

CLINICAL CASE

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## A case of nevoid basal cell cutaneous syndrome – radiological, CT and MRI findings

G.I. Kirova<sup>1</sup>, A. Stratiev<sup>2</sup>

<sup>1</sup>Department of Radiology and <sup>2</sup>Department of Maxillofacial Surgery, “Lozenetz” Hospital, Sofia, Bulgaria

### Summary

*The nevoid basal cell carcinoma syndrome (NBCCS) is a rare, still well-defined autosomal dominant disorder, characterized by multiple cutaneous basal cell carcinomas, jaw keratocysts and a variety of other tumors and developmental anomalies. The nevi turn malignant with time, and thus, early diagnosis, follow-up, and treatment are imperative.*

*This article presents a case of a 60-year-old man with classical form of NBCCS. The images from conventional radiography, CT and MRI are discussed in the context of clinical presentation of the disease, and the importance of imaging modalities in the diagnostic process is stressed.*

**Key words:** basal cell carcinoma, CT, cyst, jaws, MRI, NBCCS

### Introduction

NBCCS, also known as Gorlin-Goltz syndrome, is an ecto-mesodermic polydysplasia characterized by four primary symptoms: multiple nevoid basal cell epitheliomas that usually undergo malignant transformation; jaw keratocysts that show constant growth; skeletal anomalies; and intracranial calcifications. Because of the rarity of this entity and the possibility to find it incidentally in the everyday practice, it is very important to recognize the Gorlin-Goltz syndrome because appropriate treatment and lifelong monitoring is essential for patient management.

### Case presentation

A 60-year-old man presented with multiple reddish pigmented enlarging nodules on his scalp, face, neck, trunk and extremities. He had first noticed a small pigmented lesion on his left eyebrow 10 years ago. Four years later an advanced eyelid basal cell carcinoma with orbital infiltration was treated with orbital exenteration. Since then, other lesions had appeared in many parts of his body. He had been otherwise healthy and without a history of exposure to radiation.

On physical examination, multiple reddish, dome-shaped nodules were present on his scalp, face, right forearm, chest and lower abdomen. They ranged in size from 0.5 to 2 cm. Multiple biopsy specimens from different sites showed pigmented basal cell carcinomas. Some of them had already been excised and irradiated (Figures 1A and 1B).

Mental and neurologic examinations revealed no abnormalities. Laboratory workup including chest radiography, abdominal ultrasound, serum biochemistry and full blood count were within normal limits.

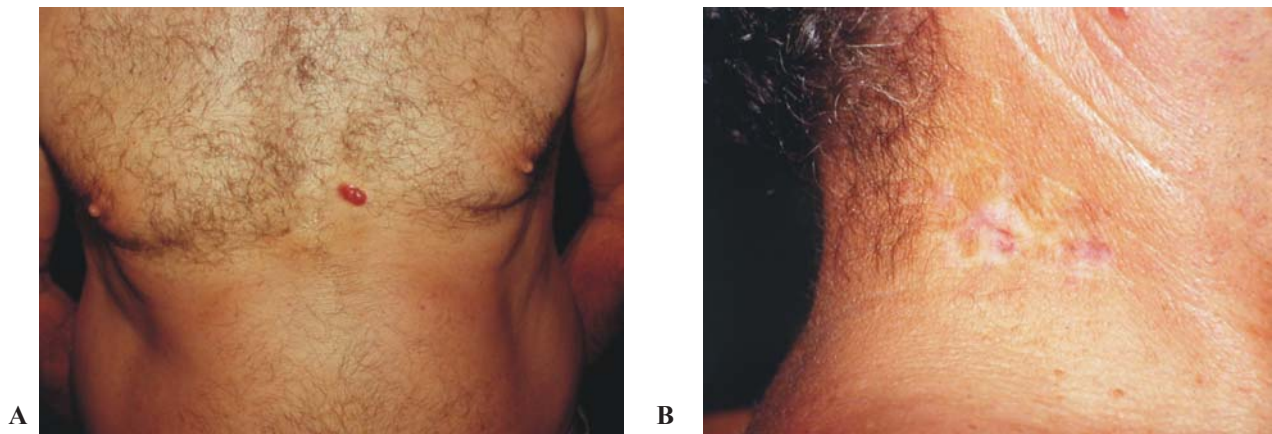
Because the patient's past dental history was one of poor compliance, with previous dental extractions, and also because the main complaints were pain

