Basal cell nevus syndrome: a case report and review of literature

Beata Bergler-Czop, Elżbieta Meszyńska, Ligia Brzezińska-Wcisło

Department of Dermatology, Medical University of Silesia, Katowice, Poland
Head: Prof. Ligia Brzezińska-Wcisło MD, PhD

Post Dermatol Alergol 2012; XXIX, 1: 56–59

Abstract

Basal cell nevus syndrome (Gorlin-Goltz syndrome, nevoid basal cell carcinoma syndrome – NBCCS) is an autosomal dominant inherited disorder. We describe a patient with symptoms of NBCCS that fulfilled the diagnostic criteria: more than 2 basal cell carcinoma (BCC) or 1 BCC before the age of 30 years or more than 10 basal cell nevi, 3 or more plantar/palmar or plantar pits, calcification of the cerebral falx, positive family history for basal cell nevus syndrome, congenital skeletal anomalies of the spine and ribs, prominent frontal tubers, cleft palate. Despite the presence of those symptoms that suggested the diagnosis, the patient was not previously informed about the diagnosis of a genetic syndrome and the consequences of such diagnosis especially about the oncological risk, the need of genetic advice before family planning.

Key words: basal cell nevus syndrome, carcinoma, Gorlin-Goltz syndrome.

Introduction

Basal cell nevus syndrome (Gorlin syndrome, nevoid basal cell carcinoma syndrome – NBCCS) (MIM#109400) is an autosomal dominant inherited disorder. Gene PTCH, located in the 9q22.3, 9q31 chromosome [1], has been identified as the cause of this syndrome and a probable cause of certain neoplastic growth [2, 3]. The disease manifests by meso- and ectodermic dysfunction that involves defects of the skin, nervous, ocular, endocrine and musculo-skeletal systems.

Homozygous PTCH1 predisposes to neoplastic growth, including basal cell carcinoma (BCC), medulloblastoma, esophageal cancer and urinary bladder cancer [2, 4].

The skin lesion in the nevoid phase is similar to melanocytic nevi. Ulceration, cicatrisation and other features of the BCC are present only in the oncogenic phase of the skin lesion. Other typical skin symptoms include: palmar and/or plantar pits and also epidermoid cysts located in the acral regions [2-4].

The diagnostic criteria for NBCCS were established by Evans *et al.* and modified by Kimonis *et al.* in 1997 [5].

Major criteria:

- more than two basal cell carcinomas or one basal cell carcinoma before the age of 30 yeras or more than 10 basal cell nevi,
- any odontogenic keratocyst or polyostotic bone cyst,
- three or more palmar or plantar pits,
- ectopic calcification: lamellar or present before the age of 20 years,
- calcification of the cerebral falx,
- positive family history of NBCCS.

Minor criteria:

- congenital skeletal anomalies involving malformations of vertebrae and ribs,
- increased size of the frontal tubers,
- cardiac or ovarian fibroma,
- medulloblastoma,
- lymphomesenteric cysts,
- other congenital malformations such as cleft palate, polydactylism or anomalies of the eyes.

The diagnosis of Gorlin syndrome can be made when two major or one major and two minor criteria are present [6, 7].

Case report

A female patient aged 51 years. The first nevoid basal cell carcinomas was present on the skin of the chest at the age of 25 years. In a short period of time the lesions have spread to the face, the scalp and the extremities. Similar skin changes were also present on the skin of the

Address for correspondence: Beata Bergler-Czop MD, PhD, 2a Lesna, 42-624 Ossy, Poland, phone/fax: +48 32 284 08 77, e-mail: bettina2@tlen.pl

