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Gorlin-Goltz Syndrome: A Case Report

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Authors' contributions

This work was carried out in collaboration among all authors. Author RBA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author MAS and AG managed the analyses of the study. Author KK managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

The Gorlin-Goltz syndrome, also known as Nevoid Basal Cell Carcinoma syndrome, is an uncommon autosomal dominant disorder caused by mutations found on chromosome 9.
This syndrome is characterized by multiple basal cell carcinomas, odontogenic keratocysts and various skeletal abnormalities. This case report presents a 63-year-old man diagnosed with Gorlin-Goltz syndrome by clinical, radiographic and histological findings. The basal cell carcinomas were treated with surgical excision for the biggest ones, and cryotherapy for some of the small ones that are located on the face with a good result.
Through this paper we aim to highlight the importance of an early diagnosis of this syndrome, leading to an early preventive treatment of basal cell carcinomas, a regular and prolonged monitoring of patients and their descendants, with a right genetic advice.

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Keywords: Nevoid basal cell carcinoma; Gorlin-Goltz syndrome; odontogenic keratocysts; surgical excision.

1. INTRODUCTION

The Gorlin-Goltz syndrome, also called as Nevoid Basal Cell Carcinoma syndrome, is an uncommon autosomal dominant disorder caused by mutations found on chromosome 9 [1].

It is characterized by a wide spectrum of developmental abnormalities and a predisposition to different cancers that makes the severity of the disease. This syndrome is mainly defined by the presence of multiple odontogenic keratocysts (75%), basal cell carcinomas (50-97%), palmar and plantar pits (60-90%), bifid ribs (40%) and ectopic calcification of the falx cerebri (37-79%) [2]. We present the case of a patient whose chief complaint was multiple and voluminous basal cell carcinomas scattered mainly on the face and the trunk.

2. CASE REPORT

A 63-year-old man was first examined by a dermatologist and then admitted in our plastic surgery department for multiple cutaneous tumors on the head and neck area, the trunk and the right shoulder which were suspect of malignancy. The disease started at the age of 31 years old with small nodular basal cell carcinomas essentially on the face. The medical history taking revealed that he was operated at an early age of odontogenic keratocysts of the jaws and that two of his four children have similar clinical symptoms.

He first underwent 4 radiotherapy sessions that led to the spreading of the lesions. No mental retardation has been noticed. Physical examination showed macrocephaly, frontal bossing, ocular hypertelorism, multiple pigmented nevi disseminated on the face (Fig. 1) and the trunk with two voluminous tumors developed on the upper half of the back and the right shoulder (Fig. 2). The endobuccal examination didn't show maxillary cysts and the aspect of the oral mucosa was normal. The neurological, cardio-vascular andophthalmologic examination didn't detect any other anomaly.

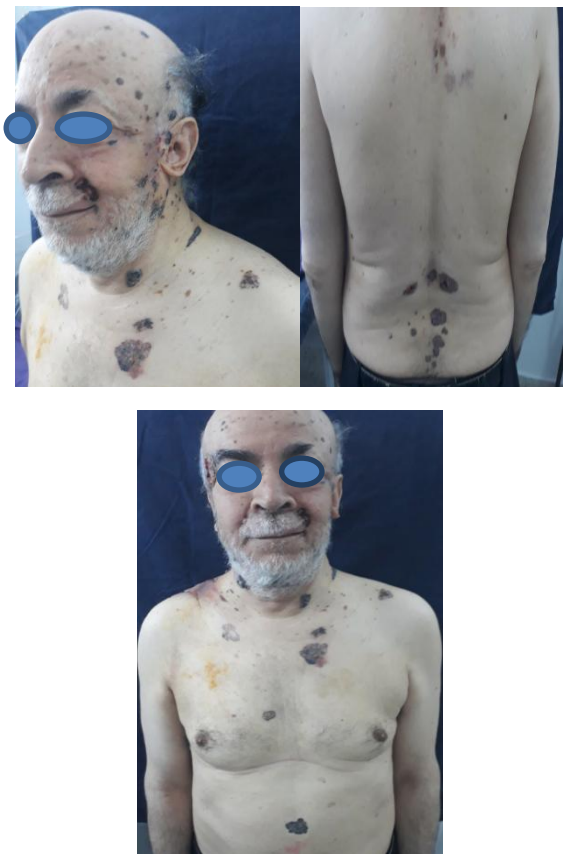

Fig. 1. Images showing multiple lesions

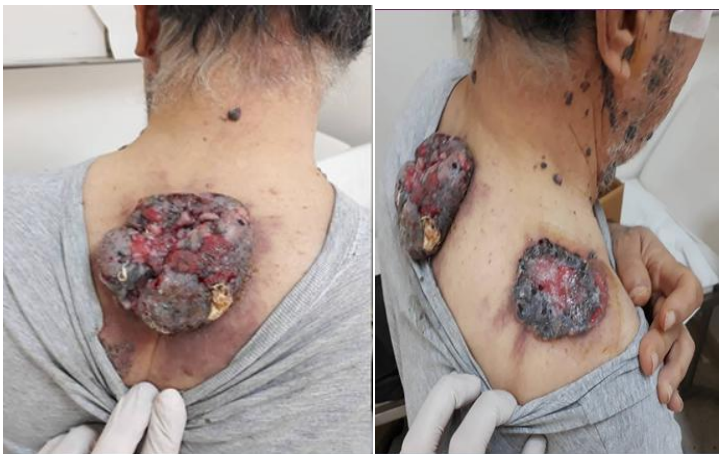

Fig. 2. Two voluminous tumors developed on the upper half of the back and the right shoulder

