Cancer Association of South Africa (CANSA)

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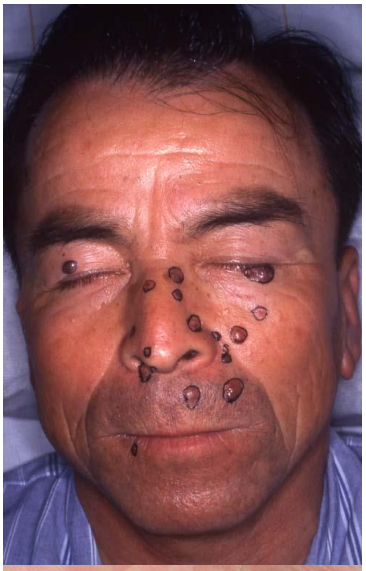
Fact Sheet
on
Gorlin-Goltz Syndrome

Introduction

Gorlin-Goltz syndrome (also known as Gorlin syndrome or Gorlin's syndrome, Gorlin Syndrome, nevoid basal-cell carcinoma syndrome (NBCCS), basal-cell naevus syndrome, and multiple basal-cell carcinoma syndrome) is an autosomal dominant disorder with a high degree of penetrance and variable expressivity. It is characterised by basal cell carcinomas, odontogenic keratocysts, palmar and/or plantar pits, and ectopic calcifications of the falx cerebri. More than 100 minor criteria have been described.

"The presence of two major and one minor criteria or one major and three minor criteria are necessary to establish a diagnosis. Early diagnosis and treatment of Gorlin-Goltz syndrome, as well as family screening and genetic counselling are essential as it may be associated in 10% of the patients with aggressive basal cell carcinomas and malignant neoplasias. "
(Jawa*, et al*.).



[Picture Credit: Gorlin-Goltz Syndrome]

The pictures on the right show the multiple typical Basal Cell Carcinoma (BCC) on the face of the patient as well as the palmar pits in the palm of the hand.

Narang A, Maheshwari C, Aggarwal V, Bansal P, Singh P. 2020. Gorlin-Goltz Syndrome with Intracranial Meningioma: Case Report and Review of Literature. *World Neurosurg*. 2020 Jan;133:324-330. j.wneu.2019.09.156. Epub 2019 Oct 9.

Background: Gorlin-Goltz syndrome is a rare hereditary disease affecting multiple organ systems. Medulloblastoma is the most common intracranial malignancy in these patients, radiotherapy makes them more susceptible to intracranial meningioma. Here we report an intracranial meningioma without radiation exposure.

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Case description: We present a case of intracranial meningioma in a young woman who was postoperatively diagnosed to have Gorlin-Goltz syndrome based on presence of calcification of bilateral tent and falx. Further clinical and radiological assessment helped us identify many other syndromic features and patient was promptly advised multispecialty consultations to screen for other malignancies and counselled regarding risk factors.
Conclusions: Early identification of the syndrome is important for prevention of secondary radiation-induced malignancies, both intracranial and extracranial. Patients need multidisciplinary approach for management.

Vetró, É., Oláh, J., Nagy, D., Széll, M., Piffkó, J. & Seres, L. 2020.
"Gorlin-Goltz syndrome, or nevoid basal cell carcinoma syndrome, is a rare disease that requires multidisciplinary approach in patient management. The disease is genetically heterogenous and has an extremely variable expressivity. Although the syndrome is in the focus of scientific research, our knowledge of it is still limited due to the relatively low number of recognised patients and the complexity of genotype-phenotype correlation. Several papers in this field have been published in the international and also in the Hungarian literature but most of these reports are single cases or small case series of families and outline general information about the disease. Authors aimed to review the literature of the syndrome and to report the genetic background and its role in the diagnosis and treatment. A review of the English and Hungarian literature was performed. The full genetic background of the syndrome is not yet discovered. Increasing the awareness of the syndrome, collecting and thoroughly analysing the medical records and performing genetic tests on the patients may lead to the better understanding of the disease; they may also help early diagnosis and treatment, positive family planning and may establish personalized medicine. Orv Hetil. 2020; 161(49): 2072-2077."

