ORIGINAL RESEARCH PAPER
Volume-9 | Issue-3 | March-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

GORLIN-GOLTZ SYNDROME- REPORT OF TWO CASES.

Oral Pathology

Heera R — Professor & Head, Department Of Oral Pathology And Microbiology, Govt. Dental College- Trivandrum.

Thatchani G V* — Postgraduate Student, Department Of Oral Pathology And Microbiology, Govt. Dental College- Trivandrum. *Corresponding Author

Shinu Koshy — Postgraduate Student, Department Of Oral Pathology And Microbiology, Govt. Dental College- Trivandrum.

ABSTRACT

Nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin-Goltz syndrome or Basal cell nevus syndrome, is a hereditary condition characterized by a wide range of developmental abnormalities and a predisposition to neoplasms. Early diagnosis and treatment of this syndrome as well as family screening and genetic counselling are essential for the patients affected with this syndrome. This syndrome may be diagnosed early by a dentist by routine radiographic examinations in the first decade of life, since the odontogenic keratocysts(OKC) are usually one of the first manifestations of the syndrome. Here, we present two cases of Nevoid basal cell carcinoma syndrome reported to our college.

KEYWORDS

Nevoid basal cell carcinoma syndrome, Odontogenic keratocyst, Patched gene, Bifid rib syndrome, Carnoy's solution.

INTRODUCTION:

Gorlin–Goltz syndrome, also known as Nevoid basal cell carcinoma syndrome (NBCCS) or Basal cell nevus syndrome or Hereditary cutaneomandibular polyoncosis or Bifid Rib Syndrome is a hereditary condition transmitted as an autosomal dominant trait with high penetrance and variable expressivity.[1] Gorlin & Goltz described the classical triad composed of multiple basal cell carcinoma, odontogenic keratocysts (OKCs) in the jaws and bifid ribs that characterized the diagnosis of this syndrome.[3] In addition to this triad, calcification of the falx cerebri, palmar and plantar epidermal pits, spine and rib anomalies, relative macrocephaly, facial milia, frontal bossing, ocular malformation, medulloblastomas, cleft lip and/or palate, and developmental malformations were also established as features of the syndrome[3,4]. Genetic studies showed that the NBCCS gene mapped to chromosome 9q22.3 and probably functioned as a tumour suppressor by deletion of this region in many of the neoplasms related to the syndrome. Cloning of the NBCCS gene showed it to be the human homologue of the *Drosophila* segment polarity gene *Patched (PTCH)*. The *PTCH* gene encodes a transmembranous protein that acts in opposition to the *Hedgehog* signalling protein (shh), controlling cell fates, patterning, and growth in numerous tissues, including tooth [2]. This syndrome existed during Dynastic Egyptian times, as shown by findings compatible with the syndrome in mummies dating back to 1,000 b.c[5]. The prevalence of NBCCS has been estimated from 1 in 57,000 [6] to 1 in 164,000 [7], but there is now general agreement that the prevalence is about 1 per 60,000 [8]. This syndrome probably presents itself in all ethnic groups, although a few cases have been published in certain human races, and affects both men and women in the same way [9]. We report two cases of Gorlin–Goltz syndrome in this article. Both patients reported with jaw swellings. Radiographic investigations showed multiple radiolucencies which were histologically confirmed as OKCs. This prompted the investigators to take chest radiograph to ascertain the presence of abnormality of ribs. The chest x-rays revealed the presence of bifid ribs and a diagnosis of Gorlin-Goltz syndrome in both the patients was made

CASE 1

A 13year old male patient presented with the chief complaint of swelling in left side of the face for 2 weeks. The patient gave no history of trauma. The swelling increased gradually and was non tender. Extraoral examination revealed facial asymmetry with a diffuse swelling of left side, hypertelorism (figure 1a) and multiple nevi over the face. Pits of plantar surface were also noted (figure 1b).

On intra-oral examination a 4x2x1 cm ovoid, bony hard swelling was noticed on the left side of mandible (figure 1c) extending from ramus to parasymphyseal region. Buccal cortical expansion with obliteration of the buccal vestibule was seen with respect to 36,37,38 region. Another diffuse, fluctuant, non-tender swelling was also noticed over the left maxillary tuberosity region.75 was mobile.24 and 25 were erupting. Retained 83,84,85.

