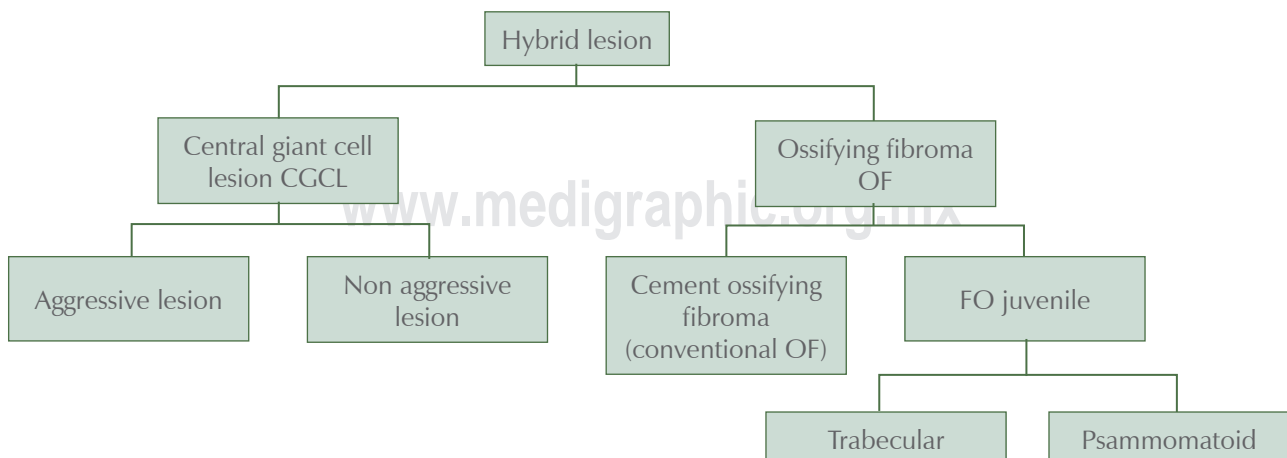


Figure 1: Central giant cell lesion and ossifying fibroma classification.

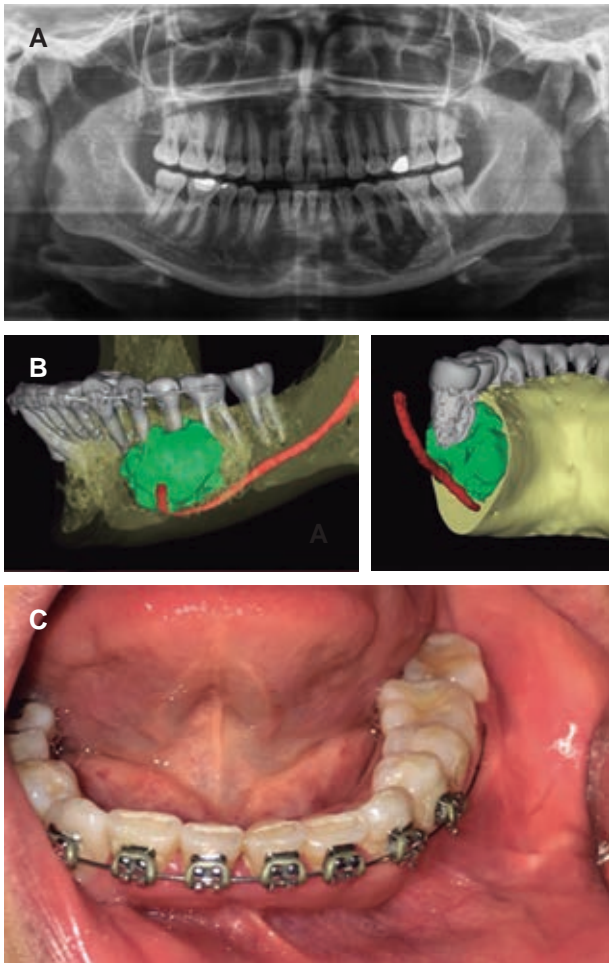


Figure 2: Clinical and imagenologic findings. **A)** Orthopantomography showing osteolytic area in the left mandibular body. **B)** Volumetric reconstruction of the same lesion. **C)** Clinical image, not showing changes in the oral mucosa, or apparent increase in volume in the left mandibular body.

