MANAGEMENT OF ODONTOGENIC KERATOCYSTS IN GORLIN-GOLTZ SYNDROME

TRATAMENTO DE QUERATOCISTOS ODONTOGÉNICOS NA SÍNDROME DE GORLIN-GOLTZ

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ABSTRACT

Introduction: Gorlin-Goltz Syndrome is presented by a dominant genetic alteration that can lead to changes throughout the body. Among the most common changes are keratocysts, intraosseous pathological lesions with a high recurrence rate in the maxillofacial regions. Early diagnosis is extremely important, since individuals with the syndrome are susceptible to developing basal cell carcinomas in epithelial tissue. **Case Report:** Patient affected by a rare syndrome (Gorlin-Goltz Syndrome) with changes diagnosed in different regions of the body such as: keratocysts, basal cell carcinomas, chest excavatum, calcification of the cerebral falx, among others. His treatment was carried out in a multidisciplinary manner associated with surgical treatment and the use of antineoplastic medication, which resulted in significant improvement in relation to his basal cell carcinomas. **Discussion:** GGS is a rare condition, with a complex diagnosis, since the syndrome can lead. **Conclusion:** to several clinical and imaging changes, which may or may not be present in the individual. Gorlin-Goltz syndrome presents several clinical manifestations, with keratocyst lesions being one of the most important. Multidisciplinary treatment is indicated, as the syndrome presents several changes, requiring long-term monitoring of these individuals.

Keywords: *Basal Cell Nevus Syndrome, Nonodontogenic Cysts, Basal Cell Carcinoma.*

RESUMO

Introdução: A Síndrome de Gorlin-Goltz apresenta-se por uma alteração genética dominante podendo levar a alterações através do corpo. Entre as alterações mais comuns estão os ceratocistos, lesões patológicas intraósseas com alta taxa de recidiva nas regiões maxilofaciais. O diagnóstico precoce é de extrema importância, uma vez que os indivíduos que possuem a síndrome são susceptíveis a desenvolverem carcinomas basocelulares em tecido epitelial. **Relato de Caso:**

Paciente acometido por uma rara síndrome (Síndrome de Gorlin-Goltz) com alterações diagnosticadas em diversas regiões do corpo como: ceratocistos, carcinomas basocelulares, peito excavatum, calcificação de foice cerebral, entre outros. Seu tratamento foi realizado de forma multidisciplinar associado tratamento cirúrgico e uso de medicamento antineoplásico, que resultou em melhora significativa em relação a seus carcinomas basocelulares. **Discussão:** A SGG é uma condição rara, de diagnóstico complexo, uma vez que a síndrome pode levar a diversas alterações clínicas e imaginológicas, sendo ainda possível, estarem ou não presentes no indivíduo. **Conclusão:** A síndrome de Gorlin-Goltz apresenta diversas manifestações clínicas, sendo as lesões de ceratocistos uma das mais importantes. O tratamento multidisciplinar está indicado, uma vez que a síndrome apresenta diversas alterações, necessitando de acompanhamento em longo prazo desses indivíduos.

Palavras chave: *Síndrome de Nevo Basocelular, cistos odontogênicos, Carcinoma Basocelular.*

INTRODUCTION

Gorlin-Goltz Syndrome (GGS) is presented by a dominant genetic alteration causing inactivation of the PTCH11 onco-suppressor gene that intervenes in cell proliferation and survival. Its prevalence is approximately 1:50,000 to 150,000, with no sex predilection.[1]

According to Neville et al. approximately 60 to 75% of patients with the syndrome have skeletal abnormalities. Among women, 15 to 25% may develop fibroids in the ovary. Radiographically, they may present calcification of the falx cerebri, multiple odontogenic keratocysts (OK), increased head circumference, and rib anomaly, among others. Although OK lesions are closely related to Gorlin-Goltz syndrome, their main characteristic is basal cell carcinomas (BCC).[2]

