

A Case Report of Gorlin-goltz Syndrome

Shima Nafarzadeh^{a*}, Fatemeh Mozaffari^b, Oveis Khakbaz^c

^aAssistant Professor, Department of Oral and Maxillofacial Pathology, Dentistry School, Babol University of Medical Sciences, Babol, Iran.

^bFaculty, Department of Oral and Maxillofacial Pathology, Dentistry School, Mazandaran University of Medical Sciences, Sari, Iran.

^cAssistant Professor, Department of Oral and Maxillofacial Surgery, Dentistry School, Babol University of Medical Sciences, Babol, Iran.

Correspondence to: Shima Nafarzadeh (email: shima.nafar2004@yahoo.com).

(Submitted: 10 June 2015 – Revised version received: 03 July 2015 – Accepted: 11 July 2015 – Published online: 26 March 2016)

Nevoid basal cell carcinoma syndrome (Gorlin syndrome) is an autosomal dominant inherited condition that exhibits high penetrance and variable expressivity. The syndrome is caused by mutations in patched (PTCH), a tumor suppressor gene that has been mapped to chromosome 9q22.3-q31. Gorlin-goltz syndrome (GGS) is characterised by the presence of multiple odontogenic keratocysts in the jaws, basal cell carcinomas, palmar and plantar pits and intracranial calcifications. Here, we present a case of familial GGS, characterised by multiple odontogenic keratocysts, broad nasal ridge, hypertelorism, enlarged head circumference and dermoid cysts.

Keywords dermoid cyst, Gorlin-goltz syndrome, odontogenic cysts

Introduction

Gorlin-Goltz syndrome (GGS), also known as nevoid basal cell carcinoma syndrome (NBCCS), is an autosomal dominant inherited disorder.¹ This syndrome is characterised by multiple odontogenic keratocysts, basal cell carcinomas of skin, palmar and plantar pits. GGS has a wide spectrum of neurological, ocular, skeletal, genitourinary disorders.² The dentist has the privilege of diagnosing the syndrome at first, as multiple odontogenic keratocysts are the first manifestations of this syndrome.³ This article reports a case of a 59-year-old patient with GGS, emphasising its clinical and radiographic manifestations.

Case Report

A 59-year-old male patient admitted to the School of Dentistry, Babol University of Medical Sciences with a complaint of bilateral, painless swelling of lower jaw with paresthesia in left mental foramen area. A history of OKC in mandible and dermoid cysts was found in the patient's brother. On extraoral examination, broad nasal ridge, hypertelorism and enlarged head circumference were inspected. Dermoid cyst was seen on the patient's hand (Fig. 1). No palpable lymph nodes were found. Intraoral examination revealed a non-tender swelling with bony hard consistency. There was no tooth mobility. The radiographic examination and CT scan from both sides of the mandible showed extensive radiolucent lesions which were then diagnosed as OKC. His first OKC was diagnosed in 2010. Incisional biopsy was performed and then surgical drain was placed on each side of the lower jaw.

In December 2010, the patient went to a dental clinic due to purulent discharge from his mandible.

The patient's last visit in January 2014 was due to bilateral facial swelling. Radiographs revealed bilateral lesions in the body and ramus of the mandible which were well defined as radiolucency with corticated margins resembling soap bubble appearance (Fig. 2). Unicystic ameloblastoma, OKC and multiple myeloma were considered as differential diagnosis.

Incisional biopsy was done for histopathological examination which showed a cystic lesion, lined by parakeratinised stratified squamous epithelium with surface corrugation (Fig. 3). Pallisading pattern in basal cells and columnar basal cell layer exhibiting reversal of polarity were seen. The epithelium and connective tissue interface was flat. Detachment of the cyst

lining from the fibrous wall was observed (Fig. 4). The connective tissue was fibrotic with blood vessels. Odontogenic epithelial islands in the connective tissue were visible (Fig. 5).

The diagnosis was OKC and considering the clinical findings the patient was found to be a case of GGS. Decompression tubes were used after performing bony windows to reduce the cysts size, and the patient was told to maintain oral hygiene and irrigate the cavity every day. The patient attended follow up sessions for 6 months, but refused to undergo enucleation surgery.

