Nevoid Basal Cell Carcinoma Syndrome: A Case Report and Review

S. Bala Subramanyam · D. Naga Sujata ·
K. Sridhar · M. Pushpanjali

Received: 13 April 2011 / Accepted: 8 July 2011 / Published online: 31 July 2011
© Association of Oral and Maxillofacial Surgeons of India 2011

Abstract Nevoid basal cell carcinoma syndrome, a rare autosomal dominant disorder, comprises of a number of abnormalities such as multiple nevoid basal cell carcinomas, skeletal abnormalities and multiple keratocystic odontogenic tumors. Diagnosis may be difficult because of the variability of expressivity and different ages of onset for different traits of this disorder. The dental clinician may be the first to encounter and identify this syndrome, when the multiple cysts like radiolucencies are discovered on panoramic view. This article reports a case of Nevoid basal cell carcinoma syndrome and provides an overview on diagnosis and management.

Keywords NBCCS · Gorlin · Goltz syndrome · Keratocystic odontogenic tumor

Introduction

The syndrome, delineated by Gorlin and Goltz in 1960 [1] was first reported in 1894 [2, 3]. NBCCS is a hereditary condition caused by mutations in the PTCH1 gene and is transmitted in an autosomal dominant manner with high penetrance and variable expressivity [4, 5]. There is no sexual predilection. Individuals with no known affected family members may comprise up to 60% of all affected

individuals [6]. The estimated prevalence varies from 1/57,000 to 1/256,000, with a male-to-female ratio of 1:1 [7–10]. Diagnosis of NBCCS can be made in the presence of two major criteria or one major and two minor criteria suggested by Kimonis et al. [11].

Major Criteria

1. Multiple (>2) BCCs or one under 20 years
2. Odontogenic keratocysts of the jaws proven by histopathology
3. Palmar or plantar pits (3 or more)
4. Bilamellar calcification of the falx cerebri
5. Bifid, fused or markedly splayed ribs
6. First degree relatives with NBCCS

Minor Criteria

1. Macrocephaly determined after adjustment for height.
2. Congenital malformation: cleft lip or palate, frontal bossing, “coarse face”, moderate or severe hypertelorism.
3. Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits.
4. Radiological abnormalities: bridging of the sella turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modeling defects of the hands and feet, or flame-shaped lucencies of the hands or feet.
5. Ovarian fibroma.
6. Medulloblastoma.

Basal cell carcinomas are reported in 90% of the patients at some stage in their life most often proliferate between

S. Bala Subramanyam · D. Naga Sujata (✉) · M. Pushpanjali
Department of Oral and Maxillofacial Surgery,
Government Dental College and Hospital, RIMS, Kadapa,
Andhra Pradesh, India
e-mail: sujatamds@gmail.com

K. Sridhar
Department of General Pathology, RIMS, Kadapa,
Andhra Pradesh, India

puberty and 35 years of age. Increased sunexposure appears to be a risk factor for BCCs which develop on body parts exposed to sun, only about 40% African Americans affected by NBCCS develop BCCs, while incidence was shown to be higher in whites approximately 90% [12].

Recurrent jaw cysts are the main oral sign, being present in 90% of patients [13]. These cysts are Keratocysts appear in the tooth bearing areas of the jaws, and are believed to arise from the dental lamina. Cysts may appear in both jaws. Keratocystic odontogenic tumors (KCOTs) are the most consistent and representative signs of NBCCS in the first and the second decades of life.

An abnormal skull configuration (characterized by frontal (25%), biparietal or temporal bossing, and large calvaria) is frequent. About 70% of patients affected by NBCCS have eyes which appear wider apart than usual. Other skeletal signs are scoliosis (40%), and abnormalities such as bifid, wide, fused, partially missing or underdeveloped ribs (30–60%). Ectopic calcifications of the central nervous system have been reported: lamellar calcification of the falx cerebri (70–85%), calcification of the tentorium cerebelli (20–40%), the petroclinoid ligament (20%) and the diaphragma sellae (60–80%), and complete or partial bony bridging of the sella turcica (25%) [13]. Cardiac and ovarian fibromas occur in approximately 2% and 20% of individuals respectively. Approximately 5% of children with NBCCS develop medulloblastoma (primitive neuroectodermal tumor [PNET]), generally the desmoplastic subtype. Peak incidence is at age 2 years. Life expectancy in NBCCS is not significantly different from average. Considering the rarity of this disease we present a case of NBCCS.

