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# Basal Cell Carcinoma, Odontogenic Cysts, Brain and Skeletal Abnormalities (Gorlin Goltz Syndrome) in a 46-Year-Old Woman

### ABSTRACT

**Objective:** To present the case of a 46-year-old woman with basal cell carcinoma, odontogenic cysts, brain anomalies and skeletal abnormalities.

**Methods:**

**Design:** Case Report  
**Setting:** Tertiary National University Hospital  
**Patient:** One

**Results:** A 46-year-old woman consulted for a non-healing, necrotic left orbital ulcer that started as a skin-colored, papilla-like lesion on the upper eyelid. There were also hyperpigmented lesions with ill-defined borders over both paranasal areas. Tissue biopsies revealed basal cell carcinoma. Radiologic imaging showed cystic lesions in the mandible, straightening of cervical vertebrae and calcifications of the falx cerebri, tentorium cerebelli, pineal gland and choroid plexus. Based on established major and minor clinical and radiologic criteria, we arrived at a diagnosis of Gorlin Goltz Syndrome or Nevoid Basal Cell Carcinoma Syndrome (NBCCS). She underwent wide excision of the left orbital mass with exenteration, excision of left and right paranasal masses, left total parotidectomy with facial nerve preservation, enucleation of mandibular cyst and cervicofacial reconstruction with skin grafts of the left orbital area and ala.

**Conclusions:** NBCCS is a rare autosomal dominant disorder with a high tendency for neoplasms and developmental anomalies. Diagnosis can easily be missed if the physician is unaware of its classic but bizarre presentation. Early recognition and prompt specialist referral is very important in order to prevent complications and provide better prognosis. Patients should be reminded of the importance of follow-up as other presentations of the syndrome may manifest later in life and family genetic screening and counseling should be undertaken.

**Keywords:** Gorlin Goltz Syndrome; Nevoid Basal Cell Carcinoma Syndrome; odontogenic keratocyst

**Physicians** are all too familiar with compartmentalization of knowledge – even Ear Nose Throat (ENT) Surgeons divide the head and neck into subspecialties. Beyond our realm the patient is likewise deconstructed-- bent spines are a job for orthopedic spine surgeons, eye problems must be seen by ophthalmologists and brain problems are left to neuroscientists. This effective “divide and conquer” strategy allows for more rapid advancement in each of our fields. But it can also make us lose sight of the larger picture and cause us to miss a rare, more complex entity. We present one such case.

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**CASE REPORT**

A 46-year-old woman from Zamboanga del Norte, Philippines consulted with a chief complaint of a non-healing, necrotic ulcer over the left orbital region. Her condition started 10 years prior when a skin-colored, non-pruritic, non-painful papilla-like lesion appeared on her left upper eyelid. She manually removed the lesion and since noted that the wound had not healed and had changed its appearance, becoming hyperpigmented with raised borders and beginning ulcer formation. It continuously enlarged, occupying the left periorbital area, with areas of necrosis, occasional bleeding and yellowish discharge.

Two years prior to consult, she developed anorexia, easy fatigability and weight loss. She also noted progressive blurring of vision. Consequently, two hyperpigmented papules appeared over her paranasal area. She consulted at a local hospital where she was advised surgery. However, due to financial constraints, she eventually transferred to our institution for further workup and management.

