Two male patients with nevoid basal cell carcinoma syndrome from Turkey

Celal Tümer[1], Nuray Er[1], Sevim Balcı[2], Atilla Ataç[3]

Departments of [1]Oral Surgery, and [3]Pedodontics, Faculty of Dentistry and [2]Clinical Genetics Unit, Department of Pediatrics, Faculty of Medicine, Hacettepe University, Ankara, Turkey

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Nevoid basal cell carcinoma syndrome, also known as Gorlin's syndrome, is a familial autosomal dominant syndrome characterized by multiple basal cell carcinomas, multiple odontogenic keratocyts of the jaws, and skeletal anomalies. Both tumors and malformations of the central nervous system occur with nevoid basal cell carcinoma. Medulloblastoma is the primary brain tumor most frequently associated with this syndrome. The authors report in this article two male patients with nevoid basal cell carcinoma syndrome: a 22-year-old male patient with multiple odontogenic keratocyts, who had medulloblastoma at two years and multiple basal cell carcinoma at 10 years of age, and a 15-year-old male patient with skeletal abnormalities and multiple odontogenic keratocyts in the jaws.

Key words: nevoid basal cell carcinoma syndrome, odontogenic keratocyst, basal cell carcinoma, medulloblastoma.

Nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin's syndrome, was first reported in 1894 by Jarisch and White, but was not delineated until 1960 by Gorlin and Goltz[1,2]. Gorlin and Goltz in 1960 suggested a well defined symptom complex consisting of multiple basal cell carcinomas, jaw cysts and skeletal anomalies[1]. The basal cell carcinomas occur on nonexposed as well as sun-exposed areas of the skin on any part of the body, but are mostly seen on the face. Other manifestations include multiple odontogenic keratocysts in the maxilla and mandible, bifid ribs, kyphoscoliosis or other vertebral anomalies, pectus excavatum or carinatum, Sprengel's deformity of the scapula, marfanoid build, mild hypertelorism, palmar and plantar pits, calcified falx cerebri, childhood medulloblastoma, craniopharyngioma and neurofibroma[3-5]. NBCCS is a rare entity, with only around 500 cases having been reported as far as we know[2,6]. In this article, we report two male patients with NBCCS.

Case Report

Case 1

A 22-year-old male patient with a history of medulloblastoma in the posterior fossa operated at two years of age and basal cell carcinoma diagnosed at 10 years of age was referred to Hacettepe University Faculty of Dentistry, Department of Oral Surgery with a complaint of swelling on his mandibular region. On clinical examination, the patient showed typical facial and physical appearance characterized by severe growth retardation (height 1.47 cm and weight 35 kg at 22 years, both below the 3rd percentile), basal cell carcinomas on the scalp and the anterior trunk (Figs. 1, 2), and palmar and plantar pits (Fig. 3). Panoramic radiograph revealed multiple odontogenic cysts in the mandible and maxilla (Fig. 4). Skeletal radiographic survey showed basal and falx cerebral calcifications, bifid ribs and fusion of the cervical vertebrae.

The jaw cysts were excised under general anesthesia. Microscopic examination of the mandibular and maxillar cysts revealed odontogenic keratocysts with hyperchromatic basal cell layer and parakeratinized surface (Fig. 5).

Based on the above, the patient was accepted as NBCCS. Family history was negative for NBCCS. The patient's family was examined and was found to have no jaw cysts. The patient had a normal 20-year-old sister and a 18-year-old brother who was mentally normal but had glaucoma. Chromosome analysis from peripheral blood was normal (46 XY) and sister chromatid exchange (SCE) was found within normal limits (4.4).

