ISSN Print: 2394-7489
ISSN Online: 2394-7497
IJADS 2022; 8(2): 233-237

www.oraljournal.com
Received: 11-01-2022
Accepted: 15-02-2022

Dr. Ashwarya Sharma
HOD and Profesor, Department of Oral Medicine and Radiology, GNDDC Sunam, Patiala, Punjab, India

Dr. Zeeza Mehboob Qazi
MDS, Department of Oral Medicine and Radiology, GNDDC Sunam, Patiala, Punjab, India

Dr. Radhika Sharma
Reader, Department of Oral Medicine and Radiology, GNDDC Sunam, Patiala, Punjab, India

Dr. Shruti Sharma
Professor,Department of Oral Medicine and Radiology, GNDDC Sunam, Patiala, Punjab, India

Dr. Puneet Goyal
Professor,Department of Paediatric and Preventive Dentistry, GNDDC Sunam, Patiala, Punjab, India

Dr. Burhan Altaf Misgar
MDS, Department of Paediatric and Preventive Dentistry, GNDDC Sunam, Patiala, Punjab, India

Corresponding Author:
Dr. Ashwarya Sharma
HOD and Profesor, Department of Oral Medicine and Radiology, GNDDC Sunam, Patiala, Punjab, India

Gorlin-Goltz syndrome (GGS): A rare case report

Dr. Ashwarya Sharma, Dr. Zeeza Mehboob Qazi, Dr. Radhika Sharma, Dr. Shruti Sharma, Dr. Puneet Goyal and Dr. Burhan Altaf Misgar

DOI: https://doi.org/10.22271/oral.2022.v8.i2d.1514

Abstract
Gorlin-Goltz syndrome (GGS) is an infrequent multisystemic disease with an autosomal dominant inherited disorder characterized by the presence of multiple keratocystic odontogenic tumors (KCOT) in the jaws, multiple basal cell nevi carcinomas, and skeletal abnormalities. Early diagnosis of Gorlin-Goltz syndrome is essential as it may progress to aggressive basal cell carcinomas and neoplasias. In this paper, a case of GGS in a 19 year old male is reported and the literature is reviewed.

Keywords: Gorlin-Goltz syndrome (GGS), Keratocystic odontogenic tumors (KCOT). Palmar pits, plantar pits

Introduction
Gorlin-Goltz syndrome (GGS), which is also well-known as nevoid basal cell carcinoma syndrome (NBCCS), is an autosomal dominant, rare multisystemic disease with a high degree of variable expressiveness and penetrance. It is characterized by basal cell nevus, odontogenic keratocysts (KCOT), ectopic calcifications of the falx cerebri, and palmar and/or plantar pits. Early diagnosis of GGS is important to reduce the severity of the complications, such as basal cell carcinomas and brain tumors, and to avoid the maxillofacial deformities related to the jaw cysts.

Case Report
A 19 year old male patient visited the department of Oral Medicine and Radiology with the chief complaint of missing teeth in front region of lower arch and complains of swelling on both sides of face since 15 days and two irregular swelling in front region of lower arch since 10 days. History of presenting illness revealed missing teeth in front region of lower arch and complains of swelling on both sides of face which was initially smaller in size and gradually increased to present size. There was no history of pain or any purulent or any blood discharge associated with it. There was also history of two irregular bulge in front region of lower arch which was initially smaller in size and gradually increased to attain the present size. It was associated with discomfort while chewing, talking with no history of pain or any purulent or blood discharge associated with it. His family and medical history was not significantly relevant. He was consuming both non vegetarian and vegetarian diet. Oral hygiene status was good and patient brushes once daily using Modified Stillmans Method. General physical examination revealed patient is well oriented to time, place and person, normesthenic and moderately nourished. All his vitals were in normal ranges. Skin examination revealed presence of multiple palmar and plantar pits of maximum diameter 1- 2mm. (Figure 1, 2)
On extraoral examination, face was bilaterally asymmetrical because of swelling on both sides of face. There was also presence of frontal bossing, and depressed nasal bridge and hypertelorism. There was no abnormality detected in TMJ/ muscles of mastication/ salivary glands, lymph nodes. There was presence of swelling on both sides of face. On right side of face, there was presence of solitary dome shaped swelling of approximate size 3cm in maximum diameter extending superoinferiorly from lower margin of ear lobe to lower border of mandible and anteroposteriorly 5cm away from outer corner of lip to angle of mandible with colour as that of surrounding skin, with smooth surface and with indistinct edges.

