

Gorlin-Goltz syndrome: A rare potentially malignant disease

George Michael N. Sosuan, Alberto C. Chacon

ABSTRACT

Introduction: The Gorlin-Goltz Syndrome is rare but well-known multi-systemic syndrome. This case report highlights a Gorlin-Goltz Syndrome with left orbital and multiple facial basal cell carcinoma, calcified falx cerebri with cyst in the right mandible. **Case Report:** A 47-year-old female presented with a 30 year history of slowly enlarging left periorbital mass eventually encroaching the left orbit. On gross examination, multiple nodular hyperpigmented masses with rolled edges on the entire left periorbital area with extension to the left orbit and globe and two 1x1 centimeter hyperpigmented nodular masses on both paranasal areas. The left globe was phthisical and enophthalmic with positive reverse relative afferent pupillary defect. The examination of the right eye, palms and phalanges was essentially normal. The patient underwent orbital exenteration, excision of left and right paranasal masses and enucleation of the right mandible cyst. The histopathology of the orbital and paranasal masses revealed basal cell carcinoma. Cranial computerized tomography revealed calcified falx cerebri. Transvaginal ultrasound revealed normal results. Chest

radiograph showed no bifid ribs. **Conclusion:** The importance of increasing awareness for early diagnosis and multi-disciplinary approach on treatment of this syndrome is of utmost importance to prevent life-threatening and vision-impairing complications of this disease. Frequent follow up and genetic counselling should be provided.

Keywords: Basal cell carcinoma, Calcified falx cerebri, Gorlin-Goltz

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INTRODUCTION

Gorlin-Goltz syndrome is a rare but well-known disorder with an autosomal dominant inheritance with a high degree of penetrance [1] and variable expressivity [2]. Males and females are affected equally with an incidence of 1 in 50,000-150,000 in the general population with a peak incidence at the third decade of life [3, 4].

The presence of multiple basal cell carcinoma, odontogenic keratocyst of the jaws, palmar or plantar pits, calcification of the falx cerebri, bifid ribs and first degree family history of basal cell carcinoma characterizes this syndrome. Many minor criteria have been described. The presence of two major or one major and two minor features establishes the diagnosis [4].

This case report discusses a case of Gorlin-Goltz Syndrome with left orbital and multiple facial basal cell carcinoma, calcified falx cerebri and right mandibular cyst.

CASE REPORT

A 47-year-old female came in the emergency department with the chief complaint of left enlarging orbital mass. History of present illness started 30 years prior to consult (PTC), the patient noted a left upper lid hyperpigmented pea-sized irregular mass. No consult was done nor medication was taken. Interim, the left upper lid mass enlarged in size and became more irregular and pigmented. Ten years PTC, the left upper lid mass increased in size and gradually encroached the left lower lid. No consult was done because of financial constraint. Few months PTC, the left upper and lower lid masses had increased rapidly in size and encroached on the left periorbital area and globe with subsequent blurring of vision. The patient had unremarkable personal, social and family history with no prolonged sun exposure or exposure to toxic chemicals. The patient came in with visual acuity of 20/20 for the right eye and light perception for the left eye. Gross examination as shown in Figure 1 showed multiple hyperpigmented mass with rolled up edges and necrosis on the entire left periorbital area extending to the left orbit and left globe. The left globe was phthisical with surrounding necrosis and enophthalmic with positive reverse relative afferent pupillary defect. Two 1x1 centimeter hyperpigmented nodular masses with telangiectasia were noted on both paranasal areas. The gross examination of the right eye was essentially normal. Examination of the palms and phalanges were essentially normal. Extraocular motility and anterior segment and fundusoscopic examination were normal for the right eye and difficult to assess for the left eye.

A palpable right mandibular mass was noted and panorex radiograph and computerized tomography (CT) scan were done. It was diagnosed as a right mandibular cyst (Figure 2).