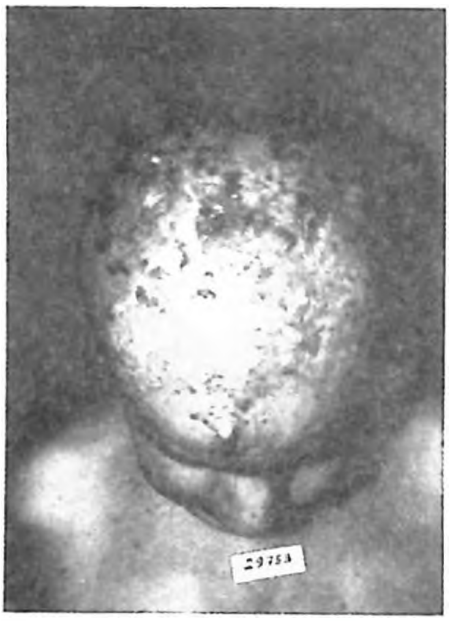

Fig. 1. General appearance of the scalp with multiple erythematous plaques and nodules.

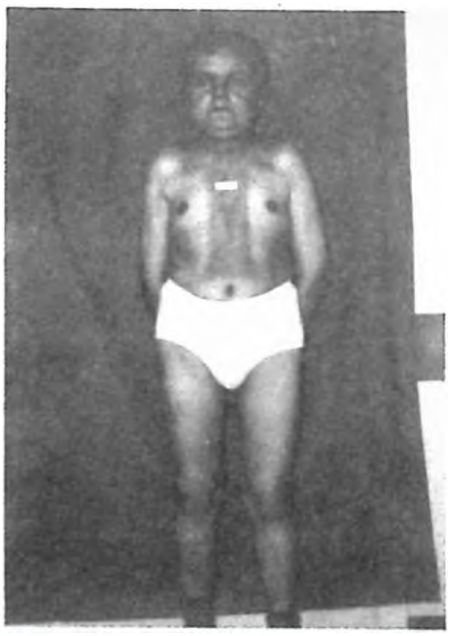

Fig. 2. Multiple erythematous plaques located on the anterior aspect of the trunk, clustered around the midline.

Case 2

15-year-old male patient who suffered from swelling on the right side of his face for two years was referred to the Department of Oral Surgery. Intraoral examination showed a fluctuating expansive mass at the right posterior mandibular alveolar ridge and another fluctuating mass between the teeth in the right anterior maxilla. On his clinical examination, the patient had characteristic facial appearance with enlarged occipitofrontal circumference (head circumference

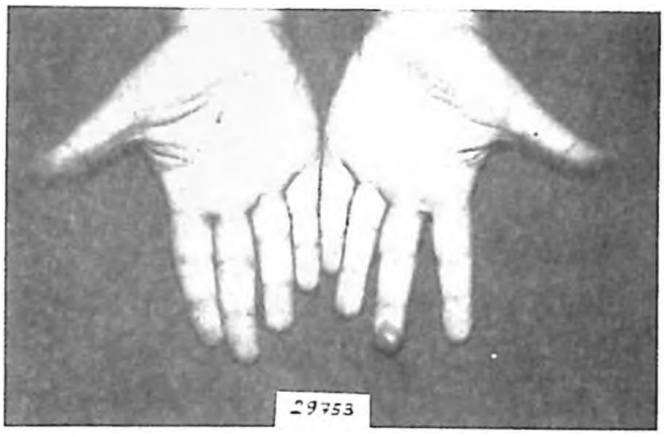

Fig. 3. Palmar and plantar pits of the first patient.

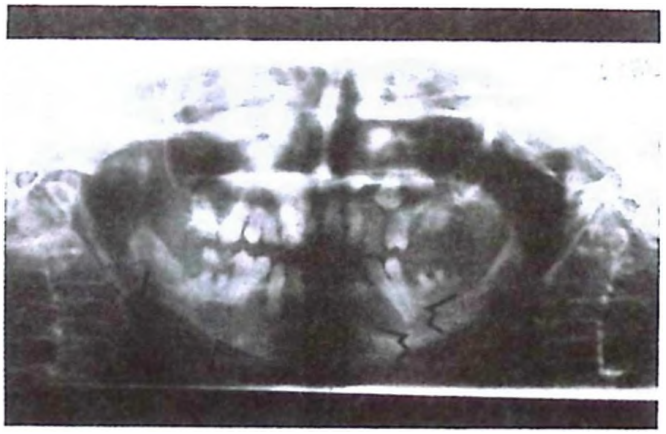

Fig. 4. Panoramic radiograph of the first patient revealing multiple odontogenic jaw cysts.