Generally, the prognosis of these patients is good, and life expectancy with the syndrome is not significantly modified, however, the morbidity of complications can be substantial. Of the patients with the syndrome, about 5% to 10% manifest medulloblastoma, a malignant brain tumor of the posterior fossa, which can be the cause of early death[3]. Treatment involves aggressive surgical resection and chemotherapy.[4]

Early diagnosis is extremely important, due to the susceptibility to developing basal cell carcinomas in epithelial tissue and brain tumor. Treatment becomes challenging for professionals since the various changes require multidisciplinary and often long-term treatment.[5]

Among the most prevalent findings in GGS is OK, which is present in 65-75% of cases of the syndrome[6]. Its predilection site is in the mandible, showing 69% of involvement compared to the maxilla, which shows 31% of cases.[7]

Most OK occur in the posterior region of the body and in the region of the mandibular ramus[8]. In general, the lesion is asymptomatic until it reaches a larger size, when it exhibits an increase in volume, pain and dental involvement[9]. In the OK aspiration puncture, a straw-coloured liquid, with a thick consistency and a large amount of keratin, is characteristic.

Clinical studies have observed cystic lesions and their correlation with the syndrome, the earlier the diagnosis, the greater the probability of the patient developing too much OK throughout life, due to its recurrence rate. Therefore, the routine and shortest possible evaluation should always be carried out. [10,11]

CASE REPORT

A 38-year-old male, leukoderma patient, was referred to the Oral and Maxillofacial Surgery

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and Traumatology Service of the Polydoro Ernani de São Thiago University Hospital – HU/UFSC/EBSERH, to perform biopsies and treatment of cystic lesions present in the jaws initially diagnosed in radiographic.

A clinical examination was performed, where the presence of BCC distributed along the face was observed (Figure 1.A), ectropion in the left lower eyelid and pain complaint in the chin region and right maxillary sinus, without paresthesia.

Radiological and tomographic examination reveals the presence of extensive deficiencies with a unilocular aspect affecting the chin region measuring 2.5x2.7 cm and a lesion in the region of the right mandibular ramus measuring 2.7x0.9 cm. A third lesion communicating in the maxillary sinus near even close to the right, lateral wall into an alveolar process, extending to ethmoid cells and presenting from superior ethmoid cells, and associated with a nasal cavity process, being 3.7x2.7cm. (Figure 1.B).

Initially, the patient underwent local anaesthesia for incisional biopsy, and decompression of the lesion in the mandibular and maxillary region, however, there was an intercurrence in the apposition of the drain in the maxillary sinus region. It was moved into the cystic lesion cavity, and an attempt was made to remove the drain where it was not possible. Mucosal suturing and the situation explained to the patient (Figure 1C, 1D). At this moment, nasal decongestants, precautions and post-surgical care were prescribed, in addition to complications such as: not smoking, avoiding blowing your nose, sneezing with your mouth open, not ingesting drinks with the help of straws.