On left side of face, there was also presence of dome shaped selling of approximate size 7 × 4.5 cm extending superoinferiorly from upper margin of ear to lower border of mandible and anteroposteriorly 3.5cm away from corner of lip to angle of mandible with colour as that of surrounding skin with smooth surface and with indistinct edges Swelling on both sides of face was non tender, soft, fluctuant, non-compressible, non-reducible, and non-pulsatile. Intraoral examination revealed that there was presence of two dome shaped bulge on right and left region of lower arch. (Figure 3, 4) On right side it was of approximate size 2 × 1 cm extending mediolaterally from distal aspect of 42 to mesial aspect of 44 and superoinferiorly from upper border of alveolar margin w.r.t. 42, 43 to respective lingual vestibule obliterating the same, pinkish in colour with smooth surface and indisinct edges. On left side it was of approximate size 1.3 × 1 cm extending mediolaterally from distal aspect of 32 to distal aspect of 33 and superoinferiorly from cememtoenamel junction w.r.t 33 to respective lingual vestibule obliterating the same, pinkish in colour with smooth surface and indisinct edges. Bulge on both sides of lower arch was non tender, hard, non-fluctuant, non-compressible, non-reducible, and non-pulsatile. Hard tissue examination revealed presence of teeth w.r.t. 11, 12, 13, 14, 15, 16, 17,21,22,23,24,25,26,27,31,34,35,36,37,41,42, 44,45,46,47 with Class I molar relation. Also the patient was having narrow and high arched palate. (Figure 5)

No abnormality was detected in buccal /labial mucosa, tongue / floor of mouth. Mouth opening is 40 mm interincisally. Based on the history taking and clinical examination, provisional diagnosis of hypodontia was made and differential diagnosis of Congenitally absent teeth, Fibromatosis gingiva, Dentigerous cyst was made.

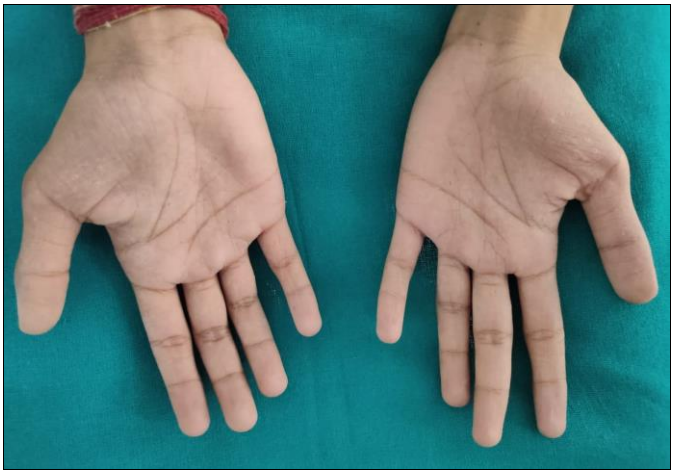


Fig 1: Skin examination revealed presence of multiple palmar pits of maximum diameter 1- 2mm

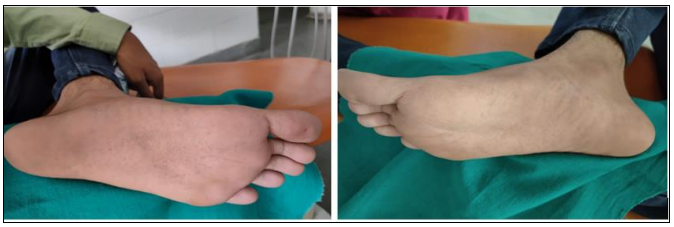


Fig 2: Skin examination revealed presence of multiple plantar pits of maximum diameter 1- 2mm