OPG (figure 1d) and brain-paranasal sinuses CT revealed 3 expansile lytic lesions of jaws- 2 in the mandible and one in maxilla (figure 1e)

On the right side of mandible, an expansile lytic lesion of 3.9 x 1.9 x 3.6cm is seen involving the body, alveolar process of incisor, premolar and molar region, engulfing their roots and also crossing the midline to 32 region. Three impacted teeth (43,44,45) are seen within the lesion.

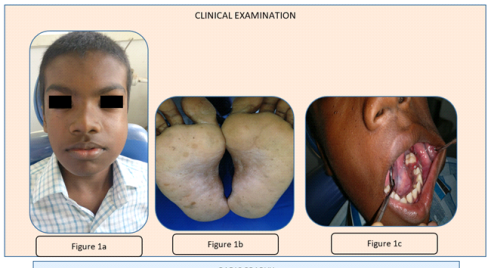
Another well defined, corticated radiolucency of size 3.6 x2.7x8.2cm is present over the left side of mandible, involving alveolar process of 35,36 and extending posterosuperior to angle, ramus and coronoid process. Crown of 37 is engulfed in the lesion,38 is displaced superiorly to the region of ramus

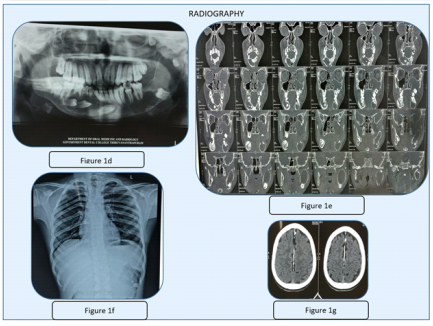
Left maxillary tuberosity region revealed ill-defined radiolucency displacing the tooth bud of 28 and causing bony erosions of anterior, posterolateral and medial wall of left maxillary sinus.

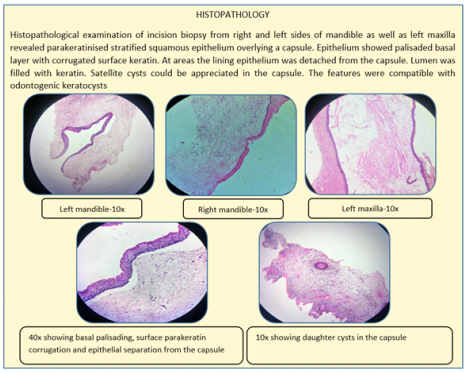
CT of brain reveals calcifications of falx cerebri (figure 1g), tentorium cerebelli and bilateral petro clinoid ligaments.

Chest x-ray showed bilateral bifid ribs (figure 1f)

A provisional diagnosis of Gorlin-Goltz syndrome was given and incisional biopsies from all 3 lesions revealed OKC with the presence of daughter cysts







CASE 2:

A 13-year old female patient presented with the chief complaint of swelling on the right side of face since 2 weeks. The swelling was of insidious onset and non-tender. Patient did not report any history of trauma.

A diffuse swelling was noted over left lower back tooth region on extraoral examination. Hypertelorism was also seen (figure 2a).

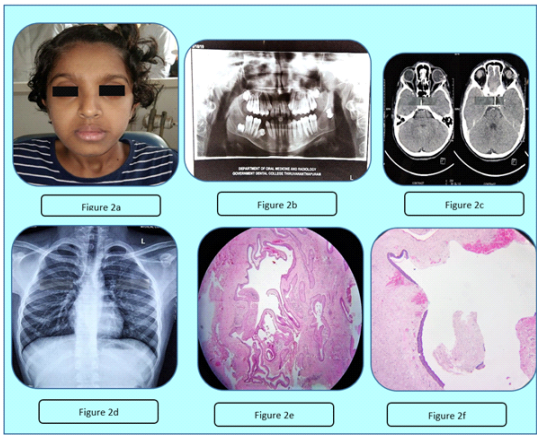
Intraoral examination revealed a diffuse swelling over left maxillary tuberosity region. On palpation the lesion was mobile, non-tender, non-fluctuant and firm in consistency. The overlying mucosa appeared normal with no evidence of secondary changes.

OPG and CT showed multiple radiolucencies in the mandible (figure 2b). A well-defined expansile lytic lesion of size 3.5x2.1 cm was noted in the body of mandible on the right side, displacing adjacent teeth. Two other similar lytic lesions were noted in the junction of body and ramus of mandible on either side. No maxillary lesions seen. 38 and 48 are unerupted and impacted.

CT brain showed calcification foci of falx cerebri and tentorium cerebelli (figure 2c) and bridging of Sella turcica.