Discussion

Nevoid basal cell carcinoma syndrome (Gorlin-Goltz syndrome) is an autosomal dominant inherited condition that exhibits high penetrance and variable expressivity.⁴ It is caused by mutations in PTCH, a tumor suppressor gene, a human homologue of a *Drosophila* segment polarity gene *PTCH* located in long arm of chromosome 9q22.3.⁴⁻⁷ The prevalence of Gorlin syndrome is estimated to be about 1 in 60,000.⁴

In 1894, Jarisch and White made the first descriptions of patients with this syndrome,^{5,8} Bettley and Ward were the first who related the presence of palmar and plantar pits with the syndrome in 1950–1960.^{5,9,10} Jaw cysts are one of the most constant features of the syndrome and are present in at least 75% of the patients.⁴ In GGS, OKC is a common lesion in the jaws.¹¹ The cysts are frequently multiple; some patients have had as many as 10 separate cysts.⁴ Less than 10% of patients with multiple OKCs have other manifestations of this syndrome; however, it has been suggested that multiple OKCs alone may be the confirmatory of the syndrome.¹² These may be bilateral, may involve both jaws and most commonly arise in the lower third molar and maxillary canine regions.¹¹ In patients with GGS, OKCs are more frequent, recur faster and more commonly, consistent with a more “aggressive” phenotype.^{11,13} The keratocysts in patients with this syndrome tend to have more satellite cysts, solid islands of epithelial proliferation and odontogenic epithelial rests within the fibrous capsule than isolated keratocysts.⁴ The increased recurrence rate of OKC in syndromic patients compared to non-syndromic patients is because of a familial tendency in this syndrome, s006F, early family detection and genetic counseling are critical.^{14,15} OKC associated with NBCCS have occasionally been reported to transform into aggressive neoplasms such as ameloblastomas and squamous cell carcinoma.^{14,16}



Fig. 1 Similar dermoid cyst on hands.



Fig. 2 Orthopantomograph showing multiple lesions in the body and ramus of the mandible.

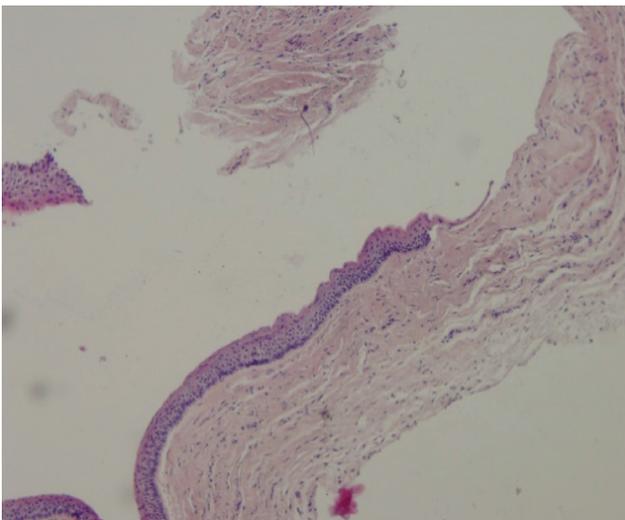


Fig. 3 Low power showing a cystic cavity lined by parakeratinised epithelium with surface corrugation.

In WHO 2005 classification of odontogenic tumors, the name of the cyst has been changed to “keratocystic odontogenic tumor” owing to its aggressive nature and recurrence rate.¹¹