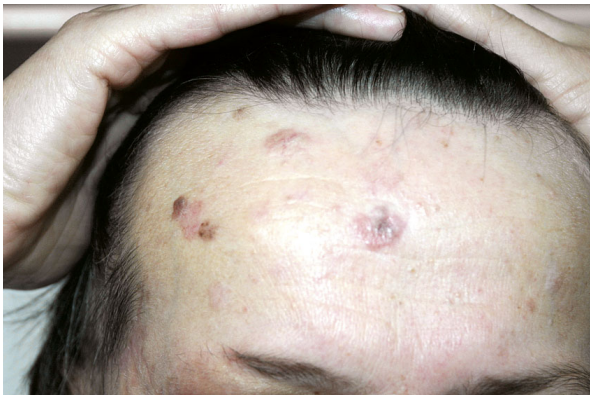

Figure 1. Carcinoma basocellulare on the forehead

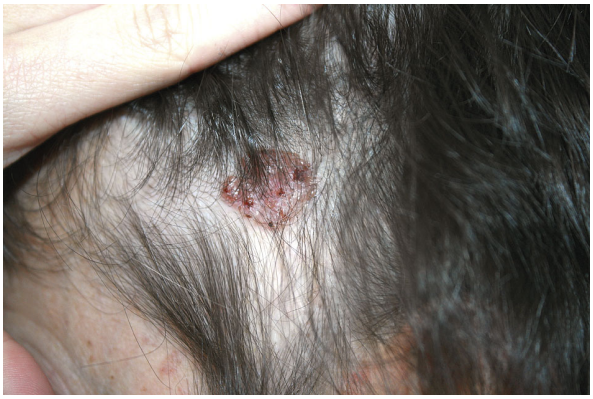

Figure 2. Carcinoma basocellulare on the temporal region

patient's father and younger sister. The father was also diagnosed with brain tumor and epilepsy (medical documentation of his case is not complete). The patient as an infant underwent surgery because of the cleft palate. As a child, the woman was also treated for Sprengel disease (congenial elevated position of scapula). The patient's son, who is 17, also suffers from Sprengel disease, without any other symptoms of the Gorlin syndrome.

In 2000, she was also diagnosed with arthrosis of the $2^{nd}/3^{rd}$ grade within medial femoral condyle and arthroscopy was performed. In 2010, she was admitted to the Department of Dermatology to undergo the first full diagnostic evaluation and qualification for chemoprevention using oral retinoids.

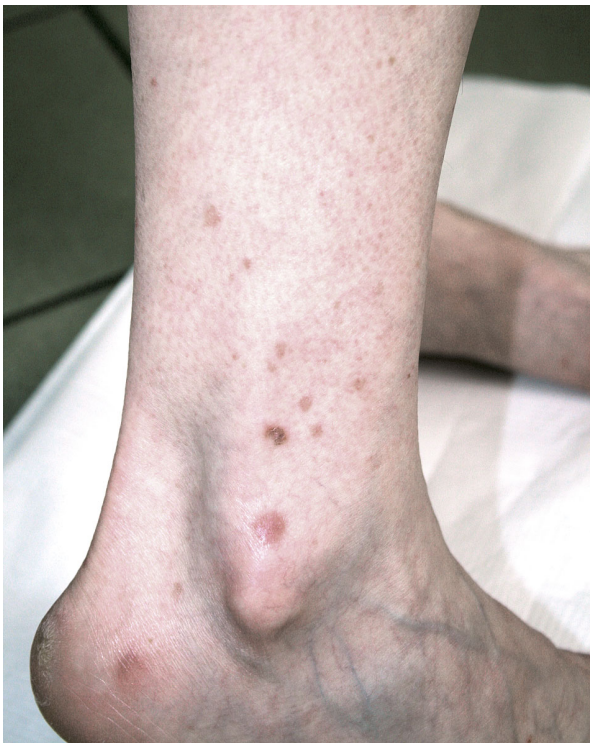

Figure 3. Carcinoma basocellulare on the leg

The thing we first noticed during the physical examination was the presence of prominent frontal tubers and hypertelorism of the orbits. Numerous, painless, flesh colored or reddish brown nodes with pearly borders were found on the skin of the face, scalp (occipital, temporal area), trunk and shanks. Changes located in the lower part of the back were pigmented maculae that resembled melanocytic nevi. This lesion occurred 2 weeks after cryosurgery. Palmar and plantar pits were present in large numbers (Figures 1-4).

