Case Report

Review of Nevoid Basal Cell Carcinoma Syndrome (Basal Cell Nevus Syndrome, Gorlin-Goltz Syndrome) and Report of a Case

Marjan Shakiba, Maryam Razzaghy-Azar*

Abstract:
Multiple odontogenic cysts, basal cell nevi and abnormalities in skeletal, nervous and endocrine systems characterize Gorlin-Goltz or nevus basal cell carcinoma syndrome.
A 12-year-old patient with odontogenic keratocysts, multiple cryptic teeth in the jaw and in the cysts, multiple nevi on the skin, nail dyskeratosis and bone abnormalities is reported and literature review is presented in this paper.

Key Words: Gorlin Goltz Syndrome; Carcinoma, Basal Cell; Nevus; Odontogenic Cyst, Iran

INTRODUCTION

Gorlin-Goltz syndrome (Nevoid or nevus basal cell carcinoma syndrome) is an infrequent multisystem disease that is inherited as an autosomal dominant trait which shows a high penetrance with variable expressivity. (1,2,3) The triad of jaw cysts, basal cell epitheliomas and skeletal anomalies is well known. (4) Other aspects of the disorder are intracranial calcifications, hypertelorism, mental retardation, cleft lip and palate, palmar and plantar dyskeratosis. (5) In 1894, Jarisch and White made the first descriptions of patients with this syndrome. (6,7) Later in 1960, Gorlin and Goltz explained a classical triad (multiple basocellular epitheliomas, keratocyst in jaws and bifid rib). (8) This triad was later modified by Rayner et al who necessitated the appearance of the cysts in combination with calcification of the falx, and palmar and plantar pits for the diagnosis of this syndrome. (9)

*** Maryam Razzaghi-Azar, MD**
Professor of Pediatrics and Pediatric Endocrinology and Metabolism
Firouzgar Hospital, Firouzgar Alley, Shahid Valadi Street, Behafarin Street, Karimkhan Zand Ave. Tehran University of Medical Sciences, Tehran, 1593748711, Iran
E-mail: mrazar_md@yahoo.com
Submission date: 25/2/2011 Acceptance Date:23/4/2011

Case Report

A 12-year-old male adolescent was visited with dental malposition, permanent dental eruption anomaly and swelling on the right side of maxilla. He was born of a non-consanguineous marriage of healthy parents and

there was no history of similar problems in the family. The patient had the history of macrocephaly from fetal life that was revealed by ultrasonography. The head circumference was 40 cm at birth, and the parents reported a delay in motor development in infancy and childhood. However, his mental status and motor movements were normal at the time of entry, and his school performance was reported well. His height was 166.5 cm that was more than 90th percentile of growth chart for age and sex and his weight was 43 kg (between 25th and 50th percentiles) (CDC 2000). The pubertal stage was consistent with stage 3 of Tanner scaling. (10) He had macrocephaly, hypertelorism, frontal bossing, miliaria, swelling on the right side of his maxilla and scar of the cleft lip that had been repaired in infancy. (Fig 1A) Severe dental malposition, a high arched palate, a narrow chest, narrow sloping shoulders, prominent scapulas and kyphoscoliosis were also noted. (Fig 1B) Multiple pigmented and palpable nevi on the upper part of the trunk and shoulders and nail dyskeratosis were observed. (Fig 1C, 1D) There were palmar pits on physical examination. Ophtalmologic examination was normal. On laboratory investigation, thyroid function tests, serum calcium, phosphorus, alkaline phosphatase and PTH were all within normal limits. IGF-1 was 221 ng/mL (normal level for stage of puberty, 249 -642) and basal GH was 2.72 IU/L. The Panorex view of the jaws showed many cryptic teeth. (Fig 2A) Brain CT scan illustrated three cysts in the mandible and maxilla containing teeth; calcification in dura, falx cerebri and tentorium were seen but there was no cerebral tumor (Fig 2B-D, 3A-B). In bone survey, kyphoscoliosis and spina bifida without rib anomaly were reported. The right and left mandibular cysts underwent operation and the result of pathologic study revealed no malignancy, and odontogenic cysts containing broken teeth were reported. Investigations showed no cardiac fibroma.