Our patient recently reported a dental pain and was seen by a dentist. A panoramic X-ray was performed and showed an odontogenic keratocyst of the lower jaw (Fig. 3).

We proceeded to the excision of the two most voluminous and embarrassing tumors located on the upper half of the back (Figs. 4). The histopathological examination concluded that it consists in basal cell carcinomas. Some of the small lesions located on the face were treated by his dermatologist with cryotherapy.

An X-ray of the chest and a cerebral MRI were performed and didn't show any abnormalities.

3. DISCUSSION

Gorlin-Goltz syndrome, also known as Nevoid Basal Cell Carcinoma Syndrome, was described

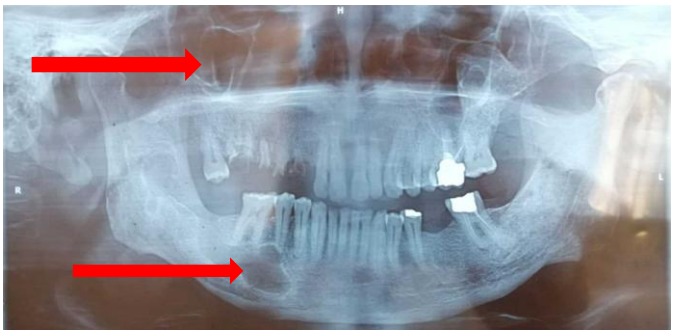

Fig. 3. Panoramic radiograph demonstrates the presence of odontogenic keratocysts

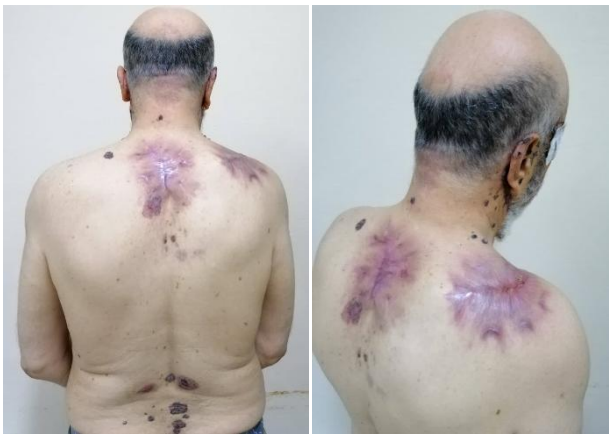

Fig. 4. Post-operative results

for the first time in 1894 from Jarisch and White in a patient with multiple basal cell carcinomas, scoliosis, and learning disability [3, 4]. In 1939, Straith described a familiar case in which multiple basocellular carcinomas and cysts appeared [5].

Binkley and Johnson in 1951, and Howell and Caro in 1959 suggested a relationship between basal cell epitheliomas and developmental malformations [4]. It was delineated only in 1960 by Robert James Gorlin and William Goltz [2] who established the classical triad (multiple basocellular epitheliomas, keratocysts in the jaws and bifid ribs) that characterizes the diagnosis of this syndrome. This triad was modified by Rayner and his colleagues who mentioned that at least cysts had to appear in combination with calcification of the falx cerebri or palmar and planter pits to maintain the diagnosis [6].

The prevalence varies from 1/ 57 000 to 1/ 256 000, with a male to female ratio of 1:1 [7].

It is due to a genetic alteration produced by a mutation in the PTCH1 (Patched) tumor suppressor gene, found on the long arm of chromosome 9 (q22.3-q31) [4,8] that is autosomal dominant inheritance gene, though sporadic cases have been found [9, 10].

The syndrome, characterized by increased predisposition to develop basal cell carcinoma and associated multiorgan anomalies, has a high level of penetrance and variable expressiveness [4, 2].

Diagnosis is based up on established major and minor clinical and radiological criteria and is ideally confirmed by DNA analysis [2, 11].

The diagnostic criteria for nevoid basal cell carcinoma, established by Evans et al. and modified by Kimonis et al. in 1997, state that there should be at least two major criteria or one major and two minor criteria for the diagnosis [3, 4, 12]:

Major criteria:

- More than two basal cell carcinomas or one basal cell carcinoma at younger than 30 years of age or more than 10 basal cell nevi.
- Any odontogenic keratocyst (proven on histology) or polyostotic bone cyst.
- Three or more palmar or plantar pits (present in about 65% of patients).
- Bifid, fused, or markedly splayed ribs.
- Ectopic calcification: lamellar or early at younger than 20 years of age.
- Falx cerebri calcification.
- Positive family history of nevoid basal cell carcinoma.
- Some authors take plurilamellar appearance of the falx cerebri calcification as a pathognomonic symptom of Gorlin-Goltz syndrome.