Chest X-ray showed bilateral cervical ribs and bifid rib on left side (figure 2d)

Incisional biopsy confirmed a diagnosis of odontogenic keratocyst on left side (figure 2e) and right-side mandible (figure 2f). Daughter cysts were also seen.



SUMMARY OF BOTH CASES

	CRITERIA	PATIENT 1	PATIENT 2
MAJOR CRITERIA			
1.	Multiple or single basal cell carcinomas occurring under the age of 20 years	-	-
2	Histologically proven OKCs of the jaws.	+ ve	+ ve
3	Palmar or plantar pits (three or more).	+ ve	-
4	Bilamellar calcifications of the falx cerebri.	+ ve	+ ve
5	Bifid, fused, or markedly splayed ribs.	+ ve	+ ve
6	First degree relative with NBCC	-	-
MINOR CRITERIA			
1	Macrocephaly (adjusted for height).	+ ve	-
2	Congenital malformation:	hypertelorism	hypertelorism.
3	Other skeletal abnormalities:	-	-
4	Radiological abnormalities	-	Bulging of sella turcica
5	Ovarian fibroma.	-	-
6	Medulloblastoma	-	-

DISCUSSION:

Gorlin–Goltz syndrome (NBCCS) was first recognized in 1894 by Jarisch and White. Dr. Robert Gorlin and Dr. Robert Goltz (1960) delineated the different clinical features in their study on "multiple naevoid basal cell epithelioma, jaw cysts and bifid rib syndrome." The main clinical manifestations of this syndrome include multiple BCC, KCOTs of jaws, palmer-plantar pits, rib and skeletal anomalies and facial dysmorphism, cleft lip/palate, eye anomalies like cataract, Bitot's spots, etc.). Various low frequency neoplasms such as MEDs, meningiomas, ovarian and cardiac fibromas, epidermoid cysts, and defects of stomatologic system, including mandibular prognathism, high arched palate, malocclusion, impacted teeth, ameloblastoma, squamous cell carcinoma, and odontogenic myxoma, have also been reported[10]. Very few cases of NBCCS had been reported previously in Indian literature probably representing under recognition. A search in medical literature (MEDLINE and others) of reports of NBCCS in Indian patients revealed 69 case reports from 1977 to 2019. Combining our cases of 2 patients with 69 additional cases of NBCCS reported in Indian patients[11-34]. In 1993, Evans, et al. first established major and minor criteria for the diagnosis of NBCCS, which was later modified by Kimonis, et al. in 2004. The presence of two major and one minor or one major and three minor criteria are essential to confirm the diagnosis of NBCCS.

MAJOR CRITERIA[11]

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

MINOR CRITERIA

- Macrocephaly (adjusted for height).
- Congenital malformation: Cleft lip or cleft palate, frontal bossing, coarse face moderate or severe hypertelorism.
- Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits.
- Radiological abnormalities: Bulging 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.
- Ovarian fibroma.
- Medulloblastoma.

Multiple OKCs can occur in association with other syndromes, such as an orofacial digital syndrome, Ehlers-Danlos syndrome, Simpson Golabi–Behmel syndrome, and Noonan syndrome[12]. Woolgar *et al*. in 1987 concluded that mean age group for syndromic cases is 10 to 30 years and females are more affected than males. In syndromic cases, more commonly maxillary molar area is affected. Recurrence rate is higher in syndromic cases (63%). Woolgar *et al*. have also noted significant differences histologically. OKC associated with Basal Cell Nevus Syndrome showed a greater number of satellite cyst, solid islands of epithelial proliferation and odontogenic rests within the capsule, and increased mitotic figures in the epithelium lining the main cavity.

OKC's falling in the category of Keratocystic Odontogenic Tumor (KCOT) may be associated with Gorlin-Goltz Syndrome in the form of multiple cystic lesions. Katase *et al*. analyzed the neoplastic nature and biological potential of sporadic and nevoid basal cell carcinoma syndrome (NBCCS)-associated KCOT. Heparanase is an endo-d-

glucuronidase enzyme that specifically cleaves heparan sulfate and the increase of its level in tumors promotes invasion, angiogenesis, and metastasis. Intense gene and protein expressions have been observed in KCOT associated with NBCCS, as compared with sporadic ones and dentigerous cyst. So, heparanase expression may be correlated with the neoplastic properties of KCOT, particularly in NBCCS-associated cases

Apart from surgical enucleation for cystic lesions, adjunctive therapies like chemical cauterization is useful to prevent recurrence by fixing the daughter cyst or remnants of epithelial lining that are not removed during the enucleation procedure. Carnoy's solution is a phenolic compound with tissue fixative properties. Voorsmit *et al*. have demonstrated that Carnoy's solution penetrates the bone to the depth 1.54 mm following a 5 minutes application without any damage to the inferior alveolar nerve[11].

