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GORLIN-GOLTZ Syndrome: Diagnosis, Management and Follow-Up of a Little-Known Pathology

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Abstract **Original Research Article**

***Introduction*:** Gorlin syndrome is a genetically predisposed inherited disorder caused by mutation of the PTCH tumour suppressor gene. Its clinical manifestations are variable, but odontogenic keratocysts, basal cell nevi and carcinomas, and costal and vertebral anomalies are the most common. ***Materials and Method*:** A retrospective study was carried out including patients operated on for maxillo-mandibular cysts in the context of basal cell nevomatosis. ***Results*:** Seven cases were collected. The mean age was 21 years, with a clear female predominance (80%). Odontogenic keratocysts were responsible for facial asymmetry in all patients. They were located twice as often on the mandible. The other major and minor criteria were variably associated. The diagnosis was based on the criteria defined by Kimonis, with confirmation by a genetic study in one patient. Treatment was surgical. Recurrences occurred in 40% of cases, with an average follow-up time of 2 years. Average follow-up was 4 years. ***Conclusion*:** Gorlin syndrome should be considered in cases of recurrent keratocysts in young subjects, associated with other signs, with long-term multidisciplinary follow-up to provide the best possible care for these patients.

Keywords: GORLIN syndrome - keratocyst - basal cell carcinoma.

INTRODUCTION

GORLIN-GOLTZ syndrome is a rare pathology described in 1960 under other names. Its syndromic character is synonymous with the association of several symptoms grouped into major and minor criteria. It classically includes the association of basal cell carcinomas, maxillo-mandibular odontogenic keratocysts and skeletal anomalies, as well as other ophthalmological, neurological and gynecological manifestations of variable expression, which may appear progressively at different ages.

This syndrome is the expression of a genetic mutation, autosomal dominant with complete penetrance of the PTCH tumor suppressor gene, whose diagnosis of certainty can be obtained by genetic study, but which is not essential.

Based on a series of 7 cases followed in our department, we will discuss diagnosis, management and follow-up.

MATERIALS AND METHOD

A retrospective study was made, including patients with a diagnosis of GORLIN-GOLTZ syndrome who were treated in our department between 2011 and 2024. We excluded patients in whom the diagnosis of GORLIN-GOLTZ syndrome was unlikely, patients who were lost to follow-up and files that could not be used.

A literature review was also carried out using the PubMed, Clinicalkey and Google Scholar search databases, using the following keywords: Gorlin-Goltz syndrome, basal cell nevomatosis, major criteria, minor criteria.

RESULTS

A total of 7 patients were selected, including 5 women and 2 men. The age of our patients ranged from 10 to 45 years, with an average age of 21,2.

The most frequent reason for consultation was facial asymmetry in connection with maxillo-mandibular

swelling, which was present in all our patients. Other manifestations were present to varying degrees from one patient to another, and others appeared during follow-up These manifestations, in order of frequency in our patients, are: multiple facial nevi, skeletal anomalies (Figure 1), palmoplantar keratoses and palmoplantar pits.

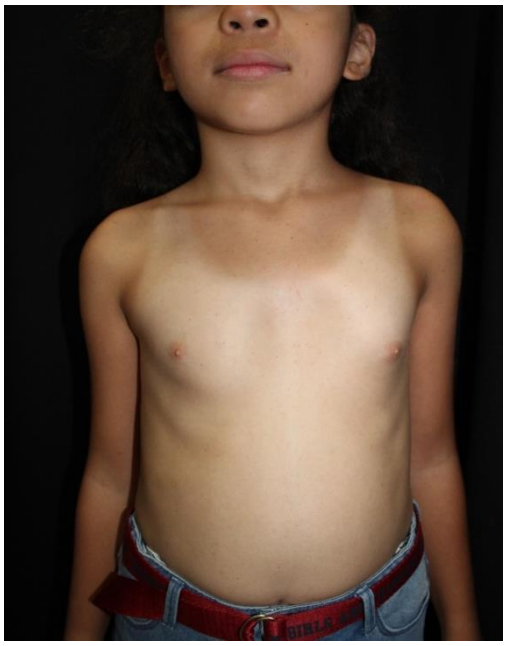

Figure 1: Thoracic deformities and multiple nevi

Dental panoramic imaging was carried out in all patients, given its availability (Figure 2), simplicity and efficiency in exploring maxillomandibular lesions. It revealed uni-locular radiolucent formations in 43.75% of cases (7 of the 16 cysts studied) and plurilocular formations in 56.25% of cases.