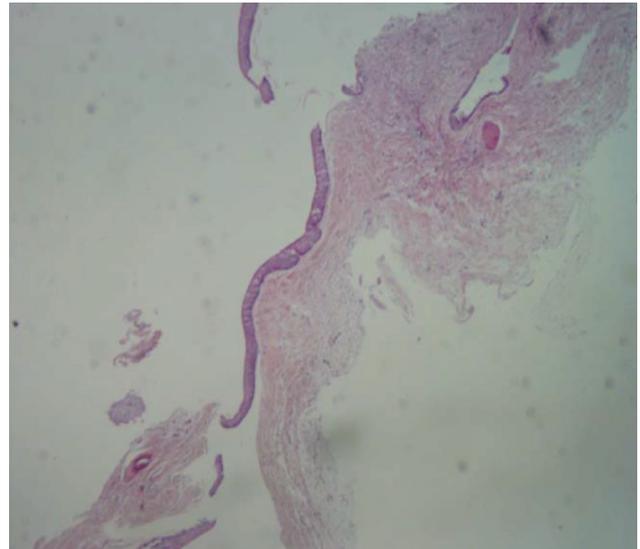


Fig. 4 Detachment of portions of the epithelium from the fibrous wall.

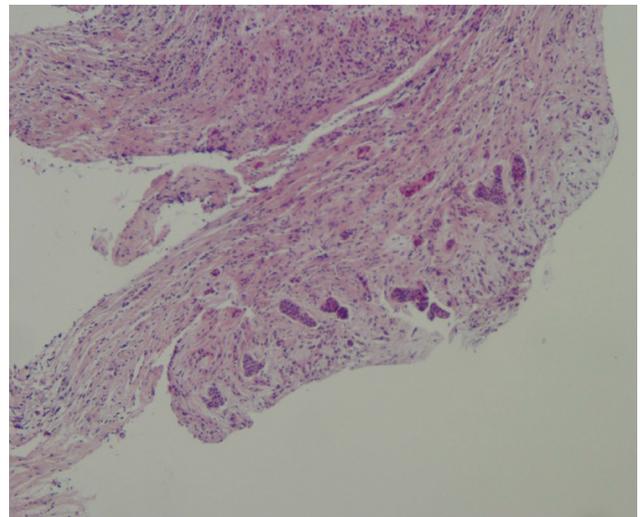


Fig. 5 Histopathologic view shows odontogenic epithelial islands in the cyst connective tissue wall.

In 1994, Evans et al., first established major and minor diagnostic criteria for this syndrome which was modified later by Kimonos et al., in 2004,^{5,17,18} the major and minor criteria are as follows:

Major criteria

- Multiple basal cell carcinomas or one occurring under the age of 20 years.
- Bifid, fused or markedly splayed ribs.
- OKCs of the jaws confirmed by histopathology.
- Palmar or plantar pits (three or more).
- First degree relative with NBCCS.
- Bilamellar calcifications of the falx cerebri.

Minor criteria

- Macrocephaly (adjusted for height).
- Skeletal abnormalities: Sprengel deformity, marked pectus deformity and marked syndactyly of the digits.

- Congenital malformation: cleft lip or cleft palate, frontal bossing, coarse face moderate, or severe hypertelorism.
- Radiological abnormalities: bridging of sella turcica, vertebral anomalies such as hemi vertebrae, fusion or elongation of vertebral bodies, modeling defects of the hands and feet, or flame-shaped hands or feet.
- Medulloblastoma, seizures, mental retardation, eningioma.
- Ovarian fibroma.

Two major criteria or one major and two minor criteria are necessary to diagnose this syndrome.⁵

Our patient had broad nasal ridge, hypertelorism, enlarged head circumference, dermoid cyst on hands and multiple OKC in the mandible. In a case report Pol et al.¹⁹ had three major features, namely palmar pits, multiple OKCs in the jaw and lamellar calcification of the falx cerebri and minor features such as macrocephaly, fontal bossing and hypertelorism,

thus suggesting it to be a case of the GGS. In their patient, the lining of the OKCs revealed the presence of parakeratinised uniform squamous epithelial lining with multiple satellite and daughter cysts in the connective tissue wall, thus indicating the association with GGS. In a case report Syyam et al.⁵ The present case fulfills the above three major criteria features like multiple OKCS, positive family history, calcification of falx cereberi and tentorial cerebella and with two minor criteria features that includes hypertelorism and neurologic disorder as the patient had episodes of seizures.