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Author and address for correspondence:

Galina Kirova, PhD  
Department of Radiology  
“Lozenetz” Hospital  
1 Koziak street  
1407 Sofia  
Bulgaria  
Tel: +359 88 401678  
E-mail: krassi@omega.bg



**Figure 1.** Basal cell nevus on the patient's trunk (A). Scar from previously removed basal cell carcinoma on the patient's right side of the neck (B).

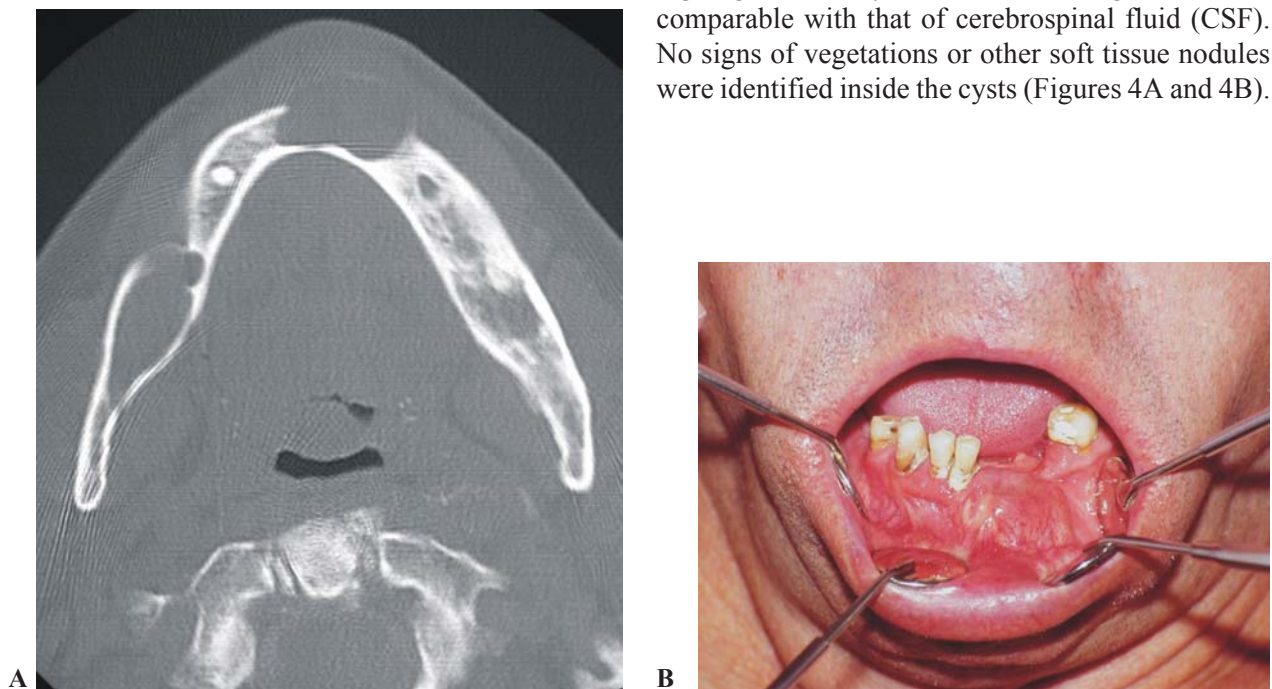
and swelling of the gingiva, a panoramic radiograph was performed which showed several well-defined radiolucencies with cortical thinning and destruction in the mandible, corresponding to the picture of multiple odontogenic cysts. Two of them were located in both rami and the biggest in the anterior mandible, causing tooth displacement and root resorption.