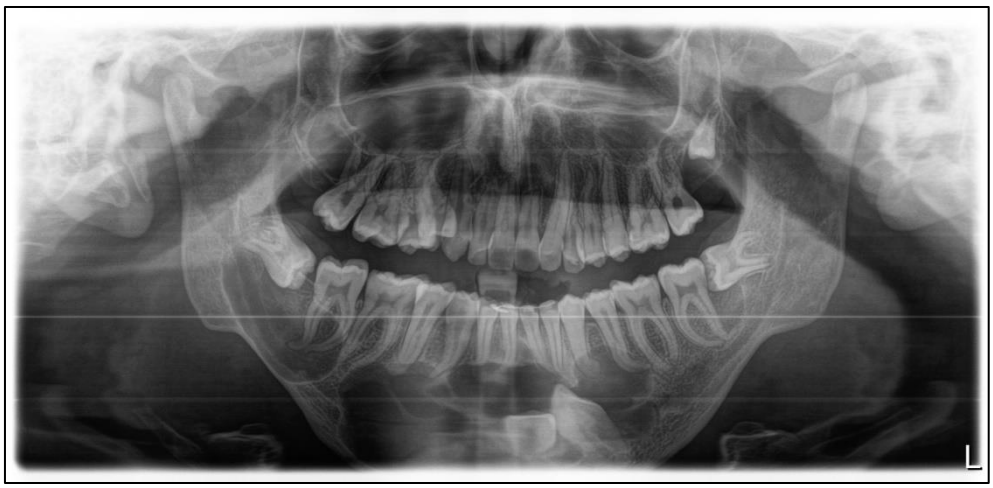

Figure 2: Dental panoramic showing multiple mandibular cysts

The most frequent localizations were the horizontal portion of the mandible (70%), the mandibular branches (60%) and the mandibular angle (40%). Other lesions included dental malposition, impacted teeth, intrasinusal teeth and reactive sinusitis. For a better analysis of the lesions, maxillofacial CT scans were requested in all patients, enabling us to determine the number of cysts (Figure 3), their size and their anatomical relationship with close organs. CT scans also revealed the presence of cerebral calcifications in 60% of cases. Other radiological examinations were carried out according to the clinical manifestations, such as chest X-rays, pelvic ultrasound and cranial X-rays (Figure 4).