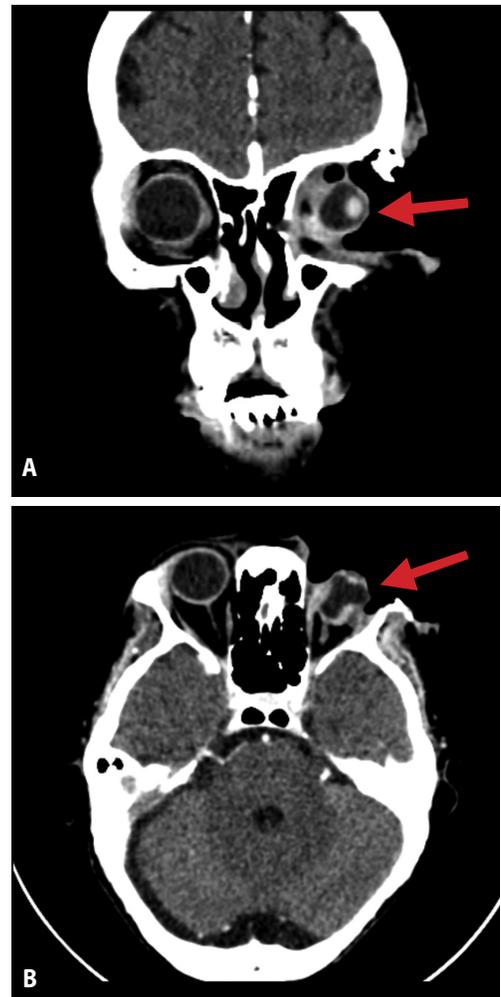
A housewife with seven children, she never smoked or drank alcohol. She had no family history of cancer or chronic sun exposure.

She presented with a 9 x 7 x 3 cm non-tender, non-pruritic ulcer with raised, rolled up border areas of necrosis and crusting occupying the left orbital region. (Figure 1) There were also hyperpigmented, raised lesions with ill-defined borders at the left nasolabial fold and right paranasal area measuring 1 x 1 x 0.5 cm. A 1.5 x 1.5 x 0.5 cm firm non-tender, non-erythematous, movable mass was palpated at the left pre-auricular area. The left upper and lower eyelids were absent and the left globe was deformed but still with light perception. The right eye was grossly normal with 20/20 vision. The rest of the ear, nose, throat, head and neck exam was normal.



**Figure 1.** Mass with necrotic areas occupying the left periorbital region and smaller hyperpigmented lesions involving both paranasal areas.

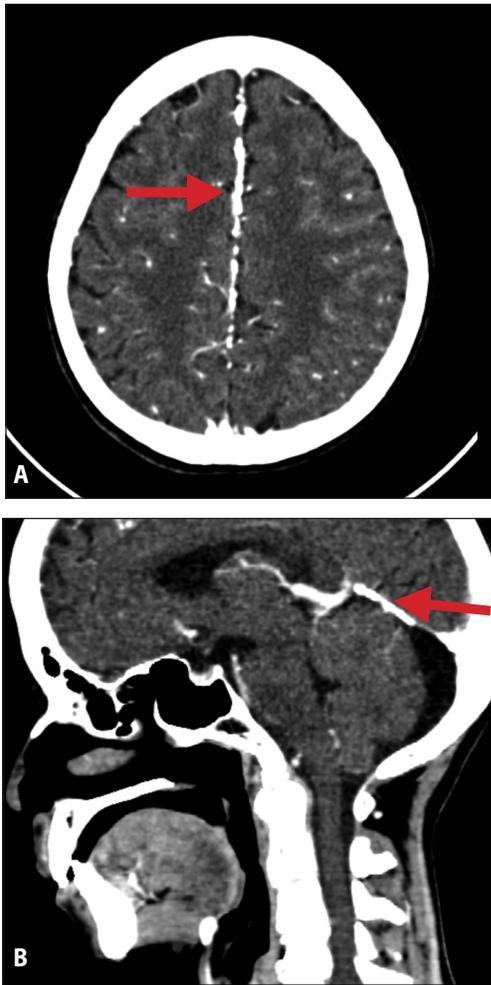
Incision biopsies of the orbital and paranasal lesions revealed Basal Cell Carcinoma. Contrast-enhanced cranial, facial and orbital CT Scans revealed an enhancing soft tissue density in the superior and lateral left intraorbital region measuring approximately 2.9 x 1.9 x 1.2 cm, with extensive ulceration involving the left eyelids and surrounding soft tissues. (Figure 2) There were dense coarse calcifications in the falx cerebri and tentorium cerebelli (Figure 3) as well as at the pineal gland and choroid plexus. The cortical sulci and lateral fissures were prominent with dilatation of the third and fourth ventricles. There were expansile lytic lesions involving the right hemimandible measuring 6.6 x 1.6 x 3.0 cm and symphyseal area measuring 2.5 x 2 x 1 cm. (Figure 4) There were lymphadenopathies in the left parotid region. A skeletal survey revealed straightened cervical vertebra with spurs and sclerosis on endplates and decreased intervertebral space between C4 and C5. A small cystic lesion was seen in the left distal radius. (Figure 5)