Incidence of Gorlin-Goltz Syndrome in South Africa
The National Cancer Registry (2017) does not provide any information regarding Gorlin-Goltz Syndrome in South Africa.

Signs, Symptoms and Diagnosis of Gorlin-Goltz Syndrom
The most common symptom of Gorlin-Goltz syndrome is the development of basal cell carcinoma early in adolescence or young adulthood. Gorlin-Goltz syndrome is also responsible for the development of other cancers early in life, including:

- medulloblastoma
- breast cancer
- non-Hodgkin's lymphoma
- ovarian cancer

People who have basal cell nevus syndrome often have unique physical features as well. Examples include:

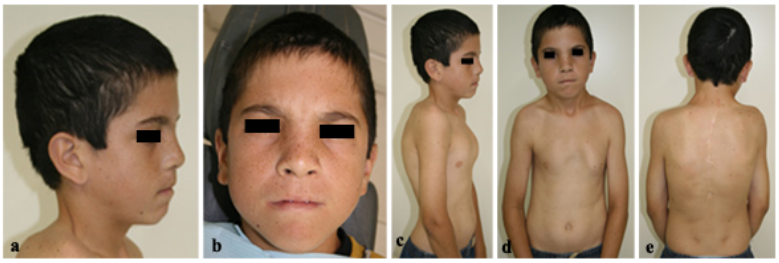
- pitting in the palms of the hands or on the feet
- large head size
- cleft palate
- eyes that are spaced far apart
- a protruding jaw

- spinal problems, including scoliosis or kyphosis

Some people with basal cell nevus syndrome will also develop tumours in their jaw. These tumours are known as keratocystic odontogenic tumours and can cause the person's face to swell. In some instances, the tumours will displace the teeth.

If the condition is severe, additional symptoms may result. For example, it can affect the nervous system. This can cause:

- blindness
- deafness
- seizures
- mental retardation



The doctor can diagnose Gorlin-Goltz Syndrome. He or she will ask about the patient's health history, if ever diagnosed with cancer, and if there is a history of the disease in the family. The doctor will also perform a physical examination to see for any of the following:

- keratocystic odontogenic tumours
- fluid on the brain that leads to head swelling (hydrocephalus)
- abnormalities in the ribs or spine

To confirm the diagnosis, the doctor may also order additional tests including:

- an echocardiogram
- MRI of the head
- biopsy (if you have tumors)
- X-ray of the head and jaw
- genetic testing

A diagnosis of Gorlin-Goltz syndrome can be made if there are 2 major or 1 major and 2 minor criteria.

Major criteria

- Multiple (>2) basal cell carcinomas at any age or one basal cell carcinoma less than 20 years or >10 basal cell naevi
- Histologically proven odontogenic keratocyst or a polyostotic bone cyst
- Palmar or plantar pits (3 or more)
- Ectopic calcification: lamellar or early (<20 years) calcification of the falx cerebri
- Family history of Gorlin-Goltz syndrome

Clinical features.
(a and b) Facial appearance of patient showed dysmorphic facial features, including relative macrocephaly (a) and ocular hypertelorism (b).
(c and d) Lateral and frontal view showing pectum excavatum.
(e) Vertebral anomaly characterized by cyphoscoliosis.
Casaroto *et al. Head & Face Medicine* 2011 **7**:2 doi:10.1186/1746-160X-7-2

Minor criteria

- Congenital skeletal defects: bifid, fused, splayed, or missing rib, or bifid, wedged, or fused vertebra
- Large head with occipitofrontal circumference >97th percentile, with frontal bossing
- Cardiac or ovarian fibroma (benign tumour in heart or ovary)
- Medulloblastoma (a malignant brain tumour that usually arises in young children)
- Lymphomesenteric cysts (abdominal cysts full of lymph fluid)
- Congenital malformation: cleft lip and/or palate, polydactyly (extra fingers or toes), congenital eye defect such as cataract, microphthalmos (small eye) or coloboma (iris tumour)

