Gorlin - goltz syndrome: a case report

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Abstract

Gorlin-Goltz syndrome, also known as basal cell nevus syndrome, is an uncommon, autosomal dominant inherited disorder, which is characterized by numerous basal cell carcinoma, odontogenic keratocysts and musculoskeletal malformations. However, medical literature documents both common and lesser known manifestations involving the skin, central nervous system, craniofacial anomalies etc. A case of Gorlin –Goltz syndrome with no family history has been reported here, the patient have multiple odontogenic keratocysts, tiny pits involving the palms and soles, rib anomalies, numerous nevi and nodes predominantly present on his face, chest and back. Histopathological study confirms the presence of multiple keratocysts in the jaws and the absence of basal cell carcinoma of the skin. Immunohistochemical study showed negatively p53 staining result. Early diagnosis and treatment is important to prevent long term sequelae including malignancy and oromaxillofacial deformation and destruction.

Keywords: Basal cell carcinoma, Gorlin syndrome, Nevoid basal cell carcinoma, Odontogenic keratocysts.

Introduction

Gorlin-Goltz syndrome is an autosomal dominant inherited syndrome manifested by multiple defects involving the skin, nervous system, eyes, endocrine system, and bones. Robert J. Gorlin and Robert W. Goltz described this distinct syndrome, it includes the presence of multiple nevoid basal cell carcinoma, jaw cysts, and bifid ribs.[1, 2] Clinical manifestations of the syndrome are grouped into the following five-categories: [3]

(A) Cutaneous anomalies: Multiple basal cell carcinoma of the skin, benign dermal cysts and tumors, palmar pitting, palmar and plantar keratosis, and dermal calcinosis.

(B) Dental and osseous anomalies: Multiple odontogenic keratocysts, mild mandibular prognathism, frontal and temporoparietal bossing, kyphoscoliosis or other vertebral defects, bifurcated ribs, spina bifida, and brachymetacarpalism.

(C) Ophthalmic anomalies: Hypertelorism, wide nasal bridge, dystopia canthorum, congenital blindness, and internal strabismus.

(D) Neurological anomalies: Mental retardation, dural calcification, bridging of sella, agenesis of corpus callosum, congenital hydrocephalus, occurrence of medulloblastoma.

(E) Sexual anomalies: Hypogonadism, ovarian tumor-like fibrosarcoma, and clinically this condition is characterized by different signs and symptoms.

Diagnosis of Gorlin-Goltz syndrome can be established when two major, or one major and two minor criteria are present. [(3,4)] The major criteria are; [3,5,6] multiple basal cell carcinoma or one occurring under the age of 20 years, histological proven odontogenic keratocyst of the jaws, palmar or plantar pits (three or more), bilamellar calcification of the falx cerebri, bifid, fused or markedly splayed ribs, and first-degree relative with nevoid basal cell carcinoma

