

A FAMILIAL CASE OF GORLIN-GOLTZ SYNDROME.

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SUMMARY:

Gorlin-Goltz syndrome (GGS) also known as Nevoid Basal Cell Carcinoma Syndrome is a rare autosomal-dominant disorder characterized mainly by the presence of multiple basal cell carcinomas (BCC), odontogenic keratocysts of the jaw and palmar pits. This syndrome is associated with a wide spectrum of developmental anomalies and neoplasms. A case of familial Gorlin-Goltz syndrome with many of the common manifestations is reported. A 29 year-old woman and her 50 year-old mother with GGS are presented. The disease started respectively at the age of 18 and 22, with multiple basal cell carcinomas on the face and upper extremities. Because of multiple odontogenic keratocysts of the jaws they two have been treated surgically. Clinical, cranial CT, histological and dermoscopy images from both patients were obtained. Multiple BCC in the mother and the daughter were detected, nodular and superficial spreading, 10 - 30 mm in diameter. The daughter has many pits on her palms. Palmar pits have a characteristic dermoscopy with red globules inside the flesh-colored, slightly depressed lesions. The histological examinations revealed different histological variants of BCC. The X-rays examination showed two jaw cysts in the daughter, calcifications of the brain falx and bridges of the sella turcica in both patients. The BCC in the patients were treated with cryosurgery and surgical excisions with good results. The patients are followed up. In conclusion our case demonstrated multisystemic involvement of GGS. The combination of clinical, imaging and histological findings is helpful in identifying GGS patients. It is important to make an early diagnosis and a proper management in GGS, which may have cancer predisposition. The genealogical analysis is important for the determination of the genetic risk and the prognosis for the proband's relatives.

Key words: Gorlin-Goltz syndrome, basal cell carcinomas, jaw odontogenic keratocysts, palmar pits, dermoscopy, cryosurgery.

INTRODUCTION:

Gorlin-Goltz syndrome also known as Nevoid Basal Cell Carcinoma Syndrome is a rare autosomal-dominant disorder characterized mainly by the presence of multiple

basal cell carcinomas, odontogenic keratocysts of the jaw and palmar pits. This syndrome is associated with a wide spectrum of developmental anomalies and neoplasms (13). We present a case of familial Gorlin-Goltz Syndrome, characterized by multiple basal cell carcinomas, odontogenic keratocysts and skeletal manifestations.

Case report:

A 29-year-old woman was admitted in our dermatological department with multiple basal cell carcinomas on the face and a 30 mm in diameter swelling in the right maxillary region. She had many pits on her palms. Her 50-year-old mother also had similar clinical symptoms. The disease started with small nodular basal cell carcinomas on the face and trunk when the daughter was 18 and the mother 22 years old. Because of recurrent skin carcinomas with or without pigment they both have been repeatedly treated surgically with transient result. They both have been operated on thrice because of odontogenic keratocysts of the jaws. Physical examination showed the patients were tall of stature – 180 and 185 cm respectively. Pathological changes affecting cardio-vascular, respiratory and the neural systems were not observed. Dermatological status in the daughter revealed multiple nodular basal cell carcinomas on the skin of her forehead, nose and temporal bone (fig. 1). She had multiple pigmented nevi on her trunk and many pits on her palms too. These pits had a characteristic dermoscopy with red globules mainly distributed inside the flesh-colored and slightly depressed lesions (fig.2, 3). Dermatological status in the mother showed multiple nodular basal cell carcinomas on the forehead, nose and chin 10 – 30 mm in diameter. Some of them were with eroded surfaces. She had two superficial spreading basal cell carcinomas in the infraorbital region on her left eye and her left arm (fig.4,5). Cranial CT revealed calcifications of the brain falx and bridges of the sella turcica in both patients (fig. 6 a, b). There were two jaw cysts in the daughter. Her right maxillary sinus was filled with a liquid formation 41/28 mm with a destructed frontal wall but without infiltration in the face tissues. A similar formation 27/25 mm without destruction and expansion was detected in the left maxillary sinus. There was a last molar retention (fig.7).The histological examinations revealed different

histological variants of the basal cell carcinomas (fig.8). X-rays examination showed a bifid rib in the mother. The genealogical analysis showed autosomal-dominant mode of inheritance (fig.9). There were no other affected relatives. A diagnosis familial Gorlin-Goltz Syndrome was made on the basis of clinical, imaging and histological findings. The basal cell carcinomas in both patients were treated with cryosurgery (liquid nitrogen) and surgical excisions with good results. The daughter was directed to surgical extirpation of the jaws cysts. The patients are followed up.