Because of the decision for surgical reconstruction, a CT of the head and lower face was performed which confirmed the presence of multiple well-defined, unilocular cyst lesions, one of them destroying

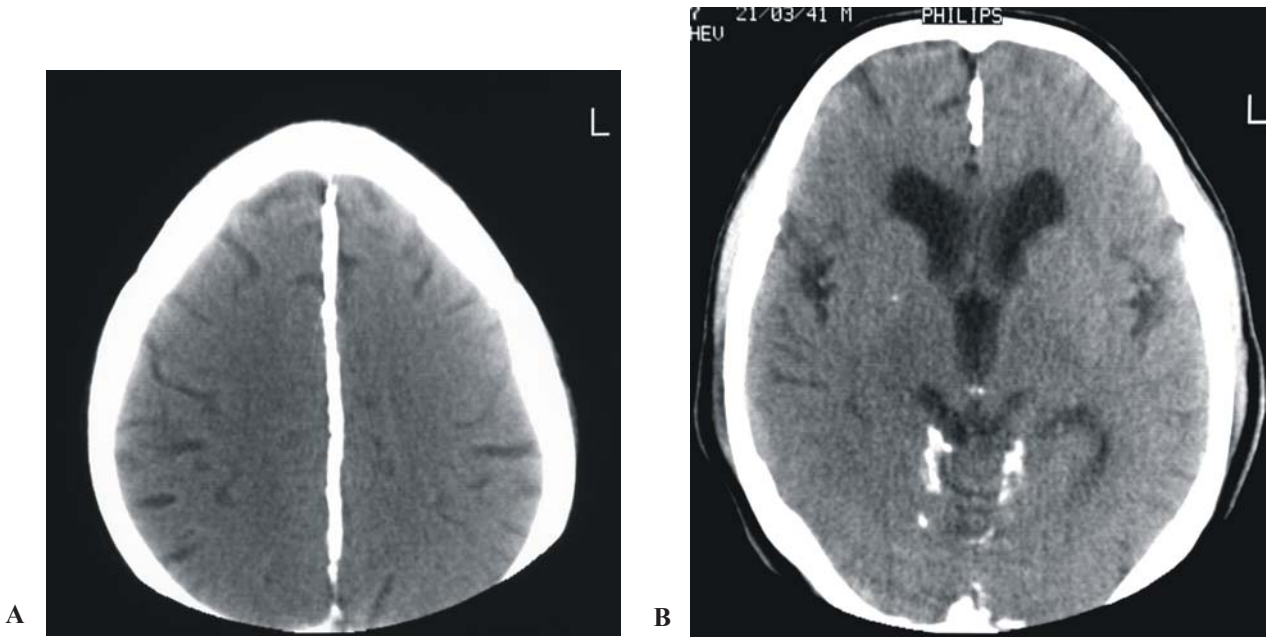
the outer cortex of the mandible. This was the cause of a painful gingival bossing near the middle line. The mandibular canal appeared displaced inferiorly. None of the cysts showed multilocularity or septations. There were no signs of periosteal reaction or new bone formation. Both temporo-mandibular joints were normal (Figures 2A and 2B).

The brain CT showed extraordinary ossifications in the falx and tentorium cerebri. No other anomalies were noted (Figures 3A and 3B).

Additional MRI of the midface revealed the presence of pure cysts in the mandible. They showed high signal intensity in T2WI and low signal in T1WI, comparable with that of cerebrospinal fluid (CSF). No signs of vegetations or other soft tissue nodules were identified inside the cysts (Figures 4A and 4B).



**Figure 2.** Axial CT scan shows 3 focal areas of decreased attenuation in the middle and both lateral parts of the mandible. All of them are unilocular, hypoattenuating with well-corticated undulating borders. The biggest one situated on the midline shows thinning of the cortex and fine perforation of the buccal plate (A). Clinical appearance of the gingival bossing near the middle line (B).