Figueira, J.A., Batista, F.R.S., Rosso, K., Veltrini, V.C. & Pavan, A.J. 2018.
"Gorlin-Goltz syndrome (GGS), also known as nevoid basal cell carcinoma syndrome, is an autosomal dominant inherited disorder with high penetrance and variable expressivity. The classic triad originally described by Gorlin and Goltz in 1960 is composed of multiple nevoid basalcell carcinomas (NBCCs), odontogenic keratocysts (OKCs) in the jaws and bifid ribs. in 1977, this triad was modified by Rayner et al, and to GGS diagnosis, the OKCs had to appear in combination with calcification of the cerebellar falx or palmar and plantar pits. It may occur that although GGS syndrome is a well-known condition, only the specific symptom could be observed by different specialists. Therefore, the patient cannot be placed in an always complex clinical panel. The authors introduce an example in this report. In the present case, the patient had NBCCs, OKCs, and probably other signs of GGS since 1998, and has been treated for this conditions separated, without a diagnosis of a syndromic condition. A 54-year-old white woman was referred to the oral medicine service due to cyst located in the right mandibular body. She had history of skin cancer and undergone surgeries and radiotherapies for the lesions treatment, scars on the skin face due to the lesions removed, and a new ulcerated lesion on the back of was diagnosed. In addition, the patient presented frontal and parietal bossing leading to increased cranial circumference, hypertelorism, strabismus, broad base, and mandibular prognathism. To the image examination, skull radiography revealed calcification of the falx cerebri; on chest X-ray bifid rib was observed and spine radiography showed vertebral osteophytes. Panoramic radiograph showed a well-defined bilocular radiolucent image located in posterior and anterior mandibular region. The whole elements induced us to investigate the patient's past medical history, which revealed that since 1998 had the diagnosis of NBCC and OKC. A multidisciplinary approach becomes necessary for the diagnosis and follow-up of patients with GGS, considering the complexity of the clinical manifestations. Therefore, it is of primary importance for dental surgeons and dermatologists to know the signs and symptoms of GGS to perform early diagnosis and to avoid progression of the oral cysts or metastasis of the skin lesions."

Manifestations of Gorlin-Goltz Syndrome

Gorlin-Goltz syndrome is a condition that affects many areas of the body and increases the risk of developing various cancerous and non-cancerous tumours.

In people with Gorlin-Goltz syndrome, the type of cancer diagnosed most often is basal cell carcinoma, which is the most common form of skin cancer. Individuals with Gorlin-Goltz syndrome typically begin to develop basal cell carcinomas during adolescence or early adulthood. These cancers occur most often on the face, chest, and back. The number of basal cell carcinomas that develop during a person's lifetime varies among affected individuals. Some people with Gorlin-Goltz syndrome never develop any basal cell carcinomas, while others may develop thousands of these

cancers. Individuals with lighter skin are more likely to develop basal cell carcinomas than are people with darker skin.

Most people with Gorlin-Goltz syndrome also develop non-cancerous (benign) tumours of the jaw, called keratocystic odontogenic tumours. These tumours usually first appear during adolescence, and new tumours form until about age 30. Keratocystic odontogenic tumours rarely develop later in adulthood. If untreated, these tumours may cause painful facial swelling and tooth displacement.

Individuals with Gorlin-Goltz syndrome have a higher risk than the general population of developing other tumours. A small proportion of affected individuals develop a brain tumour called medulloblastoma during childhood. A type of benign tumour called a fibroma can occur in the heart or in a woman's ovaries. Heart (cardiac) fibromas often do not cause any symptoms, but they may obstruct blood flow or cause irregular heartbeats (arrhythmia). Ovarian fibromas are not thought to affect a woman's ability to have children (fertility).

The Sun and Gorlin-Goltz Syndrome

Individuals with Gorlin-Goltz Sydrome have an increased sensitivity to radiation, including radiation from the sun. This means that they need to take extra care in the sun. This is the same for anyone with Gorlin-Goltz syndrome, whether they have had a skin cancer or not. Sufferers should always use a high factor sunscreen (SPF 50) and cover up properly in the sun.

Treatment of Gorlin-Goltz Syndrome

Treatment of patients with Gorlin-Goltz syndrome involves surveillance for and treatment of the associated findings. Because most of the findings involve tumours (benign and malignant), treatment is often surgical.

Patients with Gorlin-Goltz syndrome often require surgery to remove jaw cysts in their 20s. Often, it is not until they are in their 30s or 40s that the basal cell carcinomas begin to appear so the diagnosis of the syndrome is often delayed.