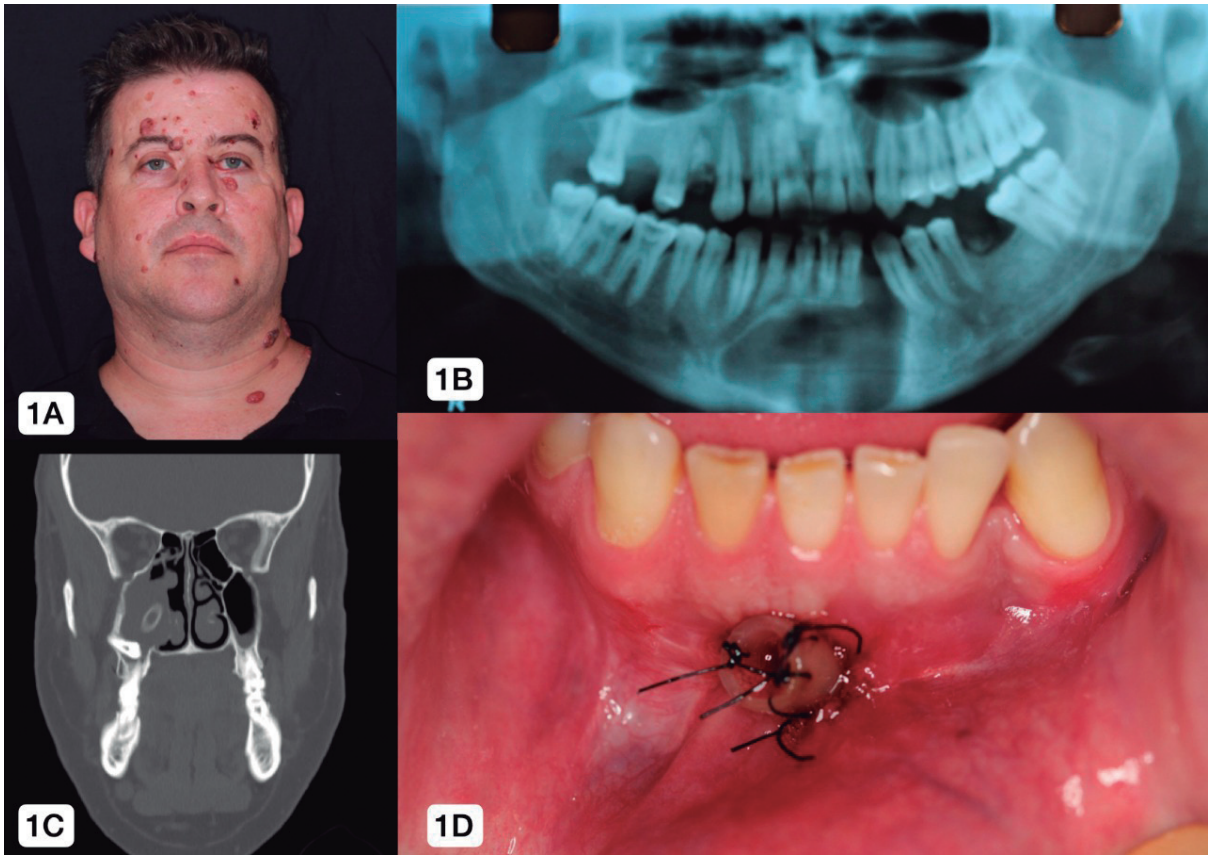

Figure 1 – **A) Frontal clinical photo at initial care B) Initial panoramic x-ray C) Face Cone Beam Tomography D) Decompression device installed in the chin region.**

It was possible to detect the presence of calcification of the falx cerebri (Figure 2A). No changes were noted in the region of the ribs or spine. (Figure 2B), In addition to the lesions of OK and chest *excavatum* (Figure 2C and Figure 2D)

In a new tomography, the presence of the drain in the maxillary sinus region was observed without great displacement, without obstruction of the right osteomeatal complex and absence of purulent secretion. It was then decided to approach the surgical centre to perform the enucleation of the lesions and a more aggressive approach to the cyst in the maxillary region.

The patient underwent surgical treatment under general anaesthesia with nasotracheal intubation. After local asepsis, local anaesthetic infiltration, intraoral incisions were made for surgical access in the symphysis region and right mandibular ramus, drain removal in the chin region and lesion enucleation, and later access in the right maxillary sinus region with drain removal. surgery followed by enucleation of the extensive cystic lesion. Adjuvant therapy was not used because it was the skull base region. Only in the mandibular region, is peripheral osteotomy under copious irrigation. (Figure 3)

Postoperative care the patient was kept on liquid and soft food for the first 48 hours, maintaining a liquid and soft diet for 05 days. After 01 postoperative days, the patient was discharged from the hospital. The patient was instructed on the correct feeding methods, as well as the hygiene methods. The patient was instructed to clean the surgical area with greater care for the first 15 days after surgery, performing oral rinse twice a day with Chlorhexidine Gluconate