DISCUSSION:

Gorlin-Goltz syndrome also known as Nevoid Basal Cell Carcinoma Syndrome was described for the first time in 1894 from Jarisch and White. The disease is an autosomal dominant disorder mainly characterized by the presence of multiple basal cell carcinomas, odontogenic keratocysts of the jaw, and volar pits (10, 14). In 1960 Robert James Gorlin and William Goltz gave a complete description of the syndrome. This syndrome is associated with a wide spectrum of developmental anomalies and neoplasms (6). Skeletal malformations are expressed by frontal, temporo-parietal bossing, prominent supraorbital ridge giving the eyes a appearance, broad nasal root, hypertelorism, mild mandibular prognathism. Other skeletal anomalies include bifid ribs, involving more than one rib unilaterally or bilaterally, kyphoscoliosis, fusion of vertebrae, spina bifida, polydactyly (8,9). The prevalence of this condition is about 1 per 60 000. Gorlin-Goltz syndrome has been mapped to the long arm of chromosome 9 q22.3-q31 (2, 4, 11). Data suggest that a product of this gene acts as tumor suppressor and Gorlin-Goltz syndrome's typical malformative patterns suggest that the main function is to control the growth and development of normal tissues. The abnormalities seen in the latter are similar to those seen in people exposed for long periods to UV radiation. These abnormalities could determine malignant cutaneous tumors removing antineoplastic protection. Gorlin-Goltz syndrome is associated with multiple keratocysts in patients in the second decade of their life. In the presented cases one of the first signs were multiple cystic lesions involving the maxilla and mandibule, which have been histopathologically diagnosed as odontogenic keratocysts. The association with odontogenic keratocysts, however not clearly understood, appears in more than 90% of the cases (7). All the other disorders are less frequent (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. 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 (10).

Despite the name of the syndrome multiple basal cell

carcinomas occur only in 50% of the cases. Basal cell carcinomas most often proliferate between puberty and 35 years of age. They may vary in number from a few to one thousand 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. Rarely they involve the waist or extremities. 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 (3). Management of superficial basal cell carcinoma without hair follicle involvement can be accomplished by topical application of 0.1 % retinoin cream, 5% 5-Flourouracil cream, imiquimod 5% cream, cryosurgery and surgical excision (5, 12, 15). Evans and colleagues proposed major and minor diagnostic criteria for Gorlin-Goltz syndrome (1). There should be at least two major criteria or one major and two minor criteria for the diagnosis. In the presented cases four of the major criteria were covered: 1. More than two basal cell carcinomas; 2. Odontogenic keratocyst (proven on histology); 3. Three or more palmarorplantar pits; 4. Ectopic calcification: lamellar falx calcification. The liquid nitrogen treatment showed very good results. The daughter was directed for surgical excision of the last maxillary cysts.

CONCLUSION:

It is important to make an early diagnosis and a proper management of Gorlin-Goltz syndrome, which has cancer predisposition. The guidelines for diagnosis include a family history, careful oral and skin examinations, chest and skull radiographs, panoramic radiographs of the jaw, magnetic resonance imaging of the brain and pelvic ultrasonography in women. The genealogical analysis is important for the determination of the genetic risk and the prognosis for the proband's relatives (1).



Fig. 1. Daughter: Nodular basal cell carcinoma on the skin of the nose.



Fig.2. Daughter: Pits on the palms.

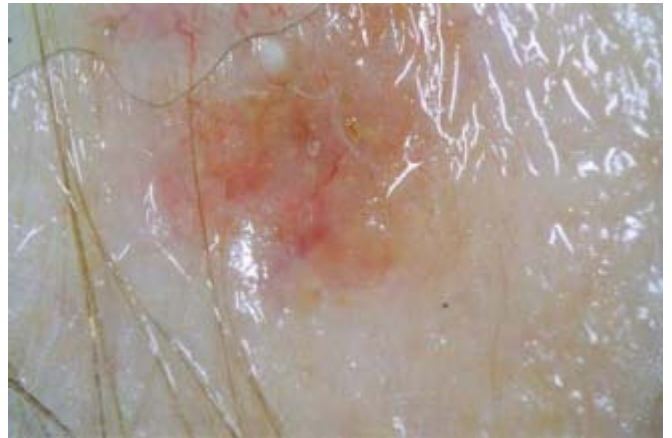


Fig. 3. Dermoscopy of the pits - red globules inside the flesh-colored and slightly depressed lesions.



Fig. 4. Mother: Multiple nodular basal cell carcinomas with eroded surfaces on the skin of the forehead, nose and chin.



Fig. 5. Mother: A superficial spreading basal cell carcinoma on the left arm.

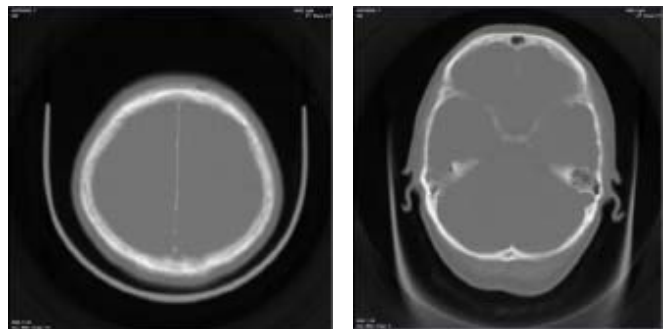


Fig. 6 a, b. Cranial CT - calcifications of the brain falx and bridges of the sella turcica.