All patients with Gorlin-Goltz syndrome should see a dermatologist for regular skin examinations so that basal cell carcinomas can be treated when they are small. This may require surgery or one of the many other treatments available for these tumours including cryotherapy, photodynamic therapy, fluorouracil cream and imiguimod cread. They should not receive treatment with irradiation as this is liable to provoke the development of more tumours.

Some patients may require long term treatment with oral retinoids such as isotretinoin or acitretin. Advanced basal cell carcinomas may sometimes be treated with vismodegib.

Sun protection is vital to reduce the number of skin cancers developing but even complete protection will not prevent all basal cell carcinomas in patients with Gorlin-Goltz syndrome.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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Sources and References Consulted or Utilised

DermNet NZ
http://www.dermnetnz.org/systemic/bcns.html

eMedicine.Medscape
http://emedicine.medscape.com/article/1101146-treatment

Figueira, J.A., Batista, F.R.S., Rosso, K., Veltrini, V.C. & Pavan, A.J. 2018. Delayed diagnosis of Gorlin-Goltz Syndrome: the important of the multidisciplinary approach. *J Craniofac Surg*. 2018 Sep;29(6):e530-e531.
doi: 10.1097/SCS.0000000000004438.

Genetics Home Reference
http://ghr.nlm.nih.gov/condition/gorlin-syndrome

Gorlin-Goltz Syndrome
http://dermaamin.com/site/atlas-of-dermatology/9-g/587-gorlin-syndrome-.html
http://www.intechopen.com/books/current-genetics-in-dermatology/nevoid-basal-cell-carcinoma-syndrome-nbccs-

Hasan A. & Akintola, D. 2018. An update of gorlin-Goltz Syndrome. *Prim Dent J*. 2018 Sep 1;7(3):38-41.

Healthline
http://www.healthline.com/health/basal-cell-nevus-syndrome#Overview1

Jawa, D.S., Sircar, K., Samani, R., Grover, N., Jaidka, S. & Singh, S. 2009. Gorlin-Goltz syndrome. *J Oral Maxillofac Pathol*. 2009 Jul-Dec; 13(2): 89–92. doi: 10.4103/0973-029X.57677 PMCID: PMC3162868

Kohli, Munish., Kohli, Monica, Sharma, N., Siddiqui, S.R. & Tulsi, S.P.S. 2010. Gorlin-Goltz Syndrome. Natl J Maxillofac Surg. 2010 Jan-Jun; 1(1):50 – 52. Doi: 10.4103/0975-5950.69171

Narang A, Maheshwari C, Aggarwal V, Bansal P, Singh P. 2020. Gorlin-Goltz Syndrome with Intracranial Meningioma: Case Report and Review of Literature. *World Neurosurg*. 2020 Jan;133:324-330. j.wneu.2019.09.156. Epub 2019 Oct 9.

National Cancer Institute
http://www.cancer.gov/clinicaltrials/learningabout/what-are-clinical-trials
http://www.cancer.gov/about-cancer/treatment/clinical-trials

National Journal of Maxillofacial Surgery
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3304191/

Robert J Gorlin
http://www.cell.com/ajhg/fulltext/S0002-9297(07)61120-3

Sanaghera, R. & Grewal, P. 2018. Gorlin Syndrome presentation and the importance of differential diagnosis of skin cancer: a case report. 2018. *J Pharm Pharm* Sci. 2018;21(1s):222s-224s. doi: 10.18433/jpps30150.

Scalia, A.C., Farulla, A., Fiocchi, F., Albaoni, C. & Torricelli, P. 2018. Imaging features of uterine and ovarian fibromatosis in Nevoid Basal Cell Carcinoma Syndrome. *J Radiol Case Rep*. 2018 Sep 30;12(9):21-30. doi: 10.3941/jrcr.v12i9.3390. eCollection 2018 Sep.

Vetró, É., Oláh, J., Nagy, D., Széll, M., Piffkó, J. & Seres, L. 2020. Genetic aspects of Gorlin-Goltz syndrome. *Orv Hetil*. 2020 Dec 6;161(49):2072-2077.