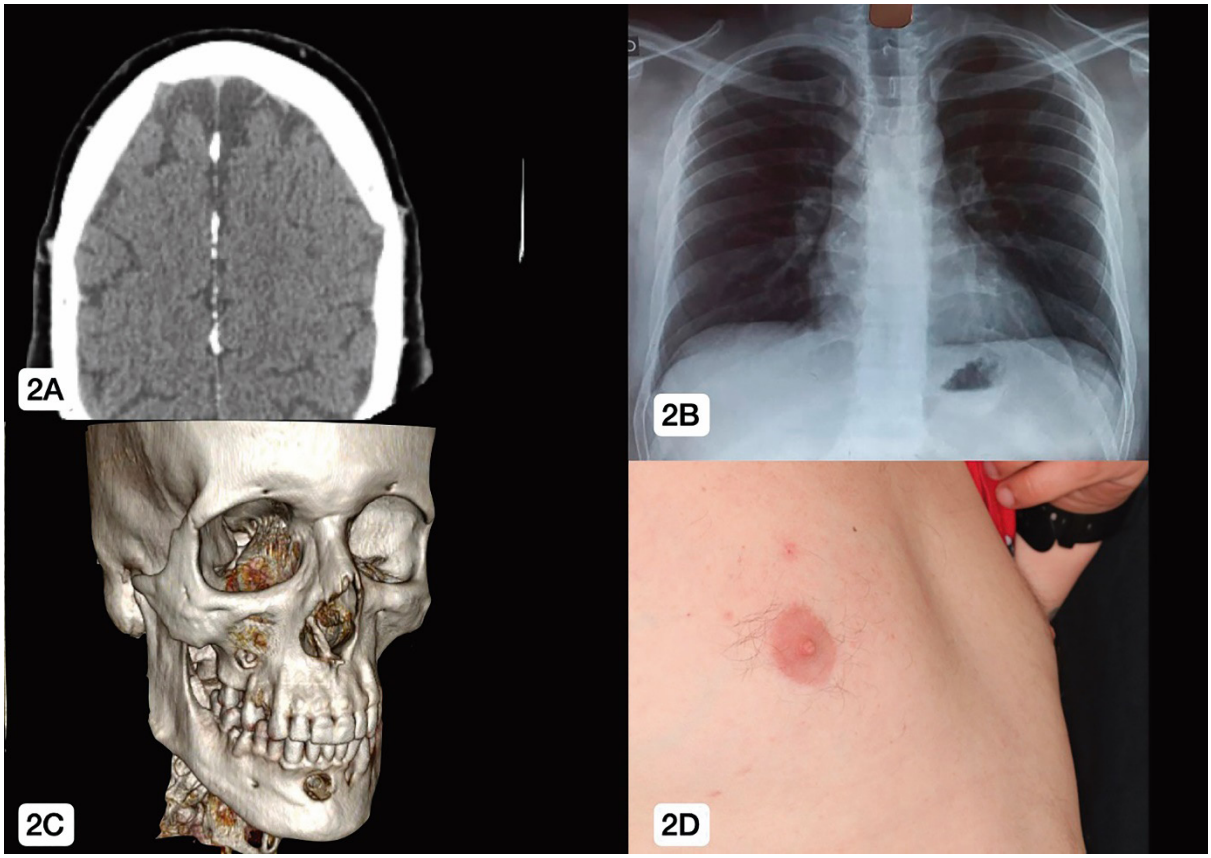

Figure 2 – **A) Axial section with cerebral falx calcification B) Anteroposterior chest x-ray C) 3D face reconstruction D) Chest** *excavatum.*