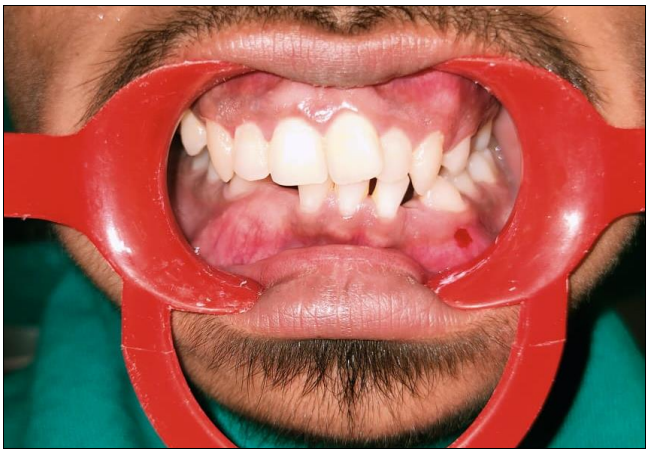


Fig 3: Bulge in canine area is seen

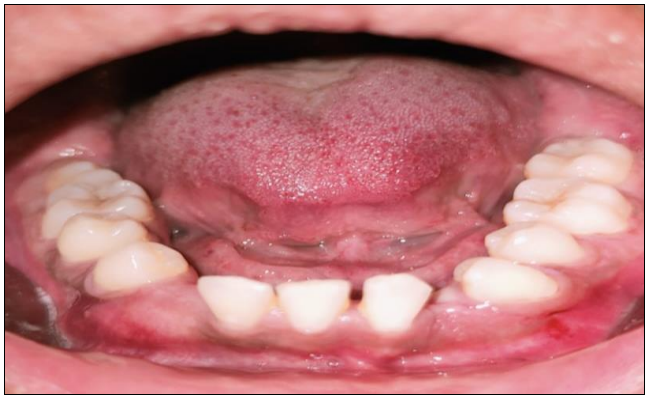


Fig 4: Mandibular arch

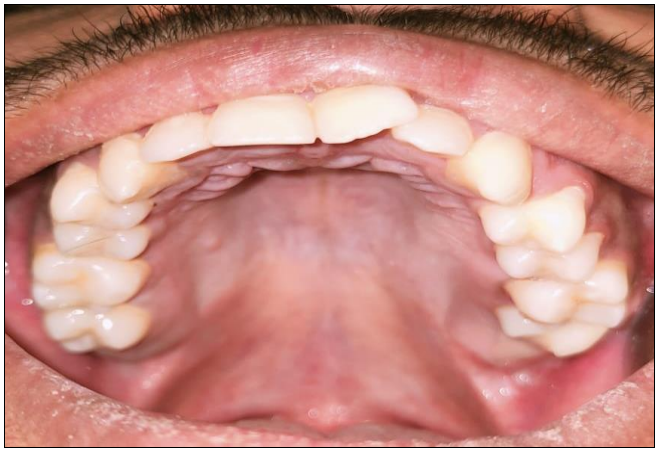


Fig 5: Maxillary arch- High arched palate

Investigations

Radiographic Investigations

Orthopantomogram revealed three unilocular well defined radiolucent lesion one being in lower anterior region of mandible and other two being on right and left rami of mandible.

Well defined unilocular radiolucency in lower anterior region of mandible is of size approx. 6.8 × 2.4 cm extending superoinferiorly from peripaical region w.r.t. 41, 42, 31 to inferior border of mandible and anteroposteriorly from mesial aspect of impacted 43 to distal aspect of 36 with corticated borders with presence of impacted teeth w.r.t. 43, 32, 33 which are displaced by enlarging cyst.