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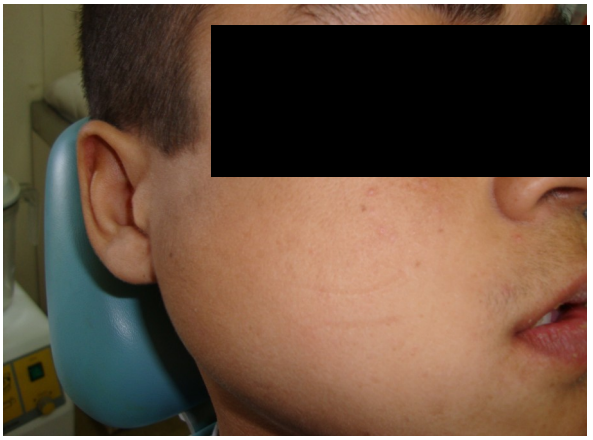
syndrome. More than 100 minor criteria have been described. The most common minor criteria are [3,5,6]; macrocephaly (adjusted for height), congenital malformation; cleft lip or palate, frontal bossing, coarse face, moderate or severe hypertelorism, other skeletal abnormalities: sprengel deformity, marked pectus deformity, marked syndactily of the digits, 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 hands or feet, ovarian fibroma, and medulloblastoma. The important potential causes of early death include the effects of medulloblastoma, which is a malignant brain tumor of the posterior fossa that develops in 10% of patients with the syndrome. In rare cases, patients die from progressively invasive basal cell carcinomas that are treated with irradiation, which causes further damage and carcinogenesis [1,7] Incidence of the Gorlin-Goltz syndrome is estimated at 1 in 50000 to 150000 in the general population. In Australia, Italy, and United Kingdom studies the prevalence is 1 per 64000, 256000, 560000 respectively. [4] Less than 10% of the patients with multiple odontogenic keratocysts have other manifestations of this syndrome. It has therefore been suggested that multiple odontogenic keratocysts alone may be confirmatory of the syndrome. [4] Generally odontogenic keratocysts which are not associated with nevoid basal cell carcinoma syndrome (NBCCS) are more common in the adult life, the peak incidence being the third decade of life. [8] However, in the Gorlin-Goltz syndrome, odontogenic keratocyst occurs at a much younger age. [9] Lo Muzio *et al*[10] observed that odontogenic keratocysts were often the first sign of NBCCS in 78% of the cases and they could be detected in patients younger than 10 years of age. Several of the developmental anomalies accumulate with age with median time of diagnosis in the second or third decades. This makes definitive diagnosis in childhood difficult in many cases. Gorlin-Goltz syndrome has equal predilection for either sex. Male to female ratio is 1:0.62 for odontogenic keratocyst not associated with NBCCS, and 1:1 for odontogenic keratocyst in NBCCS, that is, simple keratocysts are more common in males, but more females with NBCCS develop odontogenic keratocysts. [11,12] Odontogenic keratocyst associated with NBCCS have greater predilections for the mandible than the maxilla, with 69% occurring in the mandible and 31% in the maxilla. [10] The odontogenic keratocyst is now termed as 'keratocystic odontogenic tumor. It may be associated with the Gorlin-Goltz syndrome in the form of multiple cystic lesions. It is locally destructive, despite its bland histological features. [13,14] Agram *et al* [15] examined (10) odontogenic keratocysts for loss of heterozygosity of tumor suppressor genes. The loss of heterozygosity was seen in 7 of 10 cases, the mutation of genomic DNA in these cysts supports the hypothesis that they are neoplastic rather than developmental in origin. Furthermore as many as one third of patients with medullablastoma and Gorlin-Goltiz syndrome have lost the wild type allele on chromosome 9q, implying that this site may code for tumor suppressor activity. [16,17]

Case report

A 17-year-old male patient visited the Maxillofacial clinic in Rizgari Teaching Hospital in April 2010 suffering from progressing swelling in the upper and lower jaws, frontal bossing and thick eye brows with no family history of Gorlin-Goltiz syndrome (Figure1-A). The skin of his palms and soles showing hyperkeratosis with tiny pits representing focal dermal hypoplasia (Figure 1-B). Skin examination also revealed numerous nevi (Figure 2: A and B arrows) and nodes predominantly on his face, chest and the back up to 3 mm in diameter. Histopathological examination of the excisional biopsy of two nodules, one from the chest and the other from the back showed the absence of basal cell

carcinoma of the skin. The patient has a dove shape chest, and the chest radiograph shows abnormal shape thorax and rib anomalies (Figure2-C). CT scans showing the presence of the lesions in the upper right molar tuberosity area, lower left premolar area and lower right molar and ramus area (Figure-3). Histopathological examination confirms the presence of odontogenic keratocysts (Figure 4- A). The expression of p53 was evaluated in the slides using p53 monoclonal antibody (Dako Cytomation, Inc. ,Glostrip, Denmark), and no positive result was observed considering p53 tumor suppressor gene (Figure 4- B).



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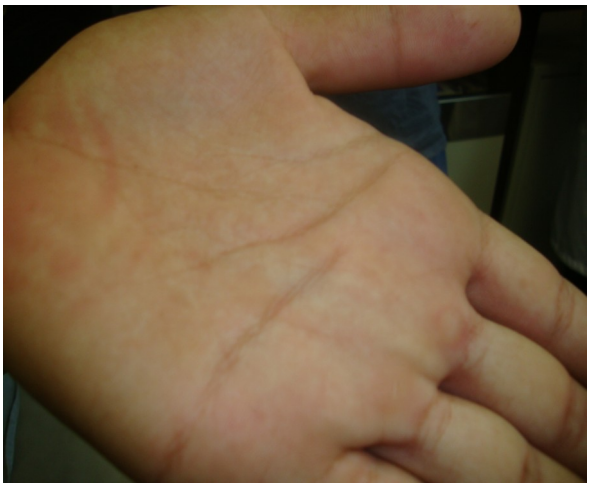

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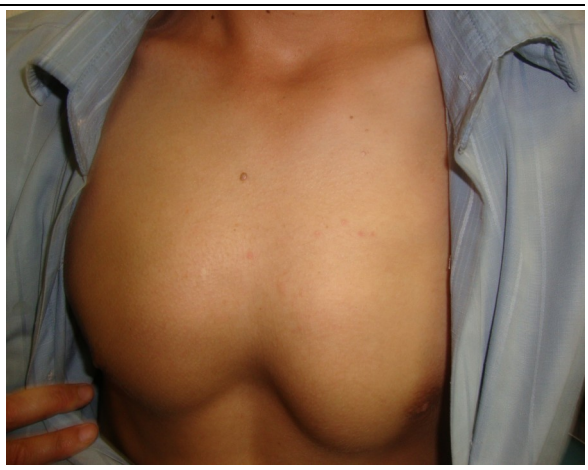
Figure-1: **(A)** 17-year-old male with swelling in the right side of the jaw.
(B) The palm showing tiny pits.