**Figure 2.** Contrast-enhanced cranial CT scans (April 2016) **A.** coronal and **B.** axial views showing an enhancing soft tissue density involving the left intraorbital region (arrows).

Our search for a multisystemic syndrome with Basal Cell Carcinoma, odontogenic cysts, brain abnormalities and skeletal anomalies led us to diagnose Gorlin Goltz Syndrome.

Our patient underwent wide excision of the left orbital mass with exenteration, excision of both paranasal masses and the alar mass, left total parotidectomy with facial nerve preservation, enucleation of mandibular cyst, and cervicofacial reconstruction with left orbital split thickness skin graft and left ala full thickness skin graft. (Figure 6) She was discharged after one week but poor graft take was noted two weeks after surgery and application of Silver Sulfadiazine cream was initiated to hasten granulation. (Figure 7A) Three weeks after surgery, she followed up at our clinic and granulation tissue formation was already noted on the defect. (Figure 7B) She has been unable to physically follow-up since as she lives in a remote village on a distant island.



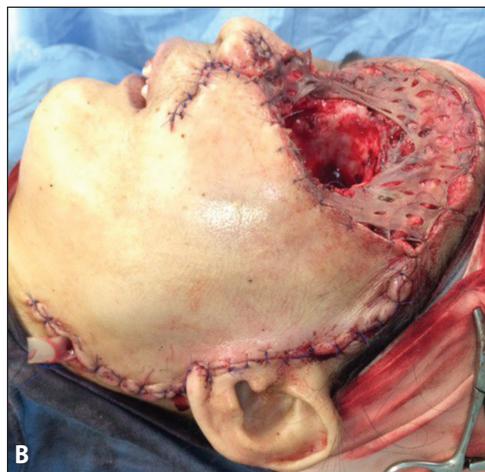
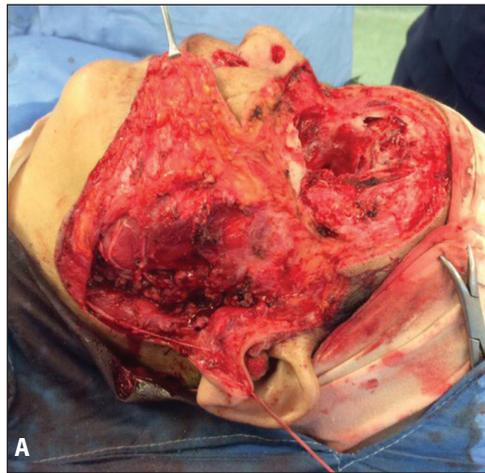
**Figure 3.** Contrast-enhanced cranial CT scans (April 2016), **A.** axial and **B.** sagittal views, showing calcification of falx cerebri and tentorium cerebelli (arrows).



**Figure 4.** Contrast-enhanced CT scans (April 2016), **A.** **B.** axial and **C.** coronal bone window views showing an expansile lytic lesion involving the right hemimandible and symphysis (arrows).



**Figure 5.** X-Ray of the left forearm (April 2016) showing a small cystic lesion at the left distal radius (arrow).



**Figure 6.** Intraoperative **A.** after orbital exenteration and total parotidectomy with facial nerve preservation **B.** cervicofacial flap and STSG.



**Figure 7.** Post-operative **A.** poor graft take over the orbital region 2 weeks after surgery **B.** granulation tissue forming on the surgical wound 3 weeks post surgery.