CONCLUSION:

Here we report two cases of Gorlin-Goltz syndrome in young patients. The patients reported with swelling of jaw bones. Further radiographic investigations led to the findings of multiple radiolucencies in both maxilla and mandible and bifid ribs. This report emphasizes the need of meticulous investigations in patients reporting with jaw swellings especially the young. The possibility of odontogenic keratocysts associated with Gorlin-Goltz syndrome should be borne in mind by the clinician while examining multiple jaw lesions. Since OKCs have a propensity for anteroposterior expansion, early diagnosis and the management of Gorlin-Goltz syndrome will enable a better prognosis and reduce morbidity in these patients.

ACKNOWLEDGEMENT:

We acknowledge the support and help of members of Department of Oral Pathology and Microbiology, Government Dental College, Triva ndrum in preparing the manuscript.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest.

REFERENCES:

1. Shafer WG, Hine MK, Levy BM, Rajendran R, Sivapathasundharam B. A textbook of oral pathology. Philadelphia: Saunders; 1983 Sep 20.
2. Shear M, Speight P. Cysts of the oral and maxillofacial regions. John Wiley & Sons; 2008 Apr 15.
3. Yamamoto K, Yoshihashi H, Furuya N, Adachi M, Ito S, Tanaka Y, Masuno M, Chiyo H, Kurosawa K: Further delineation of 9q22 deletion syndrome associated with basal cell nevus (Gorlin) syndrome: Report of two cases and review of the literature. Congenit Anom 2009, 49:8-14.
4. Cohen MM: Nevoid basal cell carcinoma syndrome: molecular biology and new hypotheses. Int J Oral Maxillofac Surg 1999, 28:216-23.
5. Satinoff MI, Wells C: Multiple basal cell naevus syndrome in ancient. Egypt Med Hist 1969, 13:294-7.
6. Farndon PA, Del Mastro RG, Evans DG, Kilpatrick MW: Location of gene for Gorlin syndrome. Lancet 1992, 339:581-2.
7. Shanley S, Ratcliffe J, Hockey A, Haan E, Oley C, Ravine D, Martin N, Wicking C, Chenevix-Trench G: Nevoid basal cell carcinoma syndrome: review of 118 affected individuals. Am J Med Genet 1994, 50:282-90.
8. Gorlin RJ: Nevoid basal cell carcinoma (Gorlin) syndrome: Unanswered issues. J Lab Clin Med 1999, 134:551-2.
9. 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.
10. Muzio LL. Nevoid basal cell carcinoma syndrome (Gorlin syndrome). Orphanet journal of rare diseases. 2008 Dec;3(1):32.
11. Joshi PS, Deshmukh V, Golgire S. Gorlin-goltz syndrome. Dental research journal. 2012 Jan;9(1):100.
12. Ali IK, Karjodkar FR, Sansare K, Salve P, Dora A, Goyal S. Nevoid Basal Cell Carcinoma Syndrome-Clinical and Radiological Findings of Three Cases. Cureus. 2016 Aug;8(8).
13. Gupta, Shalini R., et al. Nevoid basal cell carcinoma syndrome in Indian patients: a clinical and radiological study of 6 cases and review of literature. Oral surgery, oral medicine, oral pathology and oral radiology. 2012 Jan 1;113(1):99-110.
14. Lata J et.al. Gorlin–Goltz syndrome: A case series of 5 patients in North Indian population with comparative analysis of literature. Contemporary clinical dentistry. 2015 Sep;6(Suppl 1):S192.
15. Sudipto Sahu et al. An enigma of Gorlin–Goltz syndrome: Two cases reported in mother and daughter. Journal of Oral and Maxillofacial Pathology: JOMFP. 2019 Feb;23(Suppl 1):115.
16. Suchithra KS. Gorlin Goltz Syndrome–Case Series and Review of Literature. 2019;18(4):76–86.
17. Kalia V.et.al, The syndromic multiple odontogenic keratocyst in siblings: A familial study. Annals of maxillofacial surgery. 2011 Jan;1(1):77.