Total cholesterol, triglyceride level, LDL and HDL were increased. The other laboratory tests: with no abnormalities. Tumor markers: CEA, Ca 125 levels were normal. Chest X-ray: right thoracic scoliosis, elongation of the aortic arch. X-ray of sinuses and the skull: calcification of the cerebral falx (Figure 5). X-ray of the cervical spine: severe left cervical scoliosis, narrowed intervertebral space C3-C4, C5-C6. Degenerative changes in the intervertebral joints. Intervertebral joints C6-C7, C7-Th1 were not visible. X-ray of the thoracic spine: severe right thoracic scoliosis. Static deformation of Th2-Th4 vertebrae. Narrowed intervertebral space in Th2-Th4. Abdominal ultrasound, electrocardiography: no abnormalities observed. Gyne-

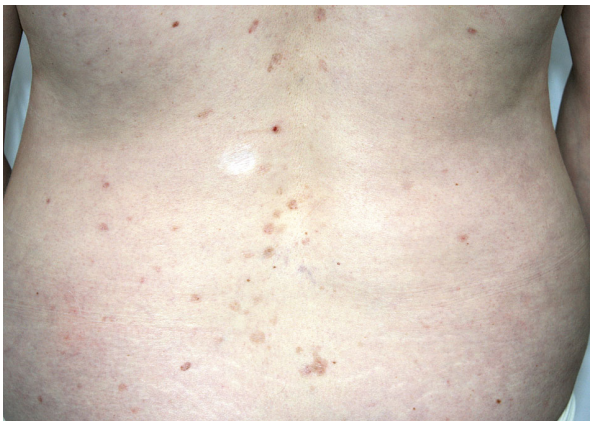

Figure 4. Carcinoma basocellulare on the trunk

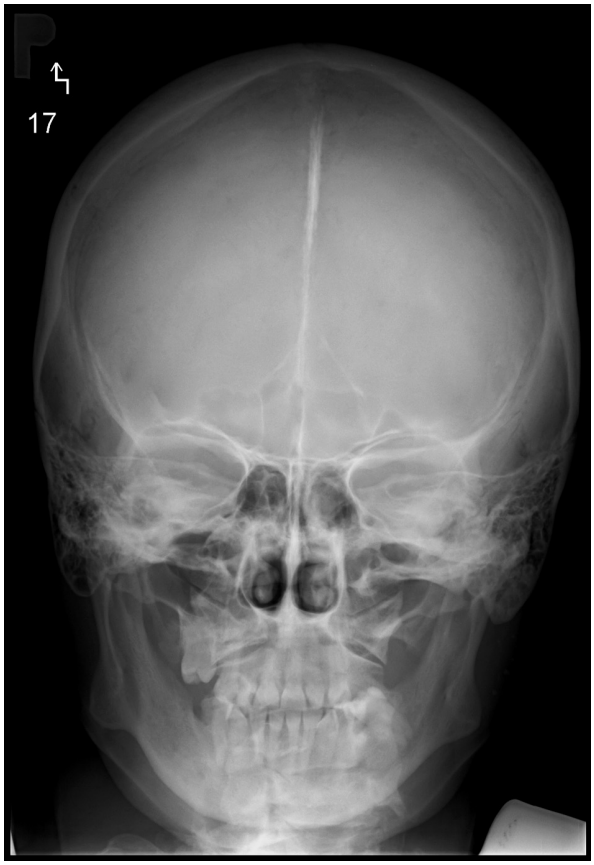

Figure 5. Calcification of the cerebral falx (front)

cological, ophthalmological and laryngological consultations: no abnormalities.

Based upon the surgical consultation, lesions located on the forehead, the temples and occiput were qualified for surgical treatment, other lesions for cryosurgery. The patient was referred for further treatment to our outpatient clinic – smaller lesions were treated with cryosurgery and bigger were removed surgically. Because of the altered level of lipids the patient was disqualified from chemoprevention using oral retinoids (isotretinoin).