Most of the anomalies in nevoid basal cell carcinoma syndrome are minor and usually not life threatening.⁴ The prognosis generally depends on the behaviour of the skin tumors.⁴ The jaw cysts are treated by enucleation. Infection of the cysts in patients with this syndrome is also relatively common.⁴ ■

References

1. Sabbia T, Bovone S, Camera A, Gambini C, Balbi P. [Gorlin-Goltz syndrome with odontogenic keratosis. Report on a patient followed for 10 years]. *Minerva Stomatol.* 1994 Jul-Aug;43(7-8):359-63.
2. Gorlin RJ, Goltz RW. Multiple nevoid basal-cell epithelioma, jaw cysts and bifid rib. A syndrome. *N Engl J Med.* 1960 May 5;262:908-12.
3. Karthiga KS, Sivapatha Sundharam B, Manikandan R. Nevoid basal cell carcinoma syndrome. *Indian J Dent Res.* 2006 Jan-Mar;17(1):50-3.
4. Neville B, Damm D, Allen C, Bouquot J. *Oral and Maxillofacial Pathology.* 3rd ed. Philadelphia: WB Saunders; 2009.
5. Sunder S, Babburi S, Guduguntla S, Raju P. Gorlin-Goltz syndrome: a rare case report. *J Dr NTR Univ Health Sci.* 2013;2(2):150.
6. Casaroto AR, Loures D, Moreschi E, Veltrini VC, Trento CL, Gottardo VD, et al. Early diagnosis of Gorlin-Goltz syndrome: case report. *Head Face Med.* 2011;7:2.
7. Shakya H, Mubeen K. Gorlin-Goltz syndrome with situs inversus: a rare case report; Síndrome de Gorlin-Goltz com situs inversus: relato de um caso raro. *Rev Clín Pesq Odontol.* 2009;5(2):175-84.
8. Jarisch W. Zur lehre von den hautgeschwulsten. *Arch Dermatol Syph.* 1894;28:163-222.
9. Bettley FR. Two cases of multiple naevoid basal cell epitheliomata? porokeratosis of Mantoux. *Br J Dermatol.* 1953 Jun;65(6):219-21.
10. Ward W. Nævoid basal celled caecinoma associated with a dyskeratosis of the palms and soles. A new entity. *Australasian J Dermatol.* 1960;5(4):204-8.
11. Kalia V, Kaushal N, Kalra G. The syndromic multiple odontogenic keratocyst in sibilings: a familial study. *Ann Maxillofac Surg.* 2011;1(1):77.
12. Agrawal A, Murari A, Vutukuri S, Singh A. Gorlin-goltz syndrome: case report of a rare hereditary disorder. *Case Rep Dent.* 2012;2012:475439.
13. Zedan W, Robinson P, Markham A, High A. Expression of the sonic Hedgehog receptor 'PATCHED' in basal cell carcinomas and odontogenic keratocysts. *J Pathol.* 2001;194(4):473-7.
14. Tarakji B, Baroudi K, Hanouneh S, Azzeghaiby S, Nassani M. Possible recurrence of keratocyst in nevoid basal cell carcinoma syndrome: a review of literature. *Eur J Dent.* 2013;7(5):126.
15. Wang XX, Zhang J, Wei FC. Familial multiple odontogenic keratocysts. *J Dent Child. (Chic).* 2006;74(2):140-2.
16. Reisner KR, Riva RD, Cobb RJ, Magidson JG, Goldman HS, Sordill WC. Treating nevoid basal cell carcinoma syndrome. *J Am Dent Assoc.* 1994;125(7):1007-11.
17. Rayner C, Towers J, Wilson J. What is Gorlin's syndrome? The diagnosis and management of the basal cell naevus syndrome, based on a study of thirty-seven patients. *Br J Plastic Surgery.* 1977;30(1):62-7.
18. Evans D, Ladusans E, Rimmer S, Burnell L, Thakker N, Farndon P. Complications of the naevoid basal cell carcinoma syndrome: results of a population based study. *J Med Genet.* 1993;30(6):460-4.
19. Pol CA, Ghige SK, Kalaskar RR, Gosavi SR. Gorlin-Goltz syndrome: a rare case report. *Contemp Clin Dent.* 2013;4(4):547.