therapy with the presence of cells of different lines in the same pathology. Hybrid lesions of CGCL with other entities such as: odontogenic fibroma,^{17,18} aneurysmal bone cyst,¹⁹ fibrous lesions,^{5,20,21} ameloblastoma^{2,22} and keratocystic odontogenic tumor²³ have been described. Based on the published cases of hybrid lesions of CGCL and OF,^{1,2,5,6} a higher frequency is observed in the female gender with five cases, appearing between the ages five to 68 years, with five cases reported in the mandible with a predominance in the posterior region, Kaplan reported the recurrence of one of his cases at a three years follow-up,^{2,6} these data is consistent with the characteristics of our patient, which has not presented recurrence at two years follow-up. The differential diagnosis of these lesions is a challenge

because they do not have a well-defined behavior.¹ Surgical treatment was proposed in the published cases, in case of marginal mandibular resections, the objective of the reconstruction is to achieve the placement of implants to allow prosthetic rehabilitation. The treatment used for the reconstruction of our patient was a free anterior iliac crest graft, due to literature recommendation of the use of free grafts for defects less than 5 mm. The anterior iliac crest is an adequate source of corticospongeous graft allowing osseointegration of dental implants,^{24,25} with survival and success rates of 96.7% and 93.3% respectively.²⁶ Infection, dehiscence and graft loss, are among the most common complications associated with free grafts for mandibular reconstruction, with a success

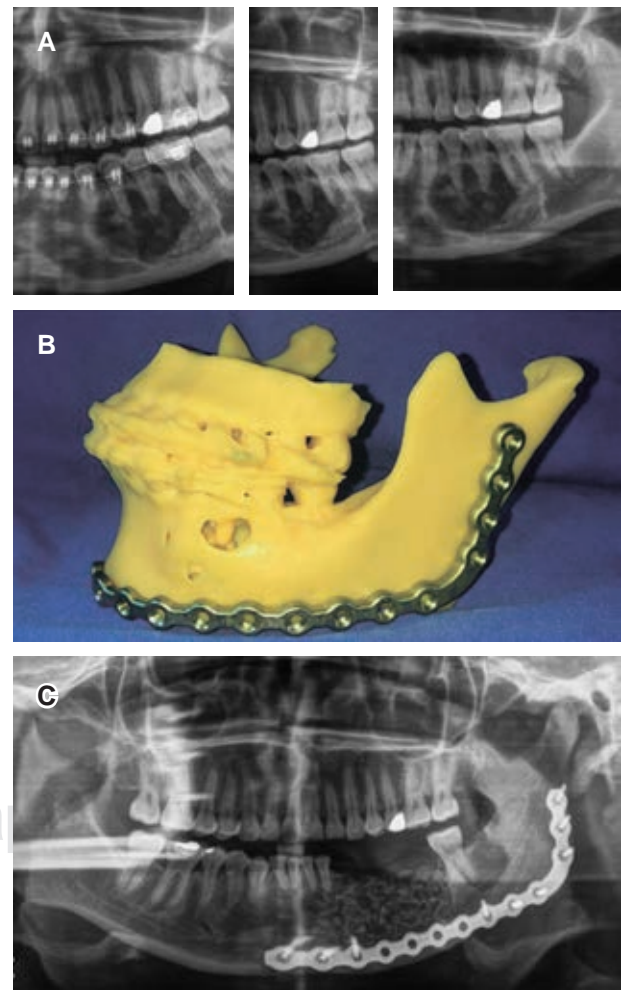


Figure 3: **A)** Initial comparative orthopantomography, one month and six weeks after infiltration with triamcinolone. **B)** Stereolithography used for adaptation of reconstruction plate. **C)** Immediate postresection and reconstruction image.

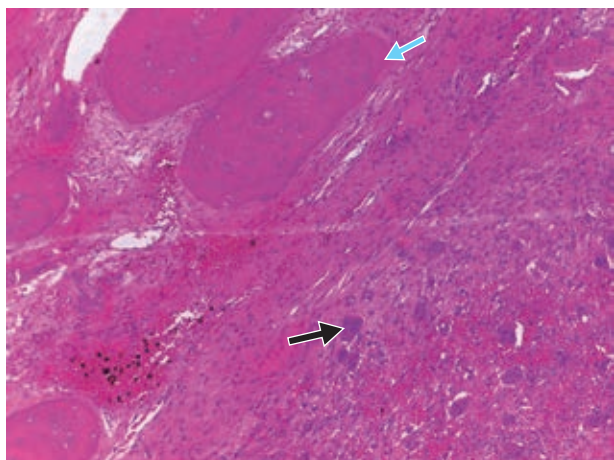


Figure 4: H&E 100× photomicrograph showing a collision tumor consisting of a giant multinucleated cells proliferation (black arrow), separated by a fibroconnective tissue band from a fibro-osseous component displaying osteoid-like material and abundant fibroblasts (blue arrow) consistent with ossifying fibroma.