18. Baliga SD, Rao SS. Nevoid-basal cell carcinoma syndrome: a case report and overview on diagnosis and management. Journal of maxillofacial and oral surgery. 2010 Mar 1;9(1):82-6.
19. Pereira T, Tamgadge A, Sapdhare S, Pujar A. Multiple keratocystic odontogenic tumors in nevoid basal cell carcinoma syndrome. Annals of maxillofacial surgery. 2015 Jul;5(2):277.
20. Kiran NK, Raj TT, Mukunda KS, Reddy VR. Nevoid basal cell carcinoma syndrome (Gorlin-Goltz syndrome). Contemporary clinical dentistry. 2012 Oct;3(4):514.
21. Subramanyam SB, Sujata DN, Sridhar K, Pushpanjali M. Nevoid Basal cell carcinoma syndrome: a case report and review. Journal of maxillofacial and oral surgery. 2015 Mar 1;14(1):11-5.
22. Anchlia S, Vyas S, Bahl S, Nagavadiya V. Gorlin-Goltz syndrome in twin brothers: an unusual occurrence with review of the literature. Bmj Case Reports. 2015;2015.
23. Mehta DN, Raval N, Patadiya H, Tarsariya V. Gorlin Goltz Syndrome. Annals of medical and health sciences research. 2014;4(2):279-82.
24. Kulkarni GH, Khaji SI, Metkari S, Kulkarni HS, Kulkarni R. Multiple keratocysts of the mandible in association with Gorlin-Goltz syndrome: a rare case report. Contemporary clinical dentistry. 2014 Jul;5(3):419.
25. Mohan RP, Verma S, Agarwal N, Singh U. Gorlin-Goltz syndrome: a rare case report. Case Reports. 2013 Jun 25;2013.
26. Tandon S, Chauhan Y, Sharma M, Jain M. Gorlin-Goltz Syndrome: A Rare Case Report of a 11-Year-Old Child. International journal of clinical pediatric dentistry. 2016 Jul;9(3):264.
27. Agrawal A, Murari A, Vutukuri S, Singh A. Gorlin-goltz syndrome: case report of a rare hereditary disorder. Case reports in dentistry. 2012;2012.
28. Pandeshwar, Padma, K. Jayanthi, and D. Mahesh. "Gorlin-goltz syndrome." Case reports in dentistry 2012 (2012).
29. Patankar AP, Kshirsagar RA, Dugal A, Mishra A, Ram H. Gorlin-Goltz syndrome: A series of three cases. National journal of maxillofacial surgery. 2014 Jul;5(2):209.
30. Ramesh M, Krishnan R, Chalakkal P, Paul G. Gorlin-Goltz syndrome: case report and literature review. Journal of oral and maxillofacial pathology: JOMFP. 2015 May;19(2):267.
31. Thomas N, Vinod SV, George A, Varghese A. Gorlin–Goltz syndrome: An often missed diagnosis. Annals of maxillofacial surgery. 2016 Jan;6(1):120.
32. Hegde S, Shetty SR. Radiological features of familial Gorlin-Goltz syndrome. Imaging science in dentistry. 2012 Mar 1;42(1):55-60.
33. Pol CA, Ghige SK, Kalaskar RR, Gosavi SR. Gorlin-Goltz syndrome: A rare case report. Contemporary clinical dentistry. 2013 Oct;4(4):547.
34. Chandran S, Marudhamuthu K, Riaz R, Balasubramaniam S. Odontogenic Keratocysts in Gorlin–Goltz Syndrome: A Case Report. Journal of international oral health: JIOH. 2015;7(Suppl 1):76.
35. Acharya S, Panda S, Dhull KS, Sahoo SR, Ray P. Gorlin syndrome with bilateral polydactyly: A rare case report. International journal of clinical pediatric dentistry. 2013 Sep;6(3):208.
36. Khaliq MI, Shah AA, Ahmad I, Hasan S, Jangam SS. Keratocystic odontogenic tumors related to Gorlin–Goltz syndrome: A clinicopathological study. Journal of oral biology and craniofacial research. 2016 May 1;6(2):93-100.
37. Bahadure RN, Jain ES, Badole GP. Gorlin and Goltz syndrome: A case report with surgical review. International journal of clinical pediatric dentistry. 2013 May;6(2):104.
38. Kumar NN, Padmashree S, Jyotsna TR, Shastry SP. Gorlin-Goltz syndrome: A rare case report. Contemporary clinical dentistry. 2018 Jul;9(3):478.