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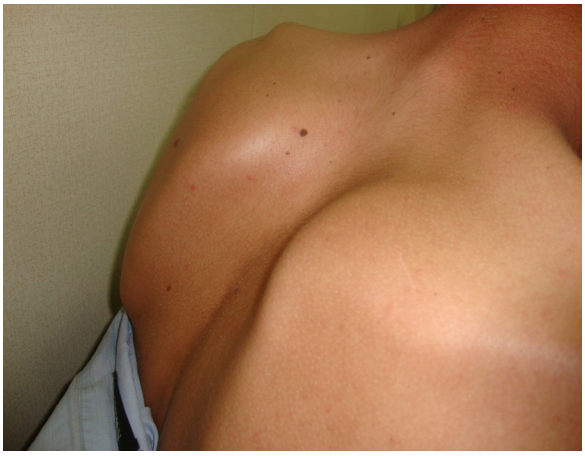

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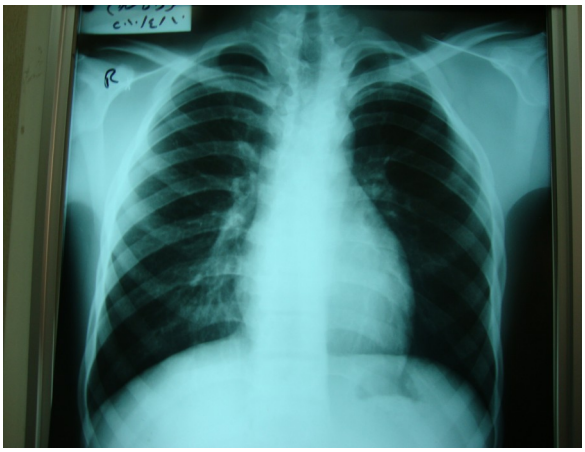

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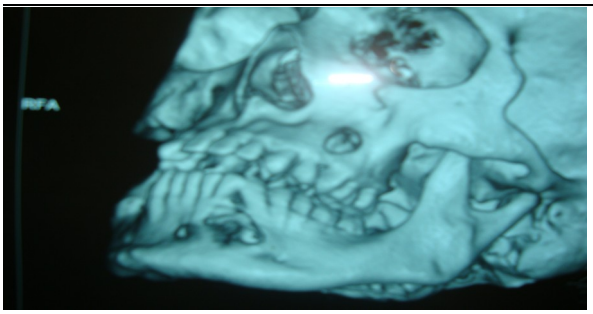
Figure-2: (A and B) Chest and the back of the patient with nodular shape nevi.
(C) Chest radiograph showing narrow abnormal shape thorax and ribs.



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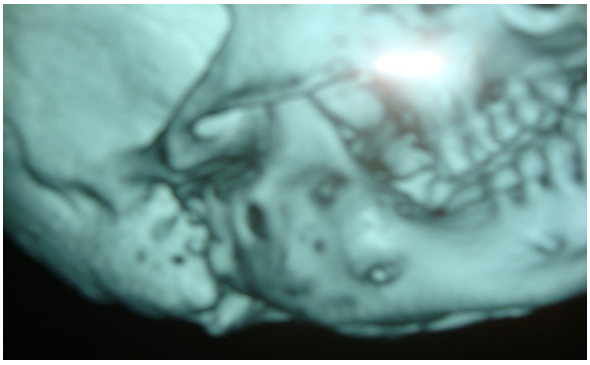

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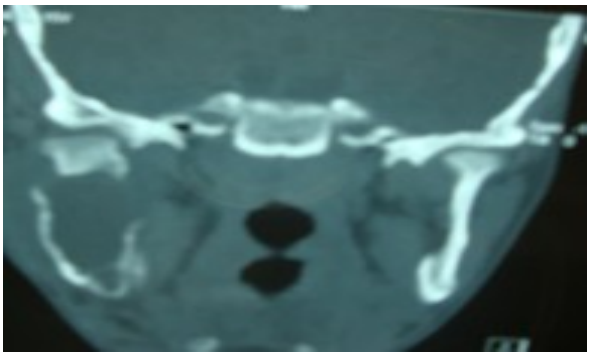