Review of literature

Gorlin syndrome is an autosomal dominant inherited disease. The tumor suppressor gene called Patched (PTCH), located in the 9q22.3 chromosome, has been identified as the cause of Gorlin-Goltz syndrome. (2, 11, 12) Mutation of this gene produces dysregulation of several genes involved in organogenesis and carcinogenesis. Consequently, the syndrome includes a wide spectrum of defects involving the skin, eyes, central nervous and endocrine systems and bones. However, the patient who is reported had healthy parents without any signs and symptoms. Perhaps its different penetrance or new mutation is considered. The estimated prevalence of this syndrome varies from 1 in 57000 to 1 in 256000 inhabitants. (13) Among the clinical manifestations of this syndrome are hypertelorism, mental retardation, cleft lip and palate. (5) Multiple odontogenic keratocysts (OKC) are common in this disease. Peak incidence of cysts is in the second and third decade of life. (14) These cysts have a high rate of recurrence after removal and may be complicated by the development of pathologic fractures, ameloblastoma and squamous cell carcinomas. (15, 16) Multiple basal cell carcinomas are predominantly seen on the face and trunk. Skin lesions other than palmar and plantar pits include sebaceous or epithelial cysts, dyskeratosis and miliaria. (1, 2, 8) Rib anomalies consist of synostosis, splaying, bifid and cervical ribs that are predominantly seen in the first to forth ones. Vertebral anomalies like block vertebra, hemi vertebra, synostosis, spina bifida oculta and kyphoscoliosis are also reported. (13) The early onset of calcification of falx cerebri, tentorium cerebelli, dura, choroid and bridging of sella turcica are seen in 6080- % of the patients. (17) Other nervous system disorders include medulloblastoma, meningioma, congenital hydrocephalus, agenesis of corpus callosum and mental retardation. (14) Abnormalities like hypogonadism, ovarian, uterus and cardiac fibroma, lymphatic mesenteric cysts, and minor kidney abnormalities may be seen in this syndrome. The patients have tendency to developing neoplastic lesions such as melanoma, rhabdomyosarcoma and leiomyoma. Dystropia canthrum, hypertelorism, congenital blindness, cleft lip and palate, pectus excavatum, narrow sloping shoulders, immobile thumbs, tall stature and characteristics similar to acromegaly are among other anomalies that are seen in this disease. (2, 3, 14) The diagnostic criteria are divided

into major and minor. Major diagnostic criteria include multiple basal cell nevus or carcinoma, odontogenic keratocysts, palmar or plantar pits, calcification of falx cerebri and a positive family history. Minor criteria are congenital skeletal anomalies, macrocrania, cardiac or ovarian fibroma, and congenital malformations (cleft lip or palate, polydactyly, eye anomaly). The presence of two major or one major and two minor criteria is diagnostic for Gorlin-Goltz syndrome. (18, 19) Our patient had three major and at least three minor criteria. Asaumi et al (20) reported 23 patients with multiple jaw cysts; 52.2% of them were diagnosed with basal cell nevus syndrome. Paveic et al (21) reported 58 OKC in 30 patients with this syndrome. Patients aged 1090- year. The peak incidence of OKC is between 2130- years of age. OKC is found predominantly in the mandible (60.34%), maxilla (15.52%), soft tissues (13.79%), and maxillary sinuses (10.34%). (21) Three patients have been reported from Mashhad and one from Isfahan. (22 – 24) Participation and cooperation of various specialists according to each clinical problem is required. As most of the basal cell carcinomas have a clinically benign course, they should not be treated with irradiation and it is often impossible to remove all of them. If they have an aggressive behavior or they are on the central areas of the face, their prompt removal is necessary. Oral retinoids are sometimes helpful in preventing the development of new tumors. Genetic counseling is also important. (25)

Conclusion: Gorlin-Goltz syndrome must be considered as a possible diagnosis in all patients with odontogenic cysts. Early diagnosis is useful for early management of neoplastic lesions and results in a better prognosis.