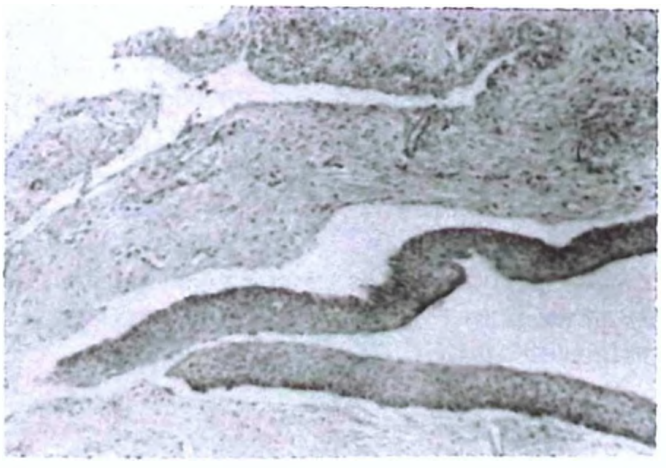

Fig. 5. Odontogenic keratocyst. Cyst epithelium with hyperchromatic basal cell layer and parakeratinized surface. Detachment of the epithelium from the capsule is obvious (HE X 200).

was 56 cm, chest circumference was 66 cm). frontal bossing, and mild hypertelorism (Fig. 6), and he had marfanoid build (height was 170 cm, weight was 43 kg), kyphoscoliosis and Sprengel's deformity of his scapulae (Figs. 7, 8). There was a surgical scar on his chest for pectus excavatum. Panoramic radiograph revealed multiple odontogenic cysts in the mandible and the maxilla (Fig. 9). Chest radiograph demonstrated bifid, fused and missing ribs, hemivertebra and scoliosis (Fig. 10). Computed tomography scans of the brain did not reveal any intracranial mass. Multiple odontogenic cysts of the jaws were excised under general anesthesia. Histopathologic examination revealed odontogenic keratocysts with daughter cysts in the fibrous wall of the cyst (Figs. 11, 12). Family history of this patient revealed that he was the second child. The patient's father, mother and the other two brothers were normal. Chromosome analysis of our patient was normal (46, XY). Based on his clinical, radiological and histopathologic findings, the patient was accepted as NBCCS, in

Fig. 6. General facial appearance of the second patient.

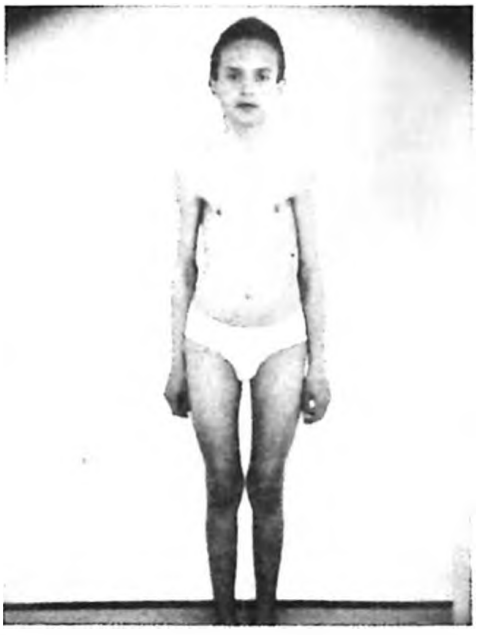

Fig. 7. Skeletal abnormalities and marfanoid appearance of the second patient.

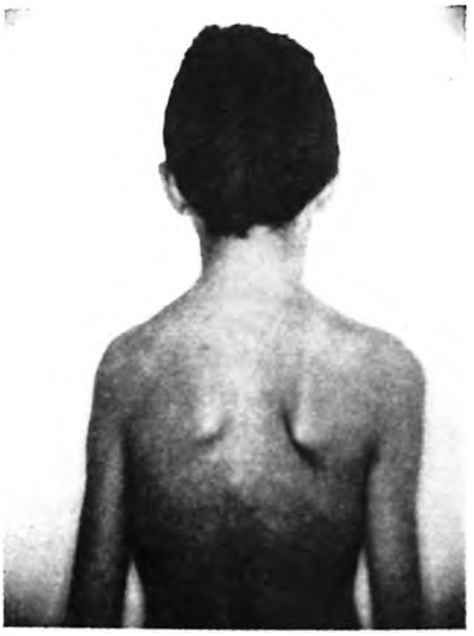

Fig. 8. Kyphoscoliosis and Sprengel's deformity of the second patient.