The patient was also informed about the need of genetic counseling and possible performance of DNA tests of her son who suffered from Sprengel disease, which is one of the symptoms of Gorlin syndrome.

Discussion

The prevalence of Gorlin syndrome is 1 in 50,000 to 150,000 in the general population. The frequency varies depending on the region of the world and is the highest in whites [7]. Typical manifestations of the syndrome are multiple basal cell carcinomas, which are often the first symptom of the disease. The incidence of BCCs varies widely among ethnic groups: black patients are affected in 60%, while whites – up to 90% [8].

The BCCs appeared in our patient at the age of 25 years. Despite the high prevalence of BCCs, the diagnosis of NBCCS is sometimes not obvious. Mackenzie and Maurice [9] reported a very interesting case of a 35-year-old patient where the presence of multiple neoplasms was said to be connected with immunosuppression that she received after kidney transplantation. Only thorough investigation led to the diagnosis of GS. The BCC rarely metastasizes, but it is still considered malignant because it can cause significant destruction and disfigurement by invading surrounding tissues. However Lamon *et al.* [10] reported a case of a 54-year-old patient having GS with multiple BCCs with metastasis in bones. In the case described by us, despite the presence of multiple BCCs, a positive family history (father and younger sister) and the early diagnosis of Sprengler disease, the diagnosis of GS was not accurately made. In 65-70% of GS cases, mandibular cysts are found, often during a radiological examination [2]. Skeletal anomalies, including Sprengler disease are described in 65-70% of NBCCS [2, 10]. Other common deformations include: hypertelorism, prominent frontal tubers (our patient has an increased distance between orbits but it does not fulfill the criteria of hypertelorism and also prominent frontal tubers) and double ribs. Calcification of the cerebral falx is also typical and was found in our case during radiological examination. The physical examination also reveals palmar and plantar pits in 60% of patients. Cases of cleft palate and lip were less frequently described. Our patient underwent surgery in childhood because of such changes. All patients with NBCCS are in a higher oncological risk group. The most commonly described neoplasms include medulloblastoma, fibromas of the heart and ovaries, meningiomas, leiomyoma, lymphomesenteric cysts [2, 6]. We have some information that the patient's father suffered from brain tumor but we do not have full documentation about the type of the neoplasm. Garrè *et al.* [11] studied the prevalence of malignant neoplasms (medulloblastoma) in the patients in a high oncological risk group. In almost 50% of cases medulloblastoma was connected with GS. Ueda *et al.* [12] described also another case of testicular thecoma in an 11-year-old patient with diagnosed NBCCS.

Reported defects of the ocular system include coloboma, congenital cataract and glaucoma. The ophthalmological consultation of our patient did not show any abnormalities.

Patients with GS require a multispecialistic team approach, including dermatologists, neurologists, surgeons, oncologists, stomatologists and geneticists. In most of the cases, because of the clinical manifestation the diagnosis is made by a dermatologist. The skin lesions can be treated with the use of local medicaments (retinoids, fluorouracil, 5% imiquimod), surgical excision (alone or together with use of oral retinoids), photodynamic therapy, cryosurgery, laser ablation [13, 14].

In the case of our patient, surgical excision together with cryosurgery was used. Ferreres *et al.* [14] and Alessi *et al.* [15] described good effects of treatment after local use of 5% imiquimod for BCC, with the exception of nodular BCC. UV exposition plays a crucial role in the development of BCC, that is why patients with GS should be informed about the absolute importance of the use of sun protection (UV protective sun glasses, avoidance of direct sun exposure during the midday, use of high-factor sunscreens – SPF30+) [5]. The information that radiotherapy, as a method of oncological treatment in this group of patients is contraindicated, is also important. Tang *et al.* [16] described the protective role of oral NSAIDs (colecoxib) in patients with GS. Oral retinoids are also chemopreventive, however our patient was disqualified from such treatment due to deviations in laboratory examination.