Well defined unilocular radiolucency on right rami of mandible is of size 5.2 × 2.2cm extending superoinferiorly 3mm below sigmoid notch to lower border of mandible and anteroposteriorly from anterior border of rami to 2mm away from posterior border of ramus with loss of trabeculation and thinning of rami with corticated borders involving displacement of impacted tooth w.r.t. 28, 38by enlarging cyst.
Well defined unilocular radiolucency on left rami of mandible is of size 3.4× 2.5cm extending superoinferiorly 6mm below sigmoid notch to 1cm above lower border of mandible and anteroposteriorly from anterior border of rami to 4mm away from posterior border of ramus with loss of trabeculation and thinning of rami with corticated borders involving displacement of impacted tooth w.r.t. 48 by enlarging cyst. (Figure 6)

Histopathologial Investigations

The H and E stained section shows epithelial lining, cystic lumen and capsular stromal components. The lining is of parakeratinised stratified squamous epithelium of 4 – 6 cells thick with columnar basal cells showing nuclear palisading. Surface epithelium shows corrugations. Split at epithelium-connective tissue interface is evident. No sign of malignancy in epithelial cells. The stromal capsue exhibits dense collagen fibres, odonogenic islands/ daughter cysts, blood capillaries and dense mixed inflammatory infiltrate of PMNLs, lymphocytes and plasma cells along with areas of hemorrhage. All these features are suggestive of odontogenic keratocyst. (Figure 7, 8).
Based on the history taking and typical clinical examination a diagnosis of Gorlin goltz syndrome was made.

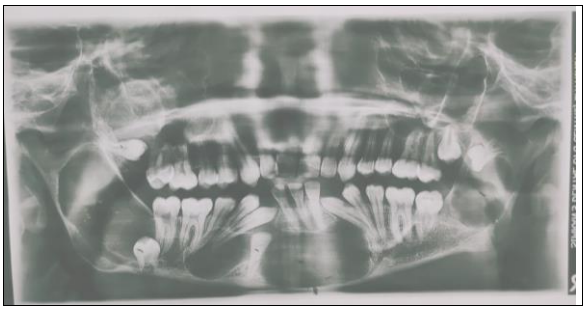


Fig 6: OPG

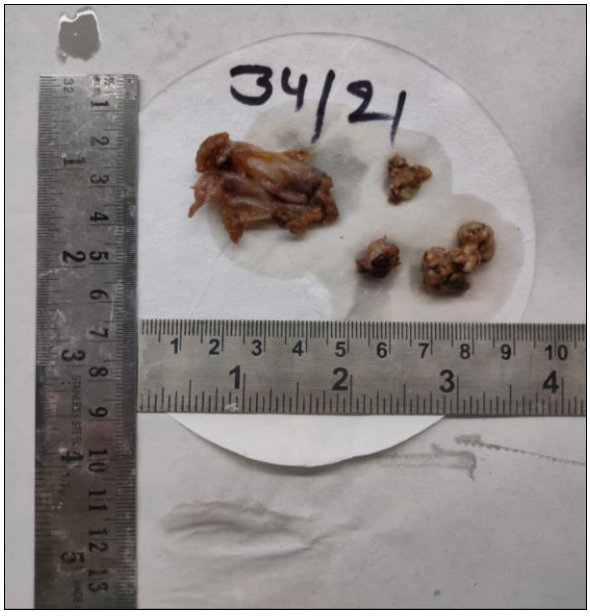
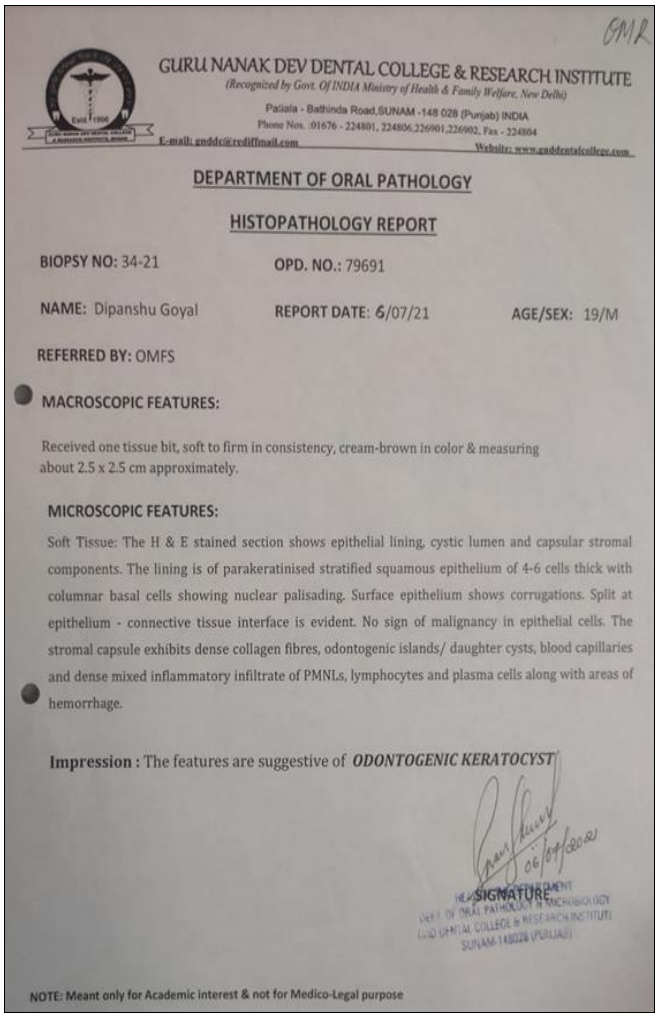