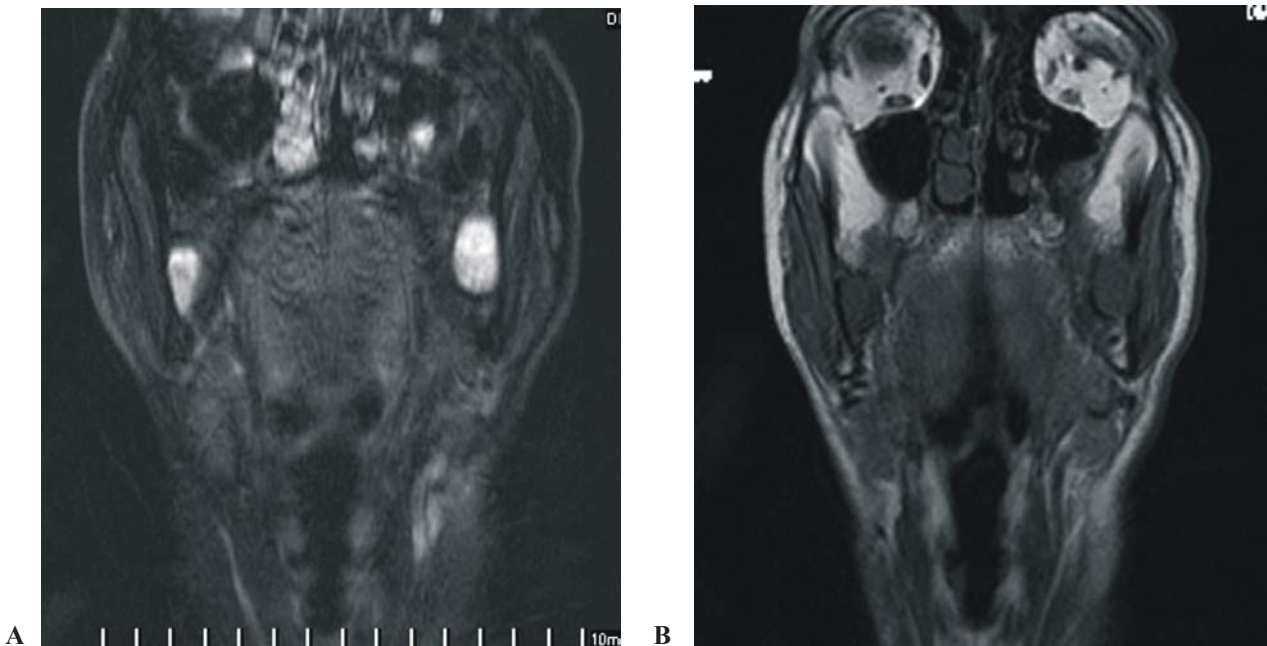
**Figure 3.** Axial CT of the brain shows no abnormalities in the brain parenchyma (A). Note the extensive calcifications in the tentorium cerebri (B).

**Discussion**

NBCCS is a familial autosomal dominant syndrome with variable penetration, characterized primarily by multiple basal cell carcinomas, multiple odontogenic keratocysts of the jaws, skeletal anomalies and ectopic calcifications of the falx cerebri and others structures [1]. A myriad of additional findings may

also be noted. Among the most frequent ones are palmar and plantar pits, a characteristic flattened facies and broad root, frontal and parietal bossing, mandibular prognathia, hypertelorism, strabismus, dystrophy of the canthi and clefts of the lip, alveolus and/or palate [2,3].

Recently, this syndrome was shown to result from germline mutations in a human patched gene, which



**Figure 4.** Coronal MRI of the midface shows the expansive cystic lesions in both mandibular rami with high SI in T2WI (A) and low SI in T1WI (B).

encodes for a membrane receptor and functions as an important developmental regulator and a tumor suppressor. Haploinsufficiency for the human patched gene locus is likely to give rise to developmental abnormalities characterized by symmetrical defects and malformed spine and ribs. Postnatal loss of the normal human patched gene allele leads to multiple basal cell carcinomas and other cancers. Human patched gene mutations and loss of the remaining wild-type allele have also been identified in sporadic basal cell carcinomas and medulloblastomas [4-8]. Unfortunately, a comprehensive family history could not be ascertained in our case, however the patient's mother had been also affected by a similar condition.