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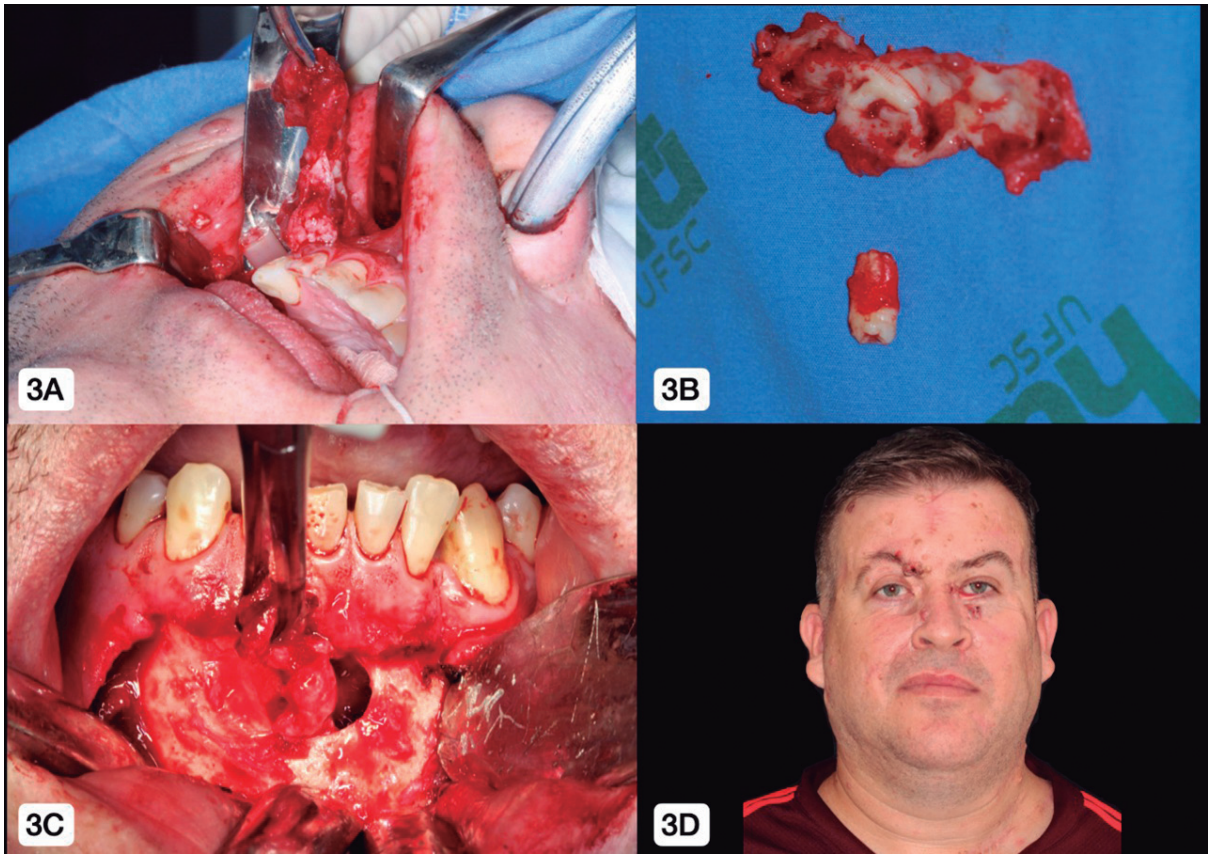

Figure 3 – **A) Excision of pathological lesion in the right maxillary sinus B) Pathological lesion associated with an impacted tooth C) Excision in the mental region D) Frontal clinical photo 7 days post-operative.**

(0.12%), remaining on a liquid and pasty diet, and performing all post-operative care. recommended operatives.

He presented evolution without pain complaints and with good healing. He remained under clinical and radiographic control until now at 14 months (Figure 4A, 4B, 4C), with no sign of lesion recurrence and with preserved bone contours. Histopathological examination showed parakeratinized stratified squamous epithelium whose diagnosis was Odontogenic Keratocyst (Figure 4D).

Currently administering Vismodegib 150 mg orally, once daily, an anticancer medication approved by the Food and Drugs Administration (FDA), and prescribed by the plastic surgery team. Resulting in the disappearance of their BCC lesions. However, it presented hair loss as a side effect. (Figure 4A).