An assessment of Gorlin-Goltz syndrome was considered in this patient and further work-up was done. Orbital CT scan showed as seen in Figures 3 soft tissue mass invading the left orbit and deforming the left globe and a calcified falx cerebri. Transvaginal ultrasound was done revealing normal results. Chest radiograph showed in Figure 4 showed no bifid ribs.

The patient underwent orbital exenteration, excision of right and left paranasal masses, total parotidectomy, enucleation of the mandibular cyst and cervico-facial reconstruction with full-thickness and split-thickness skin grafts.

The histopathology results of the orbital and paranasal masses revealed basal cell carcinoma. The mandibular cyst revealed orthokeratinized odontogenic cyst. The

parotid gland only showed reactive inflammatory infiltration. The results confirmed the diagnosis of Gorlin-Goltz syndrome.

DISCUSSION

Gorlin-Goltz syndrome, also known as nevoid basal cell carcinoma syndrome (NBCCS), is a spectrum of dermatologic, ophthalmic, neurologic, maxillo-facial, endocrine and genital manifestations. It may also be called as multiple basal cell carcinoma syndrome, Gorlin syndrome, hereditary cutaneomandibular polyoncosis, multiple nevoid basal cell epithelioma-jaw cyst or bifid rib syndrome [5].

The human patched gene (PTCH1 gene) is a 34 Kb composed of 23 exons and encodes for a transmembrane glycoprotein composed of 1447 amino acids, with 12 transmembrane domains and two large hydrophilic extracellular loops where Sonic Hedgehog (SHH) ligand binding occurs. Abnormalities in the chromosome



Figure 1: Gross Examination of the Patient.

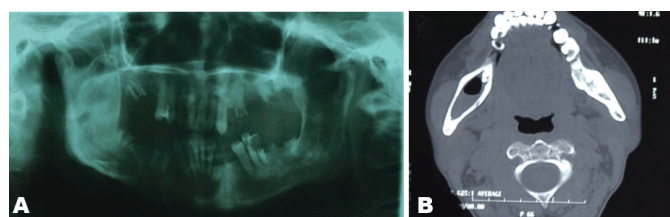


Figure 2 (A and B): (Left) Panorex Radiograph, and (Right) CT scan showing a right mandibular cyst.

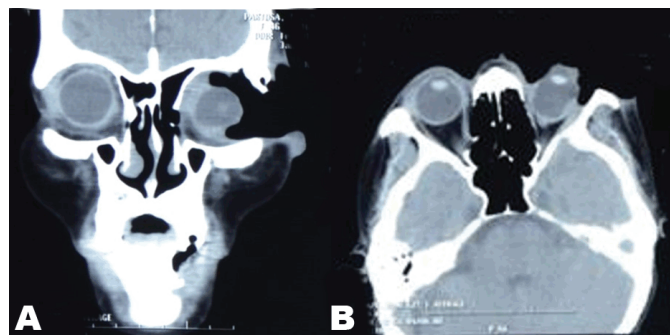


Figure 3 (A and B): (Left) Coronal, and (Right) Axial CT scan showing invasion of the left orbit, deformed left globe and a calcified falx cerebri.



Figure 4: Chest Radiograph showing no bifid ribs.

9q22.3-q31, loss of mutations in the PTCH1 gene and Patched 2 (PTCH 2) and SHH have been implicated for the pathogenesis of this syndrome [6].

Gorlin-Goltz syndrome was first described by Jarisch and White in 1894 and more detailed descriptions by Gorlin and Goltz in later years. This syndrome is diagnosed by different clinical signs and symptoms. Diagnosis of Gorlin-Goltz is established when two major or one major and two minor criteria are present.

The major criteria are, multiple basal cell carcinoma or one occurring under the age of 20 years. Histologically proven odontogenic keratocysts of the jaws. Palmar or plantar pits (three or more). Bilamellar calcification of the falx cerebri. Bifid, fused or markedly splayed ribs. First-degree relative with Nevoid Basal Cell Carcinoma syndrome.