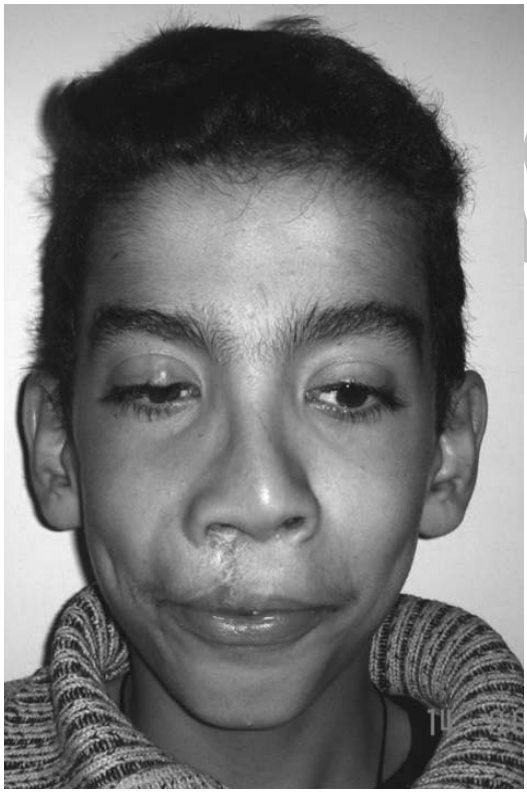

Figure 1A: The face of the patient with Gorlin-Goltz syndrome

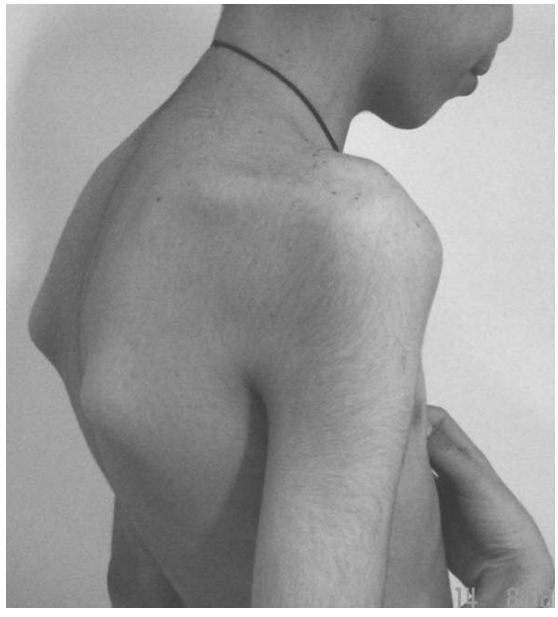

Figure 1B: The shoulder of the patient with Gorlin-Goltz syndrome

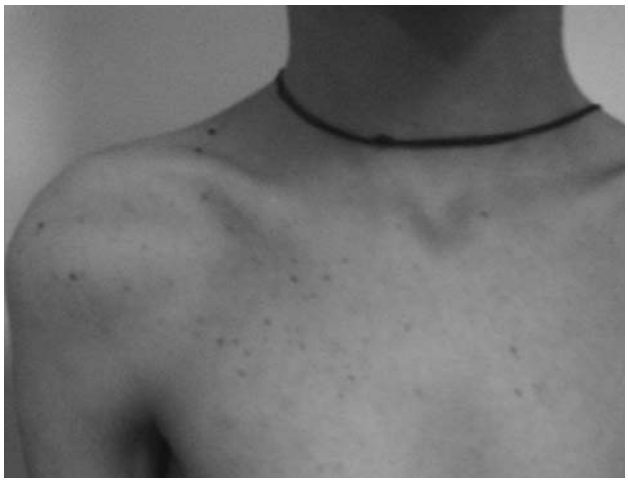

Figure 1C: Nevi on the skin of the patient with Gorlin-Goltz syndrome

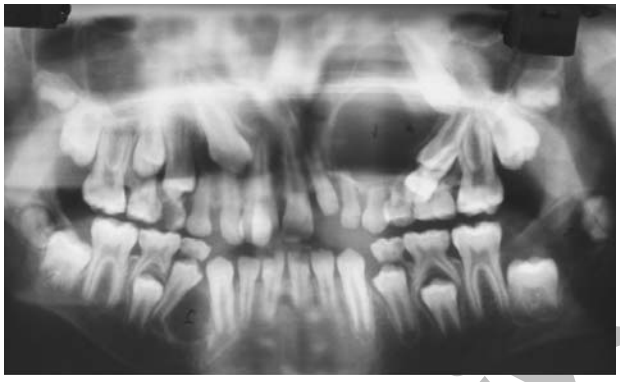

Figure 2A: Panorex view of jaws of the patient with Gorlin-Goltz syndrome

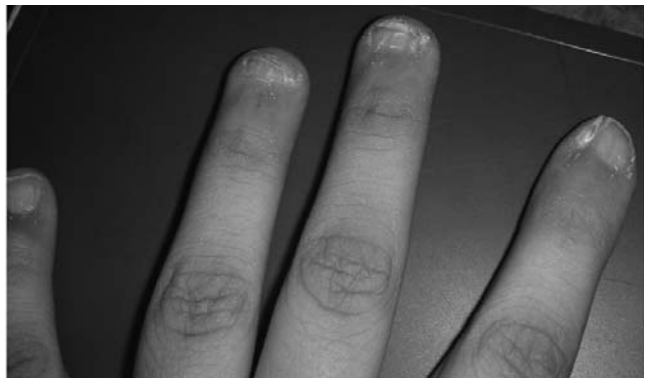