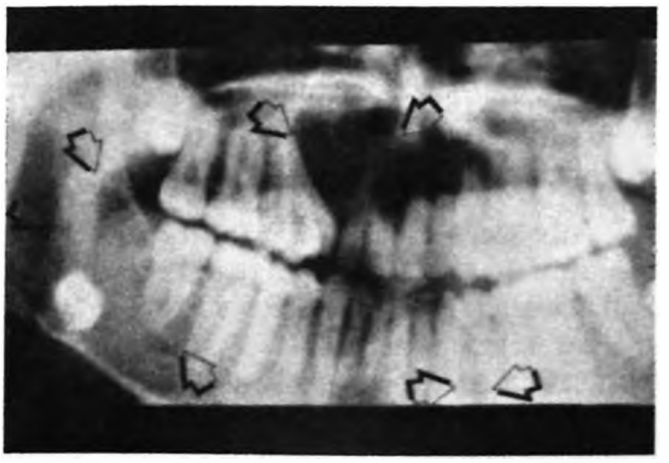

Fig. 9. Panoramic radiograph of the second patient revealing multiple odontogenic jaw cysts.

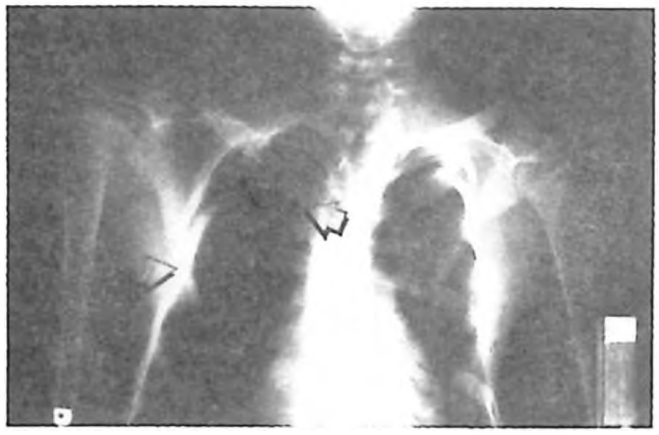

Fig. 10. Chest radiograph demonstrating rib anomalies, hemivertebra and scoliosis.

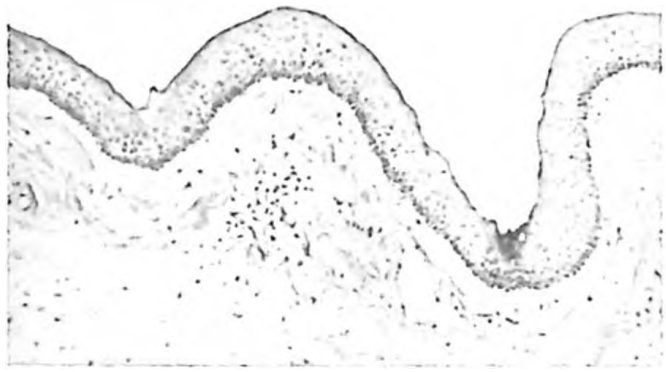

Fig. 11. Odontogenic keratocyst. Cyst epithelium shows hyperchromatic basal cell layer and parakeratinized surface (HE X 400).