The most characteristic finding of NBCCS are odontogenic keratocysts. They usually develop in the first decade of life, with a peak incidence in the second or third decade. Because of the benign nature of the cysts, the process very often is asymptomatic, particularly in early stages, and it is discovered incidentally at routine dental radiography used in orthodontia. The most common symptom is pain, which may or may not be accompanied by swelling. Other reported symptoms and signs include paresthesias and tooth displacement or morbidity, as in the presented case [9].

Odontogenic keratocysts are of special interest because of their high recurrence rate and aggressive behavior. They occur commonly in patients in the third decade of life, followed by those in the second decade. Eighty percent occur in the mandible, and the other 20% in the maxilla [10]. The mandibular molar and premolar areas are the most common sites, and the most frequent clinical manifestations at first admission are swelling, pain, or both. As the frequency of recurrence at follow-up is 60%, the cysts must be treated aggressively [11]. Histologically, the cysts are parakeratinized, orthokeratinized, or mixed types. Patients with multiple cysts all show parakeratinization. Surface corrugation, subepithelial split, suprabasal split, satellite microcysts, epithelial islands, significant inflammation, hyaline bodies, and dystrophic calcification are present [12].

An exact diagnosis of multiple jaw cysts is easily made using only the routine panoramic tomography, particularly if the topographic position of the cysts and any relationship to the dental system are taken into account [13,14]. At radiography, an odontogenic keratocyst usually appears as a unilocular, radiolucent lesion with smooth, corticated borders that is often associated with an impacted tooth. They may cause cortical thinning, tooth displacement, and root resorption. Although odontogenic keratocysts are most com-

monly located in the body and rami of the mandible, they may also occur in the anterior mandible, as in our case, or anywhere in the maxilla [15]. High resolution CT studies can exquisitely determine the extent of the cysts and pinpoint areas of cortical breakthrough, as well as involvement of the teeth [16]. Other characteristic signs revealed by cranial CT are calcifications of the falx cerebri and the so called "bridging" between processus clinoideus anterior and posterior of the sella turcica. Whilst CT displays aspects of bone morphology not visible on plain films, MRI provides the essential macropathological details of the cysts, including intracystic soft tissue masses which correlate with the histological findings of focal inflammatory ulceration of the cyst lining, orthokeratosis and cell debris. In several cases, when the cysts are large enough to destroy adjacent structures or propagate to the soft tissue planes, MRI is helpful in the preoperative planning. The features identified by these combined imaging techniques are helpful in distinguishing the odontogenic keratocysts from other cysts or neoplastic lesions and are invaluable in the surgical planning for excision of these lesions [17,18].

Many lesions that occur in the mandible have a cyst-like radiographic appearance. These lesions are often difficult to differentiate on the basis of their radiographic features alone [9]. Careful consideration of the patient history and the location of the lesion within the mandible, its borders, its internal architecture, and its effects on adjacent structures generally make it possible to narrow the differential diagnosis. Odontogenic keratocysts are more likely to show aggressive growth than other odontogenic cysts and may have undulating borders and a multilocular appearance; these characteristics make odontogenic keratocysts indistinguishable from ameloblastomas [19]. The differential diagnosis becomes difficult in cases where the peripheral compact lamella is missing or the bony border is not sharp, and in cases of honeycombed, multilocular, polycystic form. In such cases, tumors, metastases and systemic diseases must be included in the differential diagnosis of various jaw cysts [20]. Furthermore, hematological malignancies should be considered in the differential diagnosis. In cases of associated signs of multiple skin lesions, jaw keratocysts, skeletal anomalies and excessive intracranial ossifications, the diagnosis of NBCCS has to be taken into account.

In the presented case the relatively late presentation of odontogenic keratocysts, the lack of obvious skeletal anomalies and the associated history of aggressive eyelid basal cell carcinoma in the past, make the exact diagnosis difficult. The patient was of poor

socio-economic status, unable to have a regular dental care.

In our case the typical radiographic presentation of multiple odontogenic keratocysts, the presence of falx calcifications on the CT of the brain and the general aspect of the skin lesions were the clue to the diagnosis of the condition.

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