**DISCUSSION**

Gorlin Goltz Syndrome, also known as *Nevoid Basal Cell Carcinoma Syndrome (NBCCS)*, is a rare autosomal dominant disorder with a high degree of penetrance and phenotype expressiveness.<sup>1</sup> It may present with cutaneous, dental, craniofacial, skeletal, cardiac, ophthalmologic, neurological and sexual anomalies.<sup>2,3</sup> This condition is also called *Gorlin Syndrome, Multiple Nevoid Basal Cell Epithelioma, Jaw Cyst Bifid Rib Syndrome or Multiple Nevoid BCC Syndrome.*<sup>4</sup>

In 1894, Jarish and White first reported cases of this syndrome highlighting the multiple basocellular carcinomas present in patients.<sup>5,6</sup> However, it was not until the 1960s that Robert J. Gorlin and Robert W. Goltz established the classical triad of odontogenic cyst, basal cell carcinoma and bifid rib.<sup>6</sup> This triad was later modified by Rayner *et al.* who added findings of calcification of falx cerebri or palmar and plantar

pits as parts of the criteria in the diagnosis of this syndrome.<sup>7</sup>

The usual age of presentation of NBCCS is 10-30 years old with females being more affected than males.<sup>8</sup> Its prevalence is quite variable. A study in England showed a prevalence of 1 out of 55,600.<sup>9</sup> In Italy, it is 1 out of 256,000; in Australia, 1 out of 164,000; while in Japan, the prevalence is 1 out of 235,800.<sup>9</sup> In the Philippines, an incidence rate has not been established but there was one case report on NBCCS published in a dermatology journal in 2009.<sup>10</sup>

The pathogenesis of NBCCS is attributed to mutations in the patched tumor suppressor gene (PTCH) on chromosome 9q21-23 where an abnormality in the Hedgehog signaling pathway results in neoplasm formation.<sup>11</sup> However, mutations in other genes such as *Patched 2 (PTCH 2)*, *Smoothed (SMO)* and *Sonic hedgehog (SHH)* have been noted in some isolated cases.<sup>11</sup>

The diagnostic criteria for NBCCS have undergone several changes over the past years-- initially established by Evans *et al.*,<sup>12</sup> modified by Kimmons *et al.*,<sup>13</sup> reviewed by Manfredi *et al.*<sup>2</sup> and recently reviewed again at the first international conference on Basal Cell Nevus Syndrome in 2011.<sup>14</sup> From this meeting, the official list of major and minor criteria for diagnosis of NBCCS was established. Major criteria include Basal Cell Carcinoma prior to 20 years old or excessive number of BCC out of proportion to prior sun exposure and skin type, odontogenic keratocyst of jaw prior to 20 years old, palmar and plantar pitting,

lamellar calcification of the falx cerebri, medulloblastoma, typically desmoplastic and first degree relative with NBCCS. Minor criteria are as follows: rib anomalies, macrocephaly, skeletal malformation and radiologic changes (i.e., vertebral anomalies, kyphoscoliosis, short fourth metacarpals, cleft lip/palate, ovarian or cardiac fibroma and ocular abnormalities (strabismus, hypertelorism, congenital cataract, glaucoma, coloboma).<sup>14</sup> The presence of one major criterion and a molecular confirmation or two major criteria or one major and two minor criteria is necessary for the diagnosis.<sup>14</sup> Our patient satisfied 3 Major Criteria (basal cell carcinoma, odontogenic keratocyst and calcified falx cerebri) and 1 Minor Criterion (skeletal malformations).

As demonstrated by our case, the management of NBCCS requires specific treatment for each clinical condition and should involve a multidisciplinary team. Because of its aggressiveness and high rate of recurrence, it is advisable that the patient follows up every 6 months for the first 5 years and every year thereafter.<sup>12</sup> This becomes a major issue in low- and middle-income countries such as ours where people in remote island villages have poor access to health care. Since this is an autosomal dominant condition, family members should undergo genetic screening and be monitored as well, and educated about the disease- its presentation, course, prognosis and the importance of prompt consult – again, an ideal that is easier said than done.

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