Minor criteria:

- Macrocephaly determined after adjustment with height**,** telorism, wide nasal bridge.
- Mandibular prognathism.
- Skeletal anomalies: hemivertebrae, scoliosis, syndactyly, polydactyly, and shortened 4th metacarpal.
- Radiological abnormalities like bridging of sella turcica, ectopic calcification of false cerebri, vertebral anomalies, and modelling defect of hands and feet.
- Medulloblastoma.
- Ovarian Fibroma, hypogonadism.
- Spinabifida.
- Congenital malformations: cleft lip or palate, polydactylism or eye anomalies (cataract, coloboma, and microphthalmus).
- And 100 more minor criteria.

A clinical examination protocol for patients with Gorlin-Goltz syndrome was suggested by Lo Muzio [7]:

Family history:

Past medical and dental history:

Clinical examinations: oral / skin / central nervous system / head circumference / interpupillar distance / eyes / genitourinary system / cardiovascular system / skeletal system.

Genetic testing:

X-ray: Chest.
A.P. and lateral skull: panoramic radiograph / Cervical and thoracic spine-A. P. and lateral / Hands (for pseudocycts) / Pelvic (female).

Ovarian ultrasound (female) for ovarian fibroma.

Echocardiogram (children) for cardiac fibroma.

In the presented case, two of the major criteria were covered: 1. More than two basal cell

carcinomas; 2. Odontogenic keratocyst (proven on histology). Three minor manifestations were identified, which are macrocephaly, frontal bossing and ocular hypertelorism.

Despite the name of the syndrome, multiple basal cell carcinomas occur only in 50% of the cases and they most often proliferate between puberty and 35 years of age, but cases have been reported in 3-4-year-old patient also [3,7]. They may vary in number from a few to one thousand [7] and range in size from 1 to 30 mm in diameter. Basal cell carcinomas most often involve face and non-exposed areas such as the back and chest and rarely involve the waist or extremities [3]. They can vary from flesh colored papules to ulcerating plaques and may be mistaken for nevi, skin tags or hemangiomas. With cases of basal cell carcinomas radiation therapy should be avoided because it causes invasion of basal cell carcinomas years later [13].

Acral pits that are often overlooked during physical examination have a characteristic dermoscopy with red globules that are mainly distributed in parallel lines inside flesh-colored, irregular shaped, and slightly depressed lesions [3]. Dermoscopy improves the visualization of these pits. Dermoscopy can help the diagnosis of the Gorlin-Goltz syndrome as well as the management of the affected patients [14].

Treatment of multiple basal cell carcinomas in patients with Gorlin-Goltz syndrome is a therapeutic challenge because of the development of an enormous number of lesions [15] and requires a multidisciplinary approach. Management of superficial basal cell carcinomas in these patients is similar to that of sporadic basal cell carcinomas, and involves surgical excision, Mohs micrografic surgery, electrodesiccation, topical chemotherapy (0.1% Tretinoin cream/ 5% 5-Flourouracil cream/ Imiquimod 5% cream), intralesional interferon, photodynamic therapy, cryotherapy and CO2 laser therapy, while radiotherapy is a contraindication [4,14,15]. Recently topical imiquimod has become a valid option in superficial basal cell carcinomas treatment [13]. Chemoprevention involves use of vitamin A analogs [4]. Patients should avoid excessive exposure to UV rays.

A regular follow-up by a multidisciplinary team (dermatologist, plastic and maxillofacial surgeons, neurologist, dentist, specialist in genetics) is compulsory. Screening for medulloblastoma in the early years of life allows to have an early diagnosis and so to give adequate genetic advice, as it may cause early death [2].

Guidelines for follow-up have been established and include the following: neurologic examinations twice yearly, yearly cerebral MRI between ages 1-7 years, orthopantomograms every 12-18 months starting at the age of eight years, yearly skin examination, and cardiologic examination according to the signs and symptoms [16,17].

Survival in Gorlin-Goltz patients is not affected significantly but morbidity from complications is considerable [4].

Genetic consultation is mandatory and antenatal diagnosis is possible by ultrasound and DNA analysis of fetal cells, obtained by amniocentesis or by trophoblast biopsy [7,9].

4. CONCLUSION

The rarity of this syndrome, the multiplicity of its clinical manifestations and their asynchronism make the diagnosis difficult and late. Its oncological potential makes it fundamental to know the characteristics of this syndrome in order to make an early diagnosis leading to an early preventive treatment of basal cell carcinomas, a regular and prolonged monitoring of patients and their descendants with a right genetic advice.

CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

ETHICAL APPROVAL

As per international standard Ethical approval has been collected and preserved by the author.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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