We described a patient with typical symptoms of NBCCS that fulfilled the diagnostic criteria: more than 2 BCC or 1 BCC before the age of 30 years or more than 10 basal cell nevi, 3 or more plantar/palmar and/or plantar pits, calcification of the cerebral falx, positive family history for basal cell nevus syndrome, congenital skeletal anomalies of the spine and ribs (Sprengel disease), prominent frontal tubers, cleft palate. Despite the presence of those symptoms that suggested the diagnosis, the patient was not previously informed about the diagnosis of a genetic syndrome and the consequences of such diagnosis especially about the oncological risk, the need of genetic advice before family planning.

References

1. Mallory SB. An illustrated dictionary of dermatologic syndromes. Taylor and Francis (sec. ed.). London and New York 2006.
2. Braun-Falco O, Plewig G, Wolff HH, Burgdorf WHC. Gorlin syndrome. In: Dermatology. Braun-Falco O, Plewig G, Wolff HH, Burgdorf WHC (eds.). Czelej, Lublin 2002; 1441-62.
3. Maas SM, Lombardi MP, van Essen AJ, et al. Phenotype and genotype in 17 patients with Goltz-Gorlin syndrome. J Med Genet 2009; 46: 716-20.
4. Tanabe R, Fujii K, Miyashita T, et al. Clinical manifestations in 25 Japanese patients with Gorlin syndrome. No To Hattats 2009; 41: 253-7.
5. Muzio LL. Nevoid basal cell carcinoma syndrome (Gorlin syndrome). Orph J Rare Dis 2008; 3: 32.
6. Ljubenovic M, Ljubenovic D, Binic I, et al. Gorlin-Goltz syndrome. Acta Dermatovenereol 2007; 16: 166-9.
7. Hottinger AF, Khakoo Y. Neurooncology of familial cancer syndromes. J Child Neurol 2009; 24: 1526-35.
8. van der Geer S, Ostertag JU, Krekels GA. Treatment of basal cell carcinomas in patients with nevoid basal cell carcinoma syndrome. J Eur Acad Dermatol Venereol 2009; 23: 308-13.
9. Mackenzie KA, Maurice PD. Delayed diagnosis of Gorlin's syndrome in a renal transplant recipient. Australas J Dermatol 2009; 50: 121-4.
10. Lamon T, Gerard S, Meyer N, et al. Exceptional bone metastasis of basal cell carcinoma in Gorlin-Goltz syndrome. Dermatology 2010; 220: 57-9.
11. Garrè ML, Cama A, Bagnasco F, et al. Medulloblastoma variants: age-dependent occurrence and relation to Gorlin syndrome: a new clinical perspective. Clin Cancer Res 2009; 15: 2463-71.
12. Ueda M, Kanematsu A, Nishiyama H, et al. Testicular thecoma in an 11-year-old boy with nevoid basal-cell carcinoma syndrome (Gorlin syndrome). J Pediatr Surg 2010; 45: 1-3.
13. Gilchrest BA, Brightman LA, Thiele JJ, et al. Photodynamic therapy for patients with basal cell nevus syndrome. Dermatol Surg 2009; 35: 1576-81.
14. Ferreres JR, Macaya A, Jucgla A, et al. Hundreds of basal cell carcinomas in a Gorlin-Goltz syndrome patient cured with imiquimod 5% cream. J Eur Acad Dermatol Venereol 2006; 20: 877-8.
15. Alessi SS, Sanches JA, de Oliveira WR, et al. Treatment of cutaneous tumors with topical 5% imiquimod cream. Clinics (Sao Paulo) 2009; 64: 961-6.
16. Tang JY, Aszterbaum M, Athar M, et al. Basal cell carcinoma chemoprevention with nonsteroidal anti-inflammatory drugs in genetically predisposed PTCH1+/- humans and mice. Cancer Prev Res 2010; 3: 25-34.