rate of 87.6%.²⁷ In our case, graft exposure was presented, in association with a tooth that presented pulp necrosis neighboring the defect, which was solved with endodontics of the teeth involved. In the literature there is different data regarding the reabsorption of free grafts prior to implant placement,^{26,28-30} Chiapasco in his publication reports that it is higher in free grafts when compared with microvascularized grafts (3.53 mm vs 0.96 mm), however, this difference is no longer significant after the placement of dental implants;²⁶ Wilkman, in his study, presented a 2% reabsorption of the anterior iliac crest graft in the first year and a 3% reabsorption in the second year;³¹ in our case we lost approximately 50% of the graft in two months, so lyophilized human graft was placed to solve this complication. One year after this procedure, implant placement and rehabilitation was performed without complications. After two years follow-up no evidence of recurrence was seen, and the recovery of the masticatory function was achieved, improving patients life quality.

CONCLUSIONS

Hybrid lesions may not respond to pharmacological management, so surgical treatment should be considered the first option. We recommend avoiding the use of antiresorptive medication, because it could impair the results of a posterior surgical and

reconstructive treatment. Immediate reconstruction with a free anterior iliac crest graft is a predictable option in defects less than 5 cm, it is known that this

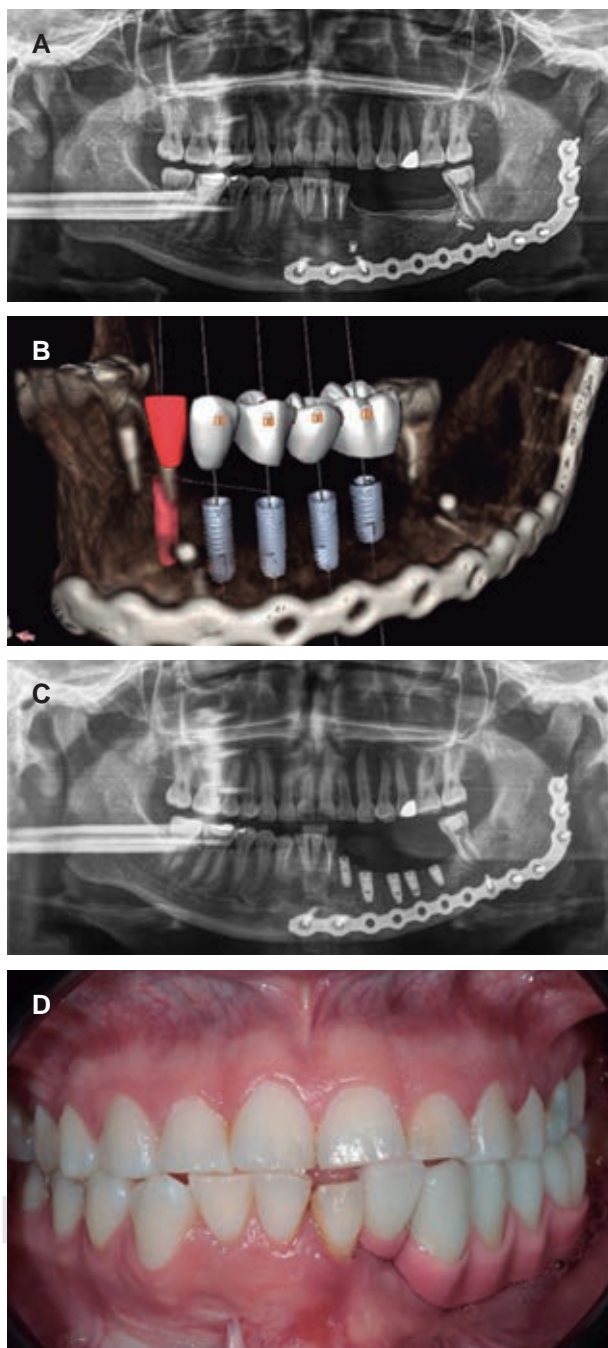


Figure 5: A) Orthopantomography after lyophilized bone graft and titanium mesh placement. B) Three-dimensional planning for implant placement. C) Control orthopantomography after dental implant placement. D) Implant supported overdenture.

option is not a complication free procedure which can be solved with the use of adjuvant grafts. The supported implant prosthetic rehabilitation allows to maintain the patient's masticatory function and quality of life. Finally, close monitoring is essential to detect possible recurrences and give them timely treatment.

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