Fig 7: Biopsy



GURU NANAK DEV DENTAL COLLEGE & RESEARCH INSTITUTE
(Recognized by Govt. Of INDIA Ministry of Health & Family Welfare, New Delhi)
Patiala - Bathinda Road,SUNAM -148 028 (Punjab) INDIA
Phone Nos. :01676 - 224801, 224806,226901,226902, Fax - 224804
E-mail: gnddc@rediffmail.com Website: www.gnddentalcollege.com

DEPARTMENT OF ORAL PATHOLOGY

HISTOPATHOLOGY REPORT

BIOPSY NO: 34-21 OPD. NO.: 79691

NAME: Dipanshu Goyal REPORT DATE: 6/07/21 AGE/SEX: 19/M

REFERRED BY: OMFS

MACROSCOPIC FEATURES:

Received one tissue bit, soft to firm in consistency, cream-brown in color & measuring about 2.5 x 2.5 cm approximately.

MICROSCOPIC FEATURES:

Soft Tissue: The H & E stained section shows epithelial lining, cystic lumen and capsular stromal components. The lining is of parakeratinised stratified squamous epithelium of 4-6 cells thick with columnar basal cells showing nuclear palisading. Surface epithelium shows corrugations. Split at epithelium - connective tissue interface is evident. No sign of malignancy in epithelial cells. The stromal capsule exhibits dense collagen fibres, odontogenic islands/ daughter cysts, blood capillaries and dense mixed inflammatory infiltrate of PMNLs, lymphocytes and plasma cells along with areas of hemorrhage.

Impression : The features are suggestive of ***ODONTOGENIC KERATOCYST***

SIGNATURE

NOTE: Meant only for Academic interest & not for Medico-Legal purpose

Fig 8: Biopsy report

Discussion

Gorlin-Goltz syndrome is an uncommon autosomal dominant inherited disorder characterized by numerous basal cell carcinomas, odontogenic keratocysts (OKCs) and musculoskeletal malformations.
NBCCS was first described by Jarish and White in 1894 and was later establish as a unique syndrome by Gorlin-Goltz in 1960. The syndrome initially consisted of triads of BCC, jaw cysts and skeletal anomalies.