Case Presentation

A 13-year-old boy was referred to department of oral and maxillofacial surgery with chief complaint of swelling in relation to right cheek region that gradually increased in size over a period of 2 months. Right facial swelling was evident that was diffuse, non tender and soft to rubbery in consistency on palpation. Intra oral examination revealed a sinus in right retromolar region through which white creamy coloured discharge was evident. Past medical history was unremarkable. Panoramic radiograph revealed three well defined radiolucencies with sclerotic borders (Fig. 1). Largest lesion measuring about 4×3 cm was located in right angle region extending into the ramus up to the condyle associated with an impacted third molar tooth bud displaced to the inferior border of mandible. The second lesion was in left angle region also associated with impacted third molar tooth bud measuring about 3×2 cms, third lesion was about 1×1 cm size in between 13 and 14. A possibility of NBCCS was considered. Thorough

Fig. 1 Preoperative panoramic radiograph revealing three well defined radiolucencies located in right ramus, left angle region of the mandible and in right anterior maxilla

Fig. 2 Photograph of patient showing relative macrocephaly and mild hypertelorism

Fig. 3 Photograph showing palmar pitting

Fig. 4 Photograph showing plantar pitting

Fig. 5 Radiograph of skull revealing macrocephaly

general examination revealed relative macrocephaly mild hypertelorism (Fig. 2), palmar and plantar pitting (Figs. 3, 4). Radiography of skull (Fig. 5), cervicothoracic spine (Fig. 6), lumbar spine (Fig. 7) and hands revealed (Fig. 8) vertebral anomalies like macrocephaly, spina bifida of cervical vertebrae, mild scoliosis and short 4th, 5th metacarpals. Laboratory reports were within normal limits. There were no familial antecedents. The patient was referred to a dermatologist for early diagnosis of future skin lesions (basocellular carcinomas).

Considering the large size of the mandibular lesions marsupialisation was carried out. In this technique a 1 cm sized window was made into the cyst and cystic lining sutured to the oral mucosa. The cystic cavity was packed open and packing consisted of gauze impregnated with chlorhexidine ointment. Pack was changed for every 3 days following thorough irrigation of the cystic cavity.

Fig. 6 Radiograph of cervicothoracic spine revealing spina bifida of cervical vertebrae

Fig. 7 Radiograph of lumbar spine revealing mild scoliosis

Fig. 8 Radiograph of hands revealing short 4th and 5th metacarpals

Fig. 9 Photo micrograph of cystic lining revealed uniform layer of stratified squamous parakeratinised epithelium

Fig. 10 Photomicrograph revealing few daughter cysts and epithelial islands

Fig. 11 Postoperative panoramic radiograph after 1 year 6 months followup revealed complete resolution of the cystic lesions

There was significant reduction in the size of the lesion after 12 weeks. Subsequently enucleation of all the cysts along with associated impacted third molar tooth buds was carried out with treatment of the bony defects with carnoys solution. The histological analysis showed that the epithelial lining of cyst composed of a uniform layer of stratified squamous epithelium, the luminal surface show flattened parakeratotic epithelial cell, which exhibited a corrugated appearance. The basal layer was composed of a palisaded layer of cuboidal or columnar epithelial cells. The interface of epithelium and connective tissue was flat and the thin fibrous wall was devoided of any inflammatory infiltration (Fig. 9). Few daughter cysts and epithelial islands were also evident (Fig. 10). This confirmed the diagnosis of Keratocystic odontogenic tumors. The cysts resolved completely clinically and radiologically. Time taken for complete resolution was 1 year. Follow up panoramic radiograph after 1 year 6 months showed complete bone healing without any evidence of recurrence (Fig. 11).

Discussion

In this case patient presented with multiple cystic lesions in the jaws leading to the suspicion of NBCCS. After thorough clinical and radiological evaluation patient had palmar and plantar pitting, ocular hypertelorism, frontal bossing, spina bifida and mild scoliosis. Characteristic nevoid basal cell carcinoma were not present in this patient as jaw cysts appear early in life than basal cell carcinomas.

KCOTs generally develop in the first, second and third decades [10, 11]. Histological analysis after incisional biopsy of cystic lesions confirmed the diagnosis one of the most problematic aspects is KCOTs associated with the syndrome have high recurrence rate [10]. The choice of treatment must take into account the patient's age, size of lesion, previous recurrence history, soft tissue involvement

and histological type, therapy can then be individually tailored for the best prognosis. In the present case, we favoured conservative treatment through decompression and marsupialization followed by a definitive enucleation at a later date with application of Carnoy's solution. Carnoy's solution was found to be effective and safe in reducing the rate of recurrence when applied to the walls of cystic cavity following enucleation [13, 14]. This will preserve the inferior alveolar nerve, and the integrity of the inferior border. This treatment should continue for several months until bony fill is noted within the cyst cavity, vital structures are free of cyst and the infection has resolved. It has been our experience that removal of the cyst lining is easier after several months of decompression/marsupialization. Proper patient education and adherence to the treatment plan is crucial to success of this conservative procedure. The patient was observed for about 1 year 6 months and demonstrated no clinical or radiographic (panoramic X-ray) evidence of recurrence.

