Basal cell carcinoma resection in an Ecuadorian patient with Gorlin-Goltz syndrome

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ABSTRACT

Gorlin-Goltz syndrome is an inherited dominant autosomal disorder characterized by a predisposition to numerous cancers. The clinical-pathological findings of this syndrome are very diverse. The objective of this report is to present an Ecuadorian patient with Gorlin-Goltz syndrome who underwent surgical resection of basal cell carcinoma compatible lesions.

Conclusion: Gorlin-Goltz syndrome encompasses a variety of clinical signs and symptoms, including important oral manifestations and skin lesions that must be recognized to achieve an early specialty referral, thus reducing the risk of malignancy through a multidisciplinary treatment.

Keywords: Basal Cell Nevus Syndrome, Gorlin-Goltz syndrome, Carcinoma, Basal Cell

Introduction

Gorlin-Goltz (G-G) syndrome or nevoid basal cell carcinoma syndrome (NBCCS) is a dominant autosomal genetic disorder with high penetrance. Fifty percent of patients who suffer from it have a mutation in the long arm of chromosome 9q22.3 in the area of the PTCH gene (protein patched homolog) (1–3), a homologue of the Drosophila patched gene (PTC), which encodes a transmembrane receptor protein (4). This protein binds to a soluble factor of the hedgehog family (Hh), thus activating the Smo (smoothened) receptor, which unblocks the transcription of several growth factors. Therefore, the PTCH gene is an oncosuppressor that is part of the Sonic Hedgehog Homolog (Shh) signaling pathway and is crucial in embryonic development, cell division control, and tumor growth (5).

Its approximate prevalence is 1 in 57000 to 1 in 256000 and the ratio of males to females is 1:1 (6). Binkley and Johnson reported this syndrome for the first time in 1951 (7), then, in 1960, Gorlin and Goltz described the association between multiple basal cell carcinoma, odontogenic keratocysts (OKC) and bifid ribs, which account for the characteristic triad (8). In 1977, Rayner et al. added additional features, including calcification of the falx cerebri and palmar/plantar fossae (9).

According to the criteria of Kimonis et al., the diagnosis of G-G syndrome requires the coexistence of at least two major criteria or one major and two minor (10).

The characteristic that is usually diagnosed first is OKC, because it can be detected during the first decade of life and appears in almost 80% of G-G syndromes.

Other manifestations include palmar and plantar ulcers that appear as shallow pits, caused by partial or complete absence of the corneal layer, which can also appear along the sides of the hands and fingers and even on
the tongue; spina bifida (10,11); medulloblastoma (can be an epiphenomenon of G-G, especially in children who are ≤5 years-old) (12); cardiac tumors, including fibromas and ventricular histiocytomas, usually congenital (13); hypertelorism, congenital cataract, nystagmus, coloboma and strabismus (14); and ameloblastoma (extremely rare) (15,16).

Early diagnosis of G-G syndrome and its subsequent treatment are very important due to neoplasm susceptibility (2).

The case of a patient with a previous diagnosis of Gorlin-Goltz syndrome who presented multiple lesions compatible with basal cell carcinoma is presented below.

Case Report

A 35-year-old male, living in Quito, Ecuador, without allergies; no history of tobacco or alcohol intake. His mother and his brother presented Gorlin-Goltz syndrome (G-G).

The patient presents hereditary and congenital G-G syndrome (multifocal basal cell carcinoma and maxillary keratocysts), whose manifestations began at the age of 22. He underwent surgery for bilateral keratocysts at the age of 25, and multiple biopsies of the upper left eyelid were taken since 2012. In August 2015, with a positive tumoral activity biopsy report, a wide resection involving 60% of the left upper eyelid plus flap reconstruction was performed.

Physical examination revealed multiple surgical scars on the left upper eyelid with tumoral activity on the eyelid margin, as well as on the outer third of the ipsilateral lower eyelid and on the right side.

In October, a wide resection of the left upper and lower eyelid was planned, plus reconstruction and transoperative study, which are performed without complications.

Subsequently, the patient attended scheduled control, reporting the presence of a left superciliary nodular lesion. Physical examination revealed multiple lesions located in the left superciliary region, left helix, concha, and antihelix, in the inner corner of the left lower eyelid, in the left parieto-temporal and occipito-temporal regions, and other small bilateral genian lesions. There were no alterations in the flap. Left external campimetry was limited. It was decided to perform a facial bone and skull simple and contrasted tomography (CT) and laboratory tests.

Then, resection of the previously mentioned lesions and resection of the lower eyelid with transoperative study, shield-type incision and external canthoplasty of the lower left eyelid was planned. A plastic surgeon was included in
Altogether, 9 skin lesions located in the left superciliary, left frontal, interparietooccipital, posterior occipital, auricular, and left retroauricular regions were resected, which were positive for basal cell carcinoma.

In the subsequent control, the patient's campimetry showed improvement.

Discussion

Reports about Gorlin-Goltz syndrome are scarce in the literature (17). The rarity and phenotypic variability of this syndrome causes a delay in its diagnosis. Syndromic associated keratocystic odontogenic tumors are often treated in the same way as nonsyndromic cases (18) and associated systemic signs can easily be missed due to lack of understanding of the syndrome. In addition, their characteristics vary globally, so doctors and even dentists must identify them in a timely manner, considering those that are more prevalent in their population or similar populations (19,20).

The pathogenesis of basal cell carcinoma (BCC) is thought to involve increased sensitivity to ultraviolet light and to involve ineffective mechanisms that repair UV-induced DNA damage. In any case, this theory is not accepted by all authors since these lesions can also appear in areas that have not been exposed to sunlight. Especially in children, patients with G-G syndrome who undergo radiotherapy for other cancers have shown to be at increased risk of radiation-induced BCC (21).

In 50% of patients with G-G syndrome, jaw keratocysts appear, characterized by a thin surrounding layer of epithelial cells, which tend to reappear locally after excision in 6 to 60% of cases, therefore, the indication for surgery should be carefully considered, also due to the possibility of intensive clinical and instrumental monitoring (22).

In recent years, new drugs have been developed to
inhibit certain components of the sonic hedgehog signaling pathway. In 2013, the FDA approved vismodegib, the first small molecule to target this pathway (11). Although these agents seem promising options for patients with G-G syndrome, their efficacy is limited by adverse effects and the development of resistance (23). Logically, a more aggressive approach is necessary if basal cell carcinoma is suspected; subsequently, depending on the lesion site and the surgery type, a reconstruction can be performed, as in the case presented in this article (24,25).

Conclusions

Gorlin-Goltz syndrome encompasses a variety of clinical signs and symptoms, including important oral manifestations and skin lesions that must be recognized to achieve early referral to a specialty, thus reducing the risk of malignancy through multidisciplinary treatment.

Ethical Responsibilities

In this case report, the informed consent of the patient was obtained. Its elaboration and all the inherent details were based on the Declaration of Helsinki.

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Conflict of interests

The authors declare the non-existence of conflicts of interest.

References