Figure 1D: Nail dyskeratosis in the patient with Gorlin-Goltz syndrome

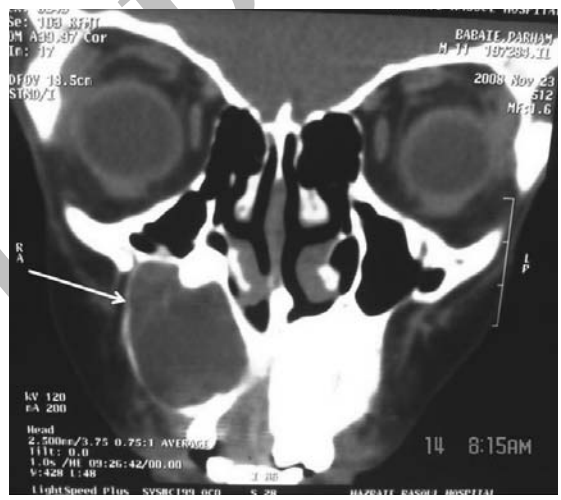

Figure 2B: Coronal view computerized tomography (CT) scan of jaws, the arrow shows the cyst in the maxilla

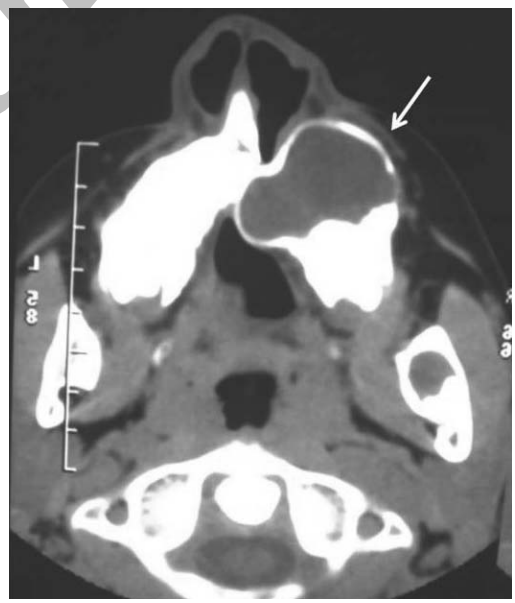

Figure 2C: Axial view CT scan of the jaws, the arrow shows the cyst in the maxilla

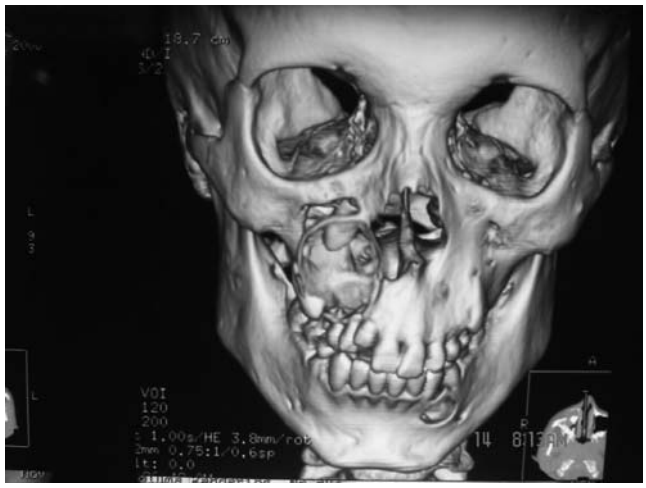

Figure 2D: Three dimension reconstructed spiral CT scan of the face which shows the cysts in maxilla and mandible contained teeth.