DISCUSSION

For the diagnosis of this syndrome to be made, it is necessary to be based on major and minor criteria[9,11,12]. In the present case, the patient presented OK lesions, basal cell carcinomas, and calcification of the falx cerebellar and pectoralis *excavatum*, which corroborates the diagnosis of GGS

The treatment of OK can be done with lesion enucleation, curettage, and enucleation associated with peripheral osteotomy or bone resection en

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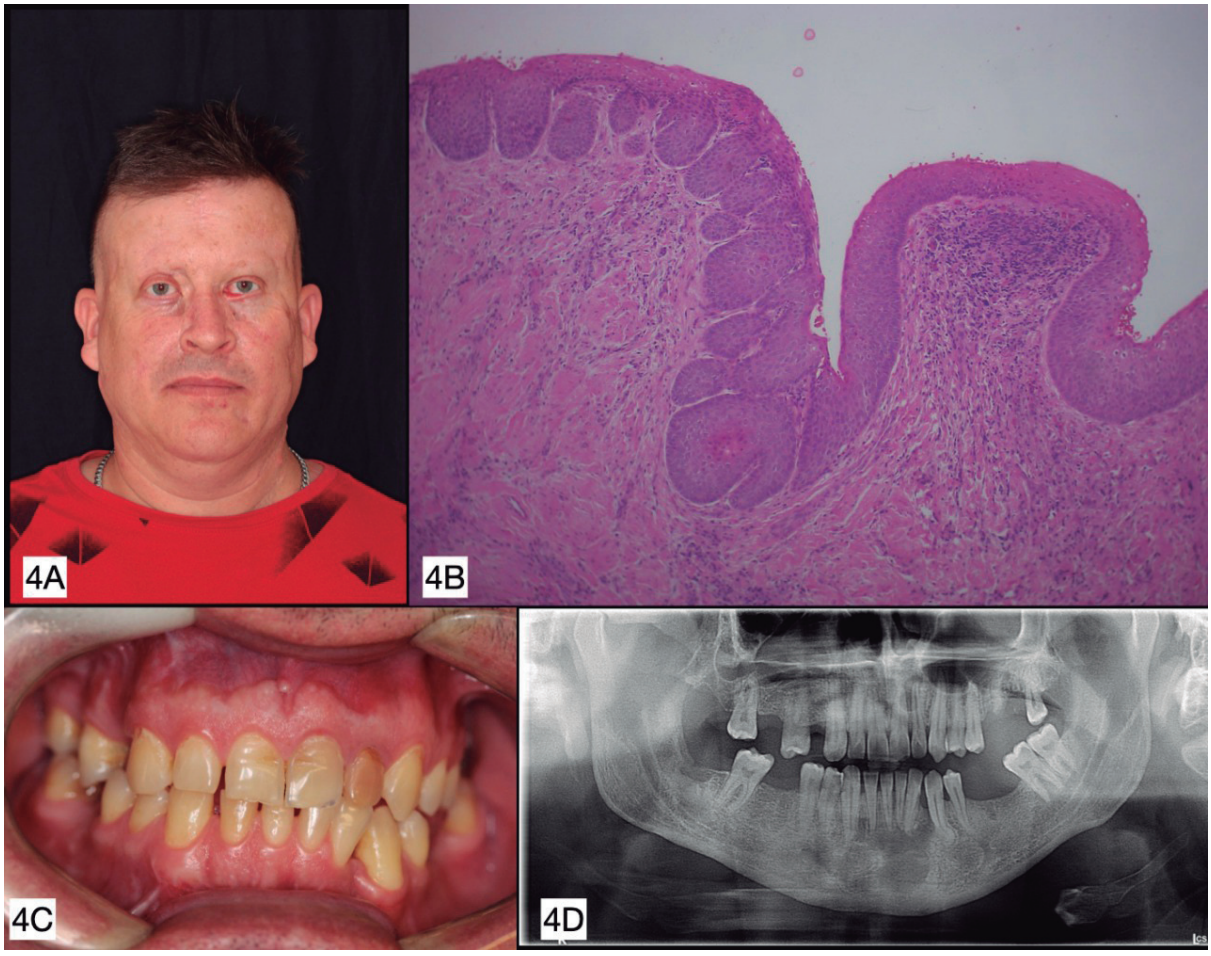