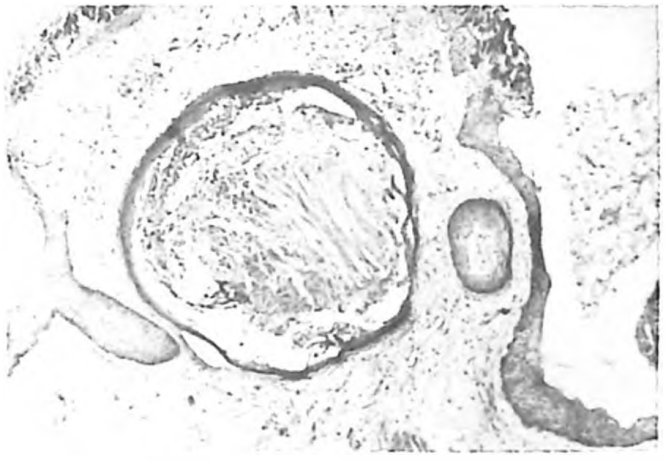

Fig. 12. Odontogenic keratocyst. Daughter cysts are seen in the fibrous wall of the cyst (HE X 100).

spite of absence of brain tumors and skin carcinomas at this age. The patient is being followed for future development of skin, intracranial or other malignancies.

Discussion

The mode of inheritance in Gorlin's syndrome is autosomal dominant[2]. The gene has been mapped to chromome 9q22-3-q31 and most likely functions as a tumor suppressor gene[6]. Recently, Cohen[8] showed that the cause of this syndrome was a single point mutation in one patched allele. This may be responsible for the malformations found in NBCCS. Inactivation of both patched alleles results in formation of tumors and cysts[8]. Older paternal age is a factor in fresh mutations. In our patients, the paternal age was 32 years in the first case and 30 years for the second case.

Evans et al.[3] reported two cases (1-2%) of NBCCS among 173 consecutive cases of medulloblastoma. This figure is lower than previous estimates. Medulloblastoma in NBCCS occurs at an average age of about two years, whereas sporadic cases of medulloblastoma occur at an average age of about six years[2,3,7]. Evans et al.[9] in his 173 consecutive cases of medulloblastoma suggested that patients with NBCCS-associated medulloblastoma tend to survive longer than patients with sporadic medulloblastoma. Ten patients with NBCCS had survived more than 10 years after removal of a medulloblastoma[3,7]. The 20-year survival of our patient after medulloblastoma resection is therefore not unusual for a patient with NBCCS.

Skin lesions are common in patients with NBCCS. Basal cell carcinomas usually appear largely between puberty and 35 years of age,

although they can be seen as early as the second year of life[2]. Approximately 2% of patients under 45 years of age with basal cell carcinomas have NBCCS. These tumors usually grow slowly, but some become invasive and if untreated cause tissue damage[10].

Odontogenic keratocysts account for 3% to 10.5% of all jaw cysts. Most odontogenic keratocysts are often asymptomatic and are discovered on routine radiological examinations[11]. The average age for diagnosis of NBCCS is 13 years, but keratocysts have been reported in patients as young as eight years. The development of odontogenic keratocysts peak[5] during the second or third decade[2,11]. This is approximately a decade earlier than the isolated odontogenic keratocysts not associated with the syndrome[2]. The most common locations, in order of decreasing frequency, are the mandibular third molar region, maxillary third molar region, and mandibular first and second molar region[11]. As these cysts have a tendency to recur, they must be treated aggressively. Enucleation of the cysts and irrigation of the cavity with Carnoy solution helps in preventing recurrence[12]. The odontogenic keratocysts in our two cases were typical for localization and time of appearance. As these cysts are usually asymptomatic, routine panoramic radiographic controls are essential in patients with NBCCS. Earlier diagnosis and treatment of these lesions will prevent the development of large jaw defects, make surgery easier and prevent tooth loss.

In this article, we report two new patients with NBCCS. It is important that these cases are all followed up by pediatricians, while the diagnosis of NBCCS is established by oral surgeons. Furthermore, in medulloblastoma and skin carcinoma cases of childhood, further evaluation for jaw cysts is necessary for the accurate diagnosis of NBCCS.

For the first time, we studied SCE in a case with NBCCS who demonstrated all of the findings of this syndrome at 22 years of age. However, the second case showed only skeletal malformations and jaw cysts. We are therefore closely following this case for the possible development of brain tumors and skin carcinomas.

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