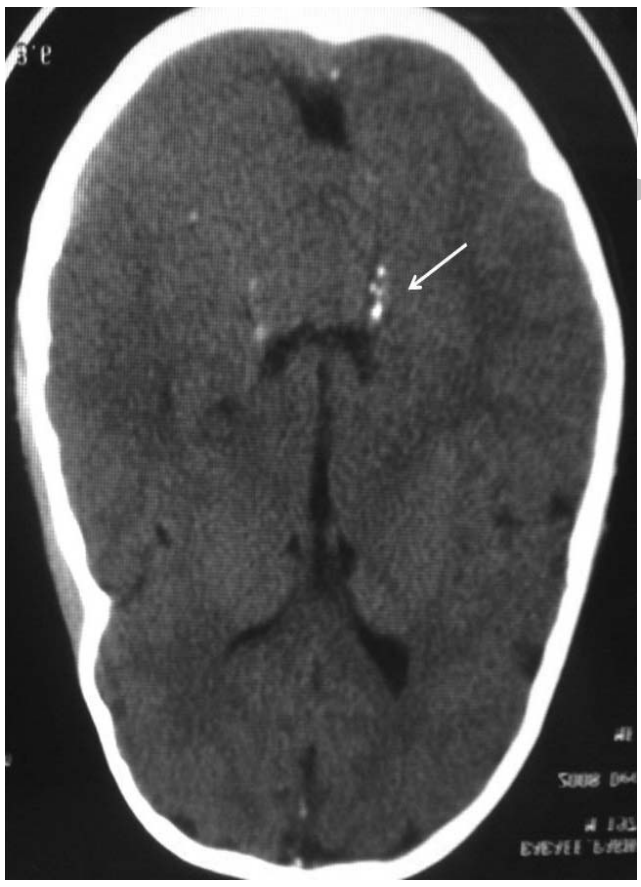

Figure 3A: Tentorial calcification in brain CT scan

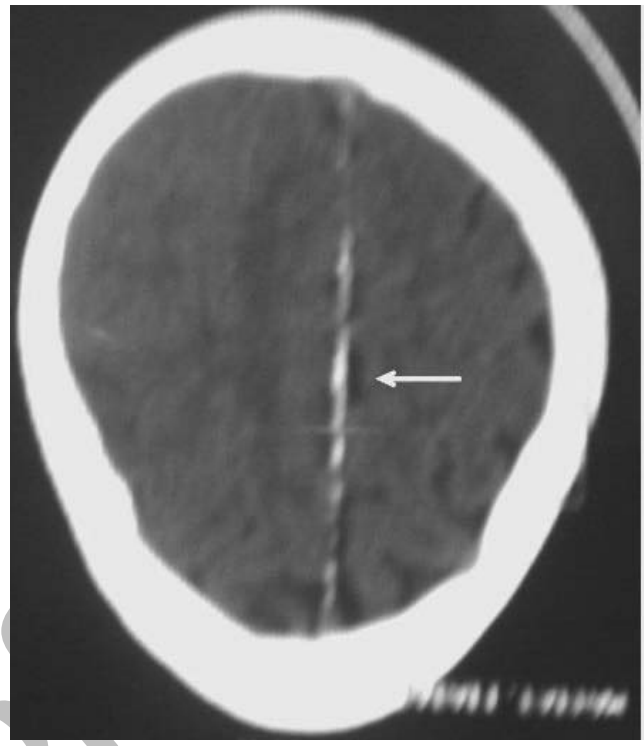

Figure 3B: Falx calcification in brain CT scan

References

1. Gu XM, Zhao HS, Sun LS, Li TJ. PTCH mutation in sporadic and Gorlin syndrome related odontogenic keratocysts. J Dent Res.2006;85;9: 85963-
2. R Yang X, Pfiffer RM, Goldstein AM,. Infuence of glutathione-S- transferase(GSTM1,GSTP1,GSTT1) and cytochrome p 450 (CYP1A1,CYP P2D6) polymorphism on numbers of basal cell carcinoma syndrome.J Med Genet. 2006;43(4)e16
3. Marsh A, Wicking C, Wain Wright B, Chenevix-Trench G. DHPLC analysis of patients with nevoid basal cell carcinoma syndrome reveals novel PTCH missense mutations in the sterol- sensing domain.Hum Mutat.2005;26;3:283
4. Gonalez Bahillo JD, Varela Patino MP, Gomez Segade L, Paz Pumpido F, Rivas Lombardero P.Case of Gorlin syndrome. AV Odontoestomatal 1989;5:5248-
5. Blanus N, Freund B, Schwartz M, Futst IM. Systematic review of the treatment and prognosis of the odontogenic keratocyst. Oral Surg Oral Med Oral Pathol Oral Radiol Endos 2000; 90:5538-
6. Jarisch W, Zur lebre von den Hautchwulsten. Archiv Fur Dermatologie ond Syphilis.1894;28:1635-
7. White JC. Multiple benign cystic epitheliomata. J Cutan Dis. 1894;12:47781-
8. Gorliun RJ ,Goltz RW. Multiple nevoid basal cell

epithelioma, jaw cyst and bifid rib: asyndrome. New Eng J Med. 1960;5:20410-
9. Rayner CRW, Towers JF, Wilson JSP. What is Gorlins syndrome? the diagnosis and management of the basal cell nevus syndrome based on a study of thirty seven patients.Br J Plast Surg. 1977; 30 (1) :627-
10. Marshall WA, Tanner JM (1969). Variations in pattern of pubertal changes in girls. Arch Dis Child 44:291.
11. Pastorino L, Cusano R, Nasti S. Molecular characterization of Italian nevoid basal cell carcinoma syndrome patients. HUM Mutat.2005; 25(3)3223-
12. Boutet N, Bignon YJ, Drouin-Garraud V, Sarda P, Spectrum of PTCH 1 mutations in French patients with Gorlin syndrome . J Invest Dermatol. 2003; 121(3) : 47881-