FIGURE 4 – **A) Frontal clinical photo with 14 months of follow-up 4. B) Intra-oral clinical photo with 14 months of follow-up C) Panoramic radiograph at 14 months of follow-up D) Histopathological examination slide.**

bloc. There are also options for adjunctive treatment, such as Carnoy's solution therapy, marsupialization or cyst decompression, topical application of 5-fluoracil, and cryotherapy. The decision must be based on its clinical and imaging characteristics, as well as the history of possible treatments already performed.[5,8,13,14]

Al-Moraissi et al. conducted another meta-analysis study, verifying the treatment of 2287 lesions in 35 studies which treatment would be most effective. Confirming again that only marsupialization as a treatment for OK has a high rate of lesion recurrence (32.3%), and enucleation associated with cryotherapy or Carnoy solution has lower rates 14.6% and 11.5% respectively. This corroborates the research by Chrcanovic, (28.7) for marsupialization only and (5.3%) for enucleation associated with the use of carnoy[15,16]

Despite these results, the study emphasizes the need for adequate treatment according to factors such as patient profile, location and size of the lesion. Being the marsupialization when added to a second intervention for cystic excision, a good indication of treatment. They also report that resections should be reserved for lesions with multiple recurrences or that do not correspond to other treatment alternatives, since this treatment is more aggressive, making the postoperative period of greater morbidity.[14,15]

The recurrence rate is higher in multilocular lesions when compared to unilocular lesions, with

no statistically significant difference by region affected or patient's sex. In patients with GGS, the recurrence rate is difficult to affirm, since the syndrome favours the development of OK lesions, leading to doubts regarding the appearance of lesions, whether recurrences or new lesions.[16,17]

Among the adjuvant therapies, it is important to highlight the possible adverse effects, for example, cryotherapy, which when not applied only locally in the region of the lesion, can cause injury to adjacent soft tissue or predisposition to mandibular fracture due to reduced bone strength. About Carnoy's solution, chloroform showed carcinogenic potential, being contraindicated for use. The new Carnoy solution no longer contained chloroform in its composition, however, its removal demonstrated a reduced effectiveness against the recurrence of OK lesions.[18,19]

5-Fluoracil is an antimetabolite agent applied to the lesion cavity after curettage or peripheral osteotomy, causing a reduction or death of satellite cysts. The literature presents a report of application in a patient with severe deficiency of the enzyme dihydropyrimidine dehydrogenase who presented a severe reaction after application in the scalp region of basal cell carcinomas.[17]

Its local application demonstrates greater safety when compared to systemic application, which can result in mucositis, granulocytopenia, neuropathy, cardiac toxicity, nausea, emesis, general malaise, hypotension or death.

Vismodegib is a selective inhibitory antineoplastic measurement of hedgehog, a signalling pathway associated with the PTCH11 gene. That is the loss of function in tumor suppressors. Resulting in the contribution of BCC oncogenesis and the presence of OK.[20.21]

Despite Being able to present complete remission with the use of the medication, discontinuation in its use is not encouraged, since the lesion may be residual or not contiguous. Enabling the lesion to grow more aggressively and drug-resistant.[22]

CONCLUSION

SGG has several clinical manifestations, with CO lesions being one of the most important. Multidisciplinary treatment by oral and maxillofacial surgeons, neurologists, neurosurgeons, dermatologists, and ophthalmologists as well as clinical monitoring is advised, as early diagnosis of possible changes leads to the most conservative treatment possible, making treatment more accessible and less morbid to the patient.

In our study, Vismodegib presented itself as a good therapy in the treatment of GGS, resulting in a reduction in BCC and KO. However, the drug presented side effects such as alopecia and gastric disorders observed clinically and by the report of the same.

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