Patients affected by Gorlin syndrome must be treated by several specialists. Many different signs and symptoms may be associated with NBCCS, basal cell carcinomas may arise in various stages of the syndrome, most often they appear between puberty and 35 years of age [15], but cases have been reported in 3 or 4 year-old patients [16, 17]; in general, the mean age of onset is about 25 years of age. Studies have indicated that the risks of BCCs show a strong positive correlation with exposure to UV radiation. Thus, these patients need to avoid excess sun exposure. In the present case patient was sent to dermatologist for monitoring of possible skin lesions. Radiotherapy should also be avoided if possible. Management of superficial BCCs without follicular involvement can be accomplished by total body application of topical 0.1% tretinoin cream [16]. Patients should be examined every 3 months, and lesions manifesting growth must be excised.

The syndrome is a hereditary condition, thus referral to a geneticist for counseling is mandatory. Clarification of the genetic status of at-risk relatives, including children, is appropriate. NBCCS is inherited in an autosomal dominant manner; offspring of an affected individual have a 50% risk of inheriting. The most common lesions accounting for NBCCS are usually not life-threatening. Medulloblastoma may be a potential cause of early death, even if NBCCS patients may have better outcome than patients with sporadic medulloblastoma. Life expectancy in NBCCS is not significantly altered but morbidity from complications can be substantial. Regular follow-up by a multi-specialist team (dermatologist, neurologist and oral surgeon) should be offered.

References

1. Gorlin RJ, Goltz RW (1960) Multiple nevoid basal-cell epithelioma, jaw cysts and bifid rib: a syndrome. *N Engl J Med* 262: 908–912
2. Jarisch W (1894) Zur Lehre von den Hautgeschwulsten. *Arch Dermatol Syphilol* 18:162–222
3. White JC (1894) Multiple benign cystic epitheliomas. *J Cutan Genitourin Dis* 12:477–484
4. Bare JW, Lebo RV, Epstein EH Jr (1992) Loss of heterozygosity at chromosome 1q22 in basal cell carcinomas and exclusion of the Basal cell nevus syndrome gene from this site. *Cancer Res* 52:1494–1498
5. Bialer MG, Gailani MR, McLaughlin JA, Petrikovsky B, Bale AE (1994) Prenatal Diagnosis of Gorlin syndrome. *Lancet* 344:477
6. Bonifas JM, Bare JW, Kerschmann RL, Master SP, Epstein EH Jr (1994) Parental origin of chromosome 9q22.3-q31 lost in basal cell Carcinomas from basal cell nevus syndrome patients. *Hum Mol Genet* 3:447
7. Farndon PA, Del Mastro RG, Evans DG, Kilpatrick MW (1992) Location of Gene for Gorlin syndrome. *Lancet* 339:581–582
8. Evans DG, Birch JM, Orton CI (1991) Brain tumours and the occurrence of severe invasive basal cell carcinoma in first degree Relatives with Gorlin syndrome. *Br J Neurosurg* 5:643–646
9. Pratt MD, Jackson R (1987) Nevoid basal cell carcinoma syndrome. A 15-year follow-up of cases in Ottawa and the Ottawa Valley. *J Am Acad Dermatol* 16:964–970
10. Lo Muzio L, Nocini PF, Savoia A, Consolo U, Procaccini M, Zelante L, Pannone G, Bucci P, Dolci M, Bambini F et al (1999) Nevoid basal cell Carcinoma syndrome. Clinical findings in 37 Italian affected individuals. *Clin Genet* 55:34–40
11. Kimonis VE, Goldstein AM, Pastakia B, Yang ML, Kase R, DiGiovanna JJ, Bale AE, Bale SJ (1997) Clinical manifestations in 105 persons with nevoid basal cell carcinoma syndrome. *Am J Med Genet* 69:299–308
12. Goldstein AM, Pastakia B, DiGiovanna JJ, Poliak S, Santucci S, Kase R, Bale AE, Bale SJ (1994) Clinical findings in two African-American families with the nevoid basal cell carcinoma syndrome (NBCC). *Am J Med Genet* 50:228–272
13. Voorsmit RACA, Stoelinga PJ, van Haelst UJ (1981) The management of keratocysts. *J Maxillofac Surg* 9:228
14. Stoelinga PJW (2003) Excision of the overlying, attached mucosa, in conjunction with cyst enucleation and treatment of the bony Defect with Carnoy solution. The odontogenic keratocyst. *Oral Maxillofac Surg Clin N Am* 15:407
15. Gorlin RJ (1995) Nevoid basal cell carcinoma syndrome. *Dermatol Clin* 13:113–125
16. Evans DG, Ladusans EJ, Rimmer S, Burnell LD, Thakker N, Farndon PA (1993) Complications of the naevoid basal cell carcinoma syndrome: results of a population based study. *J Med Genet* 30:460–464