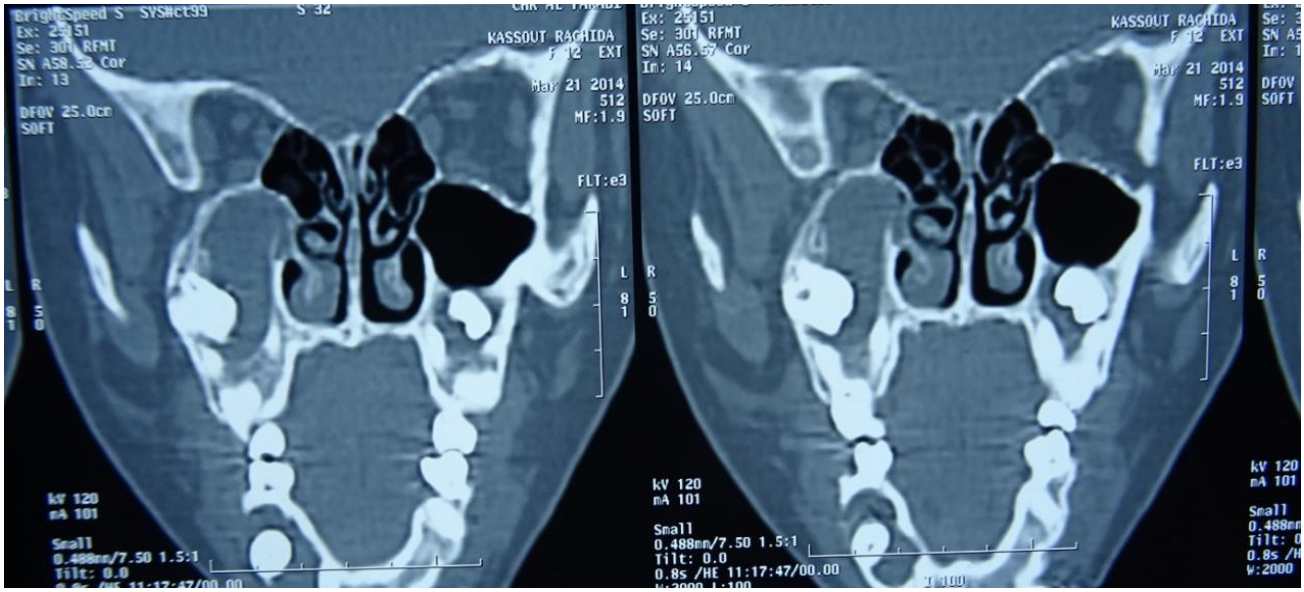

Figure 3: Maxillo-mandibular cysts on CT-scan

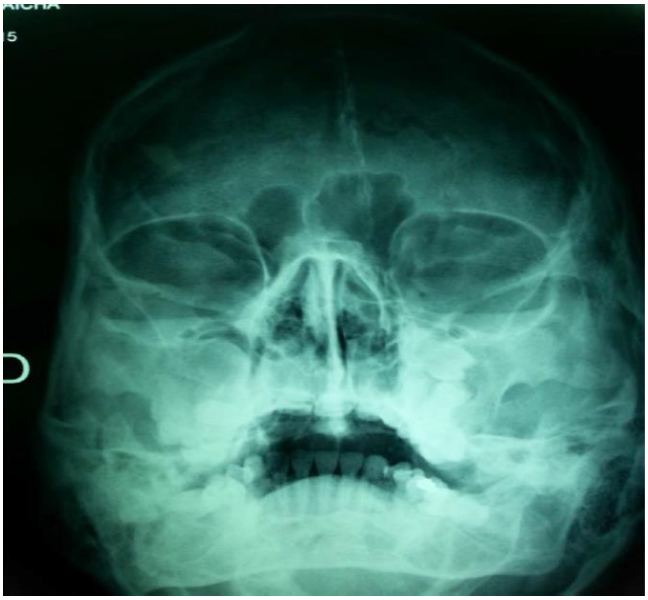

Figure 4: Calcification of the brain scythe

The diagnosis was based on the presence of major and minimal criteria, except for one patient who benefited from a genetic study that confirmed the diagnosis.

Treatment of odontogenic keratocysts was surgical in all patients, consisting of a conservative procedure performed orally under general anaesthesia with nasotracheal intubation. Enucleation of the cysts was performed in all patients, and was completed by (Figure 5):

- Ostectomy of the bone walls: 80% of cases,
- Application of Carnoy's solution in the residual bone cavity: 20% of cases.
- Extraction of impacted teeth: in 80% of cases.
- Removal of cutaneous tumors in 40% of cases.

Anatomopathological examination of cysts or cystic fragments revealed odontogenic keratocysts in 90% of cases. The remaining 10% were inflammatory cysts and dental cysts, while the skin tumours were found to be basal cell carcinoma (BCC).

Post-operative follow-up averaged 4 years, with a maximum of 9 years and a minimum of 1 year. During this follow-up period, recurrence of keratocysts was noted in 40% of cases. The average time to recurrence was 2 years, and the average number of recurrences was 5. BCC recurrence was noted in only one patient, and de novo appearance during follow-up in only one patient.

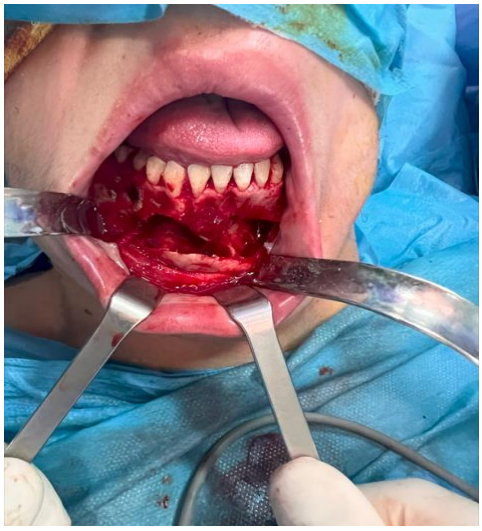

Figure 5: Ennucleation of mandibular cysts

DISCUSSION

GORLIN-GOLTZ syndrome or basal cell naevomatosis is a rare, hereditary disease with autosomal dominant transmission whose the responsible gene is PTCH of complete penetrance and highly variable clinical expression [1], several cases have been described with various symptoms and it was not until 1960 that two doctors brought these symptoms together into a syndrome named in french: "Syndrome des Multiples Carcinomes Basocellulaires", des Kystes de la mâchoires et des Côtes bifides, these two doctors are: Gorlin RJ, a dental surgeon, and Goltz RW, a dermatologist, whose names the syndrome currently bears [2].