Synonyms

Basal cell nevus syndrome, Nevoid basal cell carcinoma syndrome (NBCCS), Multiple basal cell carcinoma (BCC) syndrome, Multiple basalioma syndrome, Jaw cyst basal cell tumor skeletal anomalies syndrome, Jaw cyst bifid rib basal cell nevus syndrome.

Incidence

The incidence of this disorder is estimated to be 1 in 50,000-1, 50, 000 in the general population, varying by region. It appears in all ethnic groups, but most often in whites; males and females are equally affected. Although detected in very young children, they are commonly expressed between the ages of 17 years and 35 years.

Origin

The pathogenesis of GGS is attributed to abnormalities linked to the long arm of chromosome 9 (q22.3-q31). It has been reported that loss of human patched gene (PTCH1 gene), which is a tumor suppressor gene, could be the molecular

origin of the syndrome.
Human patched gene (PTCH1 gene) is significant for embryonic structuring and cellular cycle and thus its mutation comprises a key event for the development of this syndrome.

Clinical Features
Clinical manifestations of the syndrome can be grouped into the following nine categories.

1. **Cutaneous anomalies:** Basal cell nevus/carcinoma (50–97%), other benign dermal cysts and tumors (21%), palmar/plantar pitting (90%), palmar and plantar keratosis and dermal calcinosis.
2. **Dental anomalies:** Multiple odontogenic keratocysts (75–100%), maxillary hypoplasia, mandibular prognathism, high arched palate or prominent palatine ridges (40%), cleft lip/palate (4%), impacted teeth and/or agenesis (3%), ectopic teeth and malocclusion.
3. **Craniofacial anomalies:** Calcification of falx (37–79%), tentorium cerebellum calcification (3%), bridged sella turcica (21%), macrocephaly (40%), brachycephaly, frontal bossing (25%), parietal and temporal bossing and coarse face (50%).
4. **Skeletal anomalies:** Polydactyly (3%), syndactyly, scoliosis (15%), hemivertebrae or other vertebral defects, flame-shaped lucencies of hand/feet, spina bifida (3%), osteoporosis (3%), cervical/bifurcated/fused/splayed/absent/rudimentary ribs (26%), brachymetacarpalism and shortened fourth metacarpal (12%)
5. **Cardiac:** Cardiac fibroma (3%)
6. **Ophthalmic anomalies:** Hypertelorism (40%), dystopia canthorum, congenital blindness (15%), internal strabismus (15%), congenital amaurosis, exotropia, glaucoma (3%), ptosis and coloboma (3%)
7. **Neurological anomalies:** Mental retardation (6%), dural calcification, bridging of sella, agenesis of corpus callosum, congenital hydrocephalus (3%), medulloblastoma (3-5%), agenesis/disgenesis of corpus callosum, meningioma (1% or less) and schizoid personality
8. **Sexual anomalies:** Hypogonadism (3%), uterine and ovarian fibromas (15%), calcified ovarian cysts (3%) and supernumerary nipple
9. **Laboratory findings:** Increased serum uric acid level (3%), increased levels of alkaline phosphate and cyclic adenosine monophosphate.

Major/Minor Criteria
Evans *et al*. first established major and minor criteria for diagnosis of this rare entity, later modified by Kimonis *et al*. According to them diagnosis of GGS can be established when two major or one major and two minor features are present.

The major criteria are
1. Multiple BCC or one occurring under the age of 20 years.
2. Histologically proven OKCs of the jaws.
3. Palmar or plantar pits (three or more).
4. Bilamellar calcification of the falx cerebri.
5. Bifid, fused or markedly splayed ribs.
6. First-degree relative with NBCCS.

The minor criteria are
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, Medulloblastoma.

Differential Diagnosis
1. Sotos syndrome
2. Bazex syndrome
3. Rombo syndrome

Management
1. Jaw cysts are managed by enucleation.
2. There is greater chance of recurrence than for the isolated OKC's.
3. The recurrence rate ranges from 30 – 60% within 3-5 years after enucleation.