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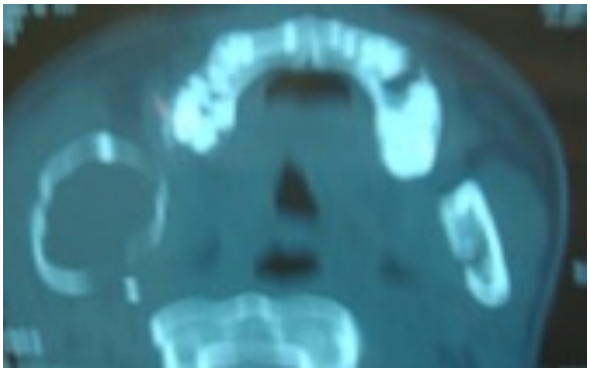
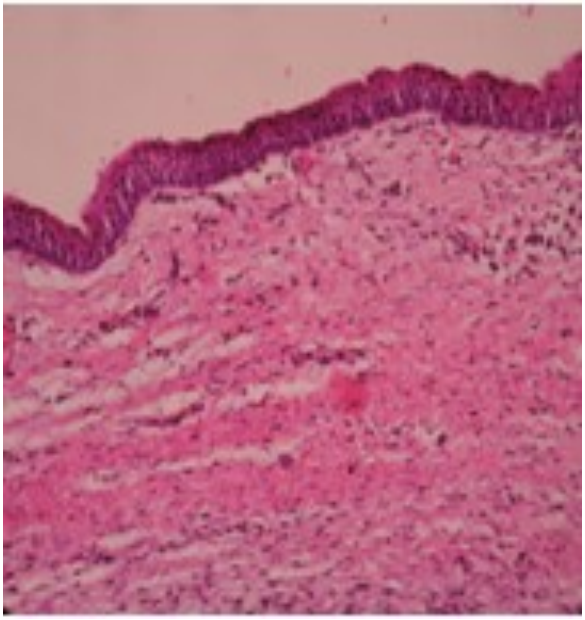


D.

Figure 3 : Different types CT scans showing the locations of the cystic lesions.



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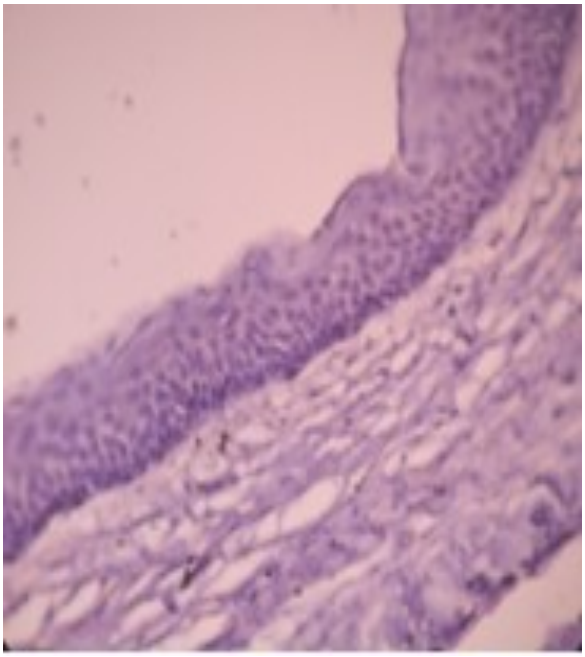

B.

Figure 4: A. Parakeratinised odontogenic keratocysts showing fibrous connective tissue wall lined by uniform thickness odontogenic epithelial lining, a flat basement membrane, and elongated palisaded basal cells (H&Ex10).
B. Negative nuclear immunoexpression in basal and suprabasal cell layer(x20).

Discussion

Patient was diagnosed as Gorlin-Goltz syndrome due to the presence of three major criteria (multiple odontogenic keratocysts, ribs anomalies, and palmar or plantar pits) and one minor criteria (frontal bossing). The differences in the frequency of major or minor criteria from other studies may be attributed to genetic and geographic differences. It is important to recognize Gorlin-Golz syndrome as early as possible, as well as the periodical follow -up examination is very important, mainly due to the skin lesions that may occur and multiple surgery is often difficult. These patients need education about the syndrome, and may need counseling and support. They should reduce UV light exposure, to minimize the risk of basal cell carcinomas. They should look for symptoms referable to other potentially involved systems: the CNS, the genitourinary system, and the cardiovascular system. [18]

Conclusion

A 17-year-old male patient with multiple odontogenic keratocyst, frontal bossing, thick eye brows, and the skin of his palms and soles showing hyperkeratosis with tiny pits representing focal dermal hypoplasia, was diagnosed as Gorlin-Goltz syndrome due to the presence numerous diagnostic criteria.

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