13. Evans DG, LadusansEJ, Rimmer S. Complications of the nevoid basal cell carcinoma syndrome. resuts of a population based study. J Med Genet . 1993; 30(6)460-4
14. Candage SG, Rahalkar M, Domkundwar S. Gorlins syndrome, radiographic and CT Manifestations. Indian J Radiol Imaging .2003;13:1922-
15. weber AL. Imaging of Cysts and odontogenic tumor of the jaw. Radiol Clin North Am 1993;31(1):101120-
16. Rater CJ, Selke AC, Van Epps EB. Basal cell nevus syndrome. Am J Roentrgenol 1968;103:589594-
17. Gorlin RJ. Nevoid basal cell carcinoma syndrome. Medicine 1987;66:98113-
18. Hll J, Johnston KA, Mcphillips JP.Nevoid basal cell carcinoma syndrome in a black child. J Am Acad Dermat 1998;38:363365-
19. Ratecliffe J, Shanlcy S, Ferguson J. The diagnostic implication of falcine calcification on plane skull radiographsin their relatives and two control groups. Br J Radioogy 1996;68:361368-
20. Asaumi JI, Murakami J, Yanagi Y, Diagnosis of multiple synchronously occurring cystic jaw lesions in 23 patients: Prognostic implication related to basal cell nevus syndrome .Oral Radiology 2007;23:1618-
21. Paveic B, Valter K, Vucicevic-Bores V. Incidence of odontogenic keratocysts in patients with Gorlin Goltz syndrome according to age, gender and location. Acta Stomatal Croat,2004;38:2325-
22. Mohtasham N, Nemati S, Jamshidi Sh, et.al. Odontogenic keratocysts in Nevoid basal cell carcinoma syndrome: a case report. Cases Journal 2009; 2:9399
23. Pakfetrat A, Falaki F, Zare Mahmoodabadi R, Saghafi Sh. Gorlin-Goltz Syndrome. Pak J Med Sci 2010;26(1):235238-
24. Shahmoradi Z, Andalib F, Siadat AH. Naevoid basal cell carcinoma syndrome Indian Journal of Dermatology Venereology and Leprology (IJDVL) 2010;76 (1): 71-73
25. Morelli J G. Tumors of the skin. In Kliegman R M, Behrman R E, Jenson H B, Stanton B F (editors): Nelson Textbook of Pediatrics, 18th ed. Philadelphia WB Saunders Elsevier 2007, PP 2767