The incidence of this syndrome varies from one country to another; in England, for example, the minimum prevalence was 1/57,000 [3], compared with 1/164,000 in Australia. In terms of age, it affects young subjects without any gender-related predilection, with a higher incidence in the light-skinned population [4].

The clinical manifestations are multiple and vary in expression from patient to patient, and are dominated by maxillo-mandibular cysts and basal cell carcinomas associated with multi-systemic involvement such as cerebral, skeletal, gynecological, ophthalmological and other abnormalities. The complexity and large number of clinical signs encountered in basal cell nevomatosis make it difficult to diagnose. What's more, not all patients present the same signs in the same way within the same family, with transmission of the mutation to offspring.

To facilitate diagnosis, these symptoms have been grouped in order of frequency into major and minor criteria. It is therefore not necessary to present all manifestations in order to make the diagnosis of basal cell nevomatosis. The presence of two major criteria, or one major and two minor criteria, is sufficient to make the diagnosis.

The major criteria are those most frequently encountered in patients with Gorlin-Goltz syndrome. There may be slight variations between authors, but 3 criteria are found throughout the literature [5]:

- The presence of several basal cell carcinomas in the same patient, or a single basal cell carcinoma in a person under the age of 30.
- The presence of one or more odontogenic keratocysts.
- The existence of palmoplantar pits.

Some authors advocate the addition of new elements to this list, arguing that certain major criteria such as basal cell carcinomas or keratocysts are not present from birth, and that since their onset tends to occur in adolescence or early adulthood, the diagnosis of basal cell nevomatosis may be delayed. For this reason, Kimonis *et al*., [6] proposed adding rib malformations to the major criteria for two reasons: firstly, their frequency, and secondly, their presence at birth, which facilitates diagnosis. He therefore retained 5 major and 5 minor criteria for the diagnosis of GORLIN syndrome [6]:

Major criteria

1. Multiple (>2) basal cell carcinomas, or a single BCC in a patient under 30 years of age, or more than 10 cutaneous naevi.
2. One (or more) odontogenic keratocyst with histological evidence.
3. Palmo-plantar pits (3 or more).
4. Cerebral calcifications.
5. Family history of basal cell nevomatosis (1st degree relative).

Minor criteria

1. Congenital skeletal anomalies: bifid, fused or missing ribs; fused or bifid vertebrae.
2. Macrocephaly (occipito-frontal circumference (+)2 standard derivations), with presence of frontal humps.
3. Cardiac or ovarian fibromas.

4. Medulloblastoma.
5. Other congenital malformations: cleft lip and/or palate, polydactyly, ocular anomalies (microphthalmia, cataract, coloboma).

At present, in addition to clinical criteria, the diagnosis can be based on the presence of a genetic mutation of the PTCH gene, although the absence of this mutation doesn't make the diagnosis any more accurate, since it hasn't been found in all patients [7].

Management of maxillo-mandibular cysts is multidisciplinary, given the multi-systemic nature of the disease, and aims to relieve the patient's pain, improve quality of life, treat curable lesions and avoid recurrence. Surgical management of maxillo-mandibular cysts should follow a conservative approach whenever possible, to preserve the patient's bone stock as much as possible and avoid damaging the growth of the facial mass, especially as these patients are candidates for iterative surgery [8].

Surgery for basal cell carcinoma can be either conventional, with carcinological margins, or Mohs micrographic surgery, the latter technique seems to be the most suitable, since it allows sparing removal of healthy tissue [9].

Clinical and radiological monitoring, depending on the symptoms found, is an essential part of management, as it enables lesions to be detected at an earlier stage, which in turn enables less invasive treatments to be carried out.

CONCLUSION

Gorlin syndrome must be brought up in the presence of recurrent odontogenic keratocysts. And it’s necessary to program a long-term multidisciplinary follow-up to support these patients.

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