Conclusion
Gorlin-Goltz syndrome is a dominant autosomal genetic process, which is of particular interest to the oral and maxillofacial health experts. Proper evaluation and characterization of the clinical features are of the utmost importance for the correct diagnosis and treatment of affected patients. In order to be able to establish early diagnosis of NBCCS, specialists should carry out clinical and imaging examinations in early ages of life. Physicians and dentists must know the features of the syndrome well.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil

Conflicts of interest
There are no conflicts of interest.

References
1. Amezaga AOG, Arregui OG, Nuño SZ, Sagredo AA, Urizar JMA. Gorlin-Goltz syndrome: Clinicopathologic aspects. Med Oral Patol Oral Cir Bucal. 2008;13:338-43.
2. Cohen MM. Nevoid basal cell carcinoma syndrome: molecular biology and new hypotheses. Int J Oral Maxillofac Surg. 1999;28:216-23. 10.1034/j.1399-0020.1999.283280314.x.
3. Dowling PA, Fleming P, Saunders ID, Gorlin RJ, Napier SS. Odontogenic keratocysts in a 5-year-old: Initial manifestations of nevoid basal cell carcinoma syndrome. Pediatr Dent. 2000;22:53-55.
4. Evans DG, Ladusans EJ, Rimmer S, Burnell LD, Thakker N, Farndon PA. Complications of the naevoid basal cell carcinoma syndrome: results of a population based study. J Med Genet. 1993;30:460-464.
5. Farndon PA, Del Mastro RG, Evans DG, Kilpatrick MW.

Location of gene for Gorlin syndrome. Lancet. 1992;339:581-2. 10.1016/0140-6736(92)90868-
6. Gorlin RJ, Goltz RW. Multiple nevoid basal cell epithelioma, jaw cysts and bifid rib: A syndrome. New Engl J Med. 1960;262:908-12. 10.1056/NEJM196005052621803
7. Gorlin RJ. Nevoid basal cell carcinoma (Gorlin) syndrome: Unanswered issues. J Lab Clin Med. 1999;134:551-2. 10.1016/S0022-2143(99)90092-6
8. Kimonis VE, Goldstein AM, Pastakia B, *et al*. Clinical manifestations in 105 persons with nevoid basal cell carcinoma syndrome. Am J Med Genet. 1997;69:299-308.
9. Manfredi M, Vescovi P, Bonanini M, Porter S. Nevoid basal cell carcinoma syndrome: a review of the literature. Int J Oral Maxillofac Surg. 2004;33:117-124. 10.1054/ijom.2003.0435
10. Nilesh K, Tewary S, Zope S, Patel J, Vande A. Dental, dermatological and radiographic findings in a case of Gorlin-Goltz Syndrome: report and review. Pan Afr Med J. 2017;27:96. 10.11604/pamj.2017.27.96.12025
11. Satinoff MI, Wells C. Multiple basal cell naevus syndrome in ancient. Egypt Med Hist. 1969;13:294-7.
12. Shanley S, Ratcliffe J, Hockey A, Haan E, Oley C, Ravine D, *et al*. Nevoid basal cell carcinoma syndrome: review of 118 affected individuals. Am J Med Genet. 1994;50:282-90. 10.1002/ajmg.1320500312
13. Sun LS, Li XF, Li TJ. PTCH1 and SMO gene alterations in keratocystic odontogenic tumors. J Dent Res. 2008;87:575-579. 10.1177/154405910808700616
14. Woolgar JA, Pippin JW, Browne RM. The odontogenic keratocyst and its occurrence in the nevoid basal cell carcinoma syndrome. Oral Surg Oral Med Oral Pathol. 1987;64:727-730.
15. Yang X, Pfeiffer RM, Goldstein AM. Influence of glutathione-S-transferase (GSTM1, GSTP1, GSTT1) and cytochrome p450 (CYP1A1, CYP2D6) polymorphism on numbers of basal cell carcinomas (BCCs) in families with the naevoid basal cell carcinoma syndrome. J Med Genet. 2006;43:e1-e16. 10.1136/jmg.2005.040188.