The minor criteria are, macrocephaly (adjusted for height). Congenital malformation: cleft lip or palate, frontal bossing, coarse face, moderate or severe hypertelorism. Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits. Radiological abnormalities: bridging of the sella turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modeling defects of the hands and feet or flame shaped hands or feet. Ovarian fibroma medulloblastoma [7].

In the patient presented, the diagnosis was established by the presence of three major criteria, i.e. multiple basal cell carcinoma, calcified falx cerebri and odontogenic cyst of the jaw. It is a rare multisystemic disease. This case is rarely reported in our country probably because of lack of awareness hence delaying diagnosis and preventing life threatening and vision impairing complications.

In Gorlin-Goltz Syndrome, the constant feature is the presence of odontogenic keratocyst mostly present in 75% of the patients. They develop in the first decade of life and peak during the second and third decade of life. Odontogenic keratocyst (OKC) not associated with BCS generally develops later in life after the fifth decade of life; however, in GCS, it presents earlier. Displacement of developing teeth may result in unerupted teeth and root resorption in young patients. At times, patient may still be asymptomatic even with widespread extension throughout the jaws, unless secondarily infected. These OKCs rarely causes pathological fractures and are detected on routine dental checkups [8].

Sixty-five percent of the patients present with palmar or plantar pits. These are approximately 2x3x2 millimeter asymmetrical pits developing on the second decade of life. Basal cell carcinomas may arise from these pits, which are characteristically more evident in warm waters. Histologically, absence of dense keratin in sharply defined areas is seen in these pits [8]. Basal cell carcinoma is seen 50–97% of patients; bifid ribs is seen in 40%; calcified falx cerebri is seen in 37–79% [9].

In the patient, since the left periorbital mass already invaded the globe and orbit, orbital exenteration was done since this procedure would be life-saving. Wide excision of the right and left paranasal masses was done with total parotidectomy for possible tumor cell invasion. Enucleation of the mandibular cyst was done for diagnosis as well as to prevent its transformation to malignancy. Cervico-facial reconstruction was done to defects with full-thickness and split-thickness skin grafts. Frequent follow is required for disease monitoring and for recurrence or development of mass. Genetic counseling is provided for chances of transmission to offspring; hence, close family surveillance is necessary.

Guidelines for follow-up have been established and include the following: cerebral magnetic resonance imaging once in a year for 1-7 years of age, neurological examination twice yearly, pantomogram every 12-18 months starting from the age of eight years, yearly skin examination and cardiologic examination according to the signs and symptoms [10].

Recently, Vismodegib (trade name Erivedge®) is a drug for the treatment of advanced basal cell carcinoma. US Food and Drug Administration (FDA)-approval for vismodegib was obtained in January 2012. Inhibition of Hedgehog signaling pathway in adults is relatively safe; except in pregnant woman, the drug is classified under category D. Most common side effects of vismodegib is muscle cramps, hair loss, weight loss, dysgeusia and fatigue [11, 12].

CONCLUSION

This case highlights the importance of awareness of this rare syndrome especially in young patients to make an early diagnosis to prevent life-threatening and

vision-impairing complications and institute proper management especially of its cancer predisposition. Multiple-disciplinary approach of health specialist like ophthalmologist, neurologist, dermatologist, otorhinolaryngologist, radiologist etc, is necessary for appropriate management. These specialist must also have a good knowledge of the characteristic features of this syndrome for timely diagnosis and management.

LITERATURE SEARCH

PubMed was searched for English-language articles on March 10, 2017, using the following terms: Gorlin-Goltz Syndrome, basal cell carcinoma, calcified falx cerebri. Sources in retrieved articles were cross-referenced.

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Author Contributions

George Michael N. Sosuan – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Alberto C. Chacon – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None

Consent Statement

Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest

Authors declare no conflict of interest.

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