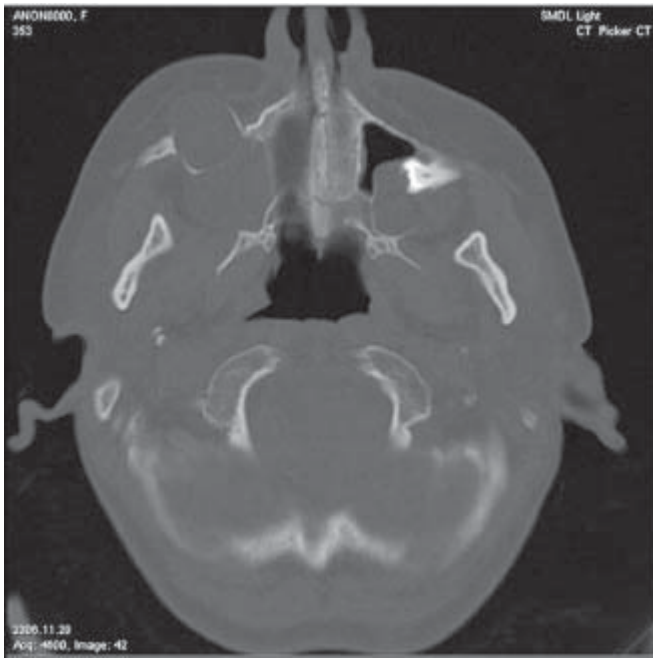


Fig. 7. Daughter: Cranial CT - two jaw cysts.

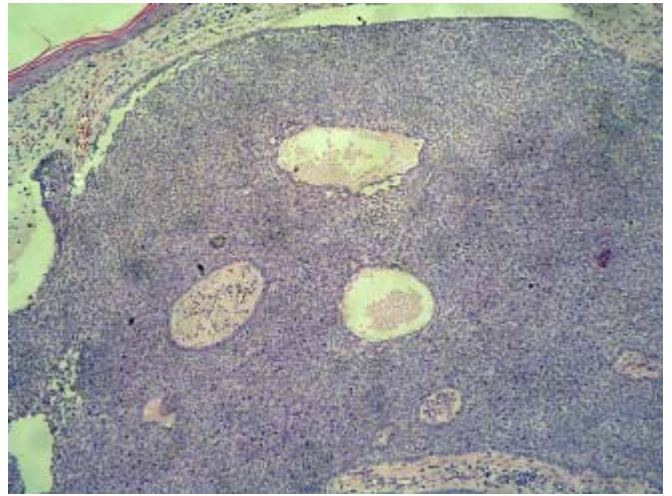


Fig. 8. A solid variant of basal cell carcinoma with central necroses and pigmented cells. HE x 10.

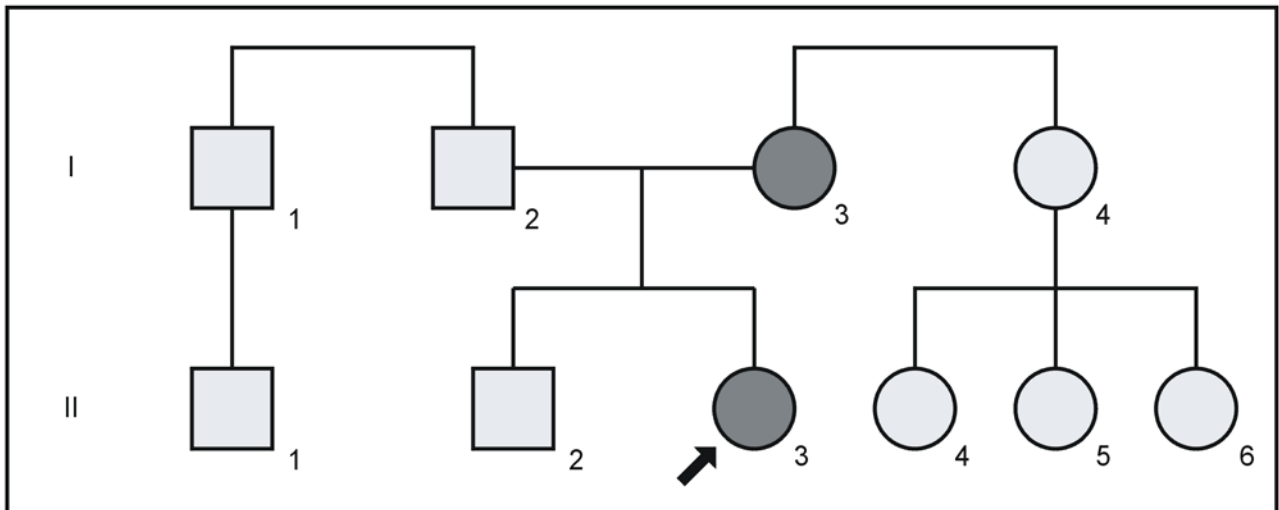


Fig. 9. Pedigree of the affected family: autosomal-dominant mode of inheritance.

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