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GORLIN-GOLTZ SYNDROME: A CASE REPORT

Maxillofacial Surgery

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ABSTRACT

Gorlin-Goltz syndrome 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 neoplasia's. This article reports a case of a 17-year-old female patient with Gorlin-Goltz syndrome.

KEYWORDS

Syndrome,Gorlin-Gotz,Odontogenics Keratocyst

INTRODUCTION

Gorlin-Goltz syndrome which is also known as nevoid basal cell carcinoma syndrome (NBCCS) is an autosomal dominant rare multisystemic disease with a variable Manifestation and Infiltration.[1] It is presented with basal cell skin growths called basal cell nevus, jawbone cysts like odontogenic keratocysts, abnormal calcium deposits in the brain's protective membrane as ectopic calcifications of the falx cerebri, and small indentations on the palms and soles called palmar/plantar pits.[2] Early diagnosis is important to reduce the severity of the complications, such as basal cell carcinomas, and brain tumours and to avoid the maxillofacial deformities related to the jaw cysts [3]. This paper presents a case of Gorlin-Goltz syndrome in a 17-year-old female patient.

Case Presentation

A 17-year-old female patient reported to the department of oral and maxillofacial surgery at King George Medical University, Lucknow with the chief complaint of swelling in the left lower tooth back region since swelling had been gradually increasing since. Meanwhile, the swelling had not increased in size and had no associated pain or discomfort. There is a h/o discharge of creamy viscous fluid from the distal gingival sulcus of the posterior left 2nd molar region. Extra oral examination revealed an increased frontal-occipital head circumference, frontal bossing, flattening of the nasal bridge, increased intercanthal distance (Figure 1), and multiple skin lesions on her hands (Figure 2)

Figure 1 – Patient having features such as Frontal bossing, wide intercanthal distance, clavicle deformity

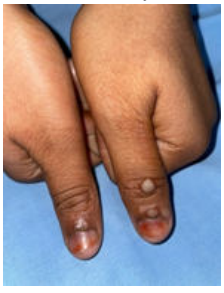

Figure 2 – Skin lesions on hands

The intra-oral examination revealed diffuse swelling of approximately 1x 0.5 cm located below the level of the attached gingival extending antero-posteriorly from the distal of 33 to the distal of 34 and supero-inferiorly from below the attached gingival to the vestibule. Tenderness on percussion was noted with mandibular teeth from 33 to 37. An orthopantomogram (OPG) showed bilateral radiolucent lesions associated with a partially erupted 18, 33,38. The left mandibular lesion was extending and involving the ramus of the mandible (Figure 3).

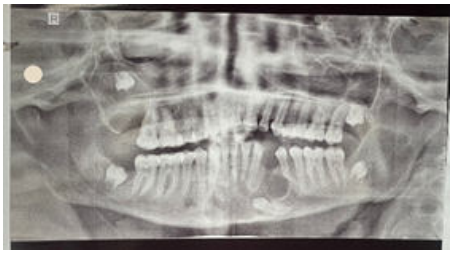

Figure 3 – Features described above seen in OPG

A skull radiograph and CT scan of the brain revealed calcification of the falx cerebri(Figure 4). In addition, the chest x-ray radiograph showed bifid right third and fourth(Figure 5). Skin lesion in the form of epidermal cyst was present .

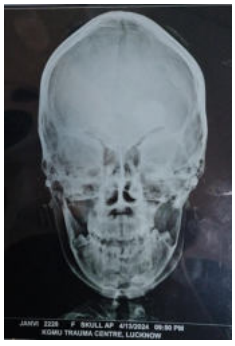

Figure 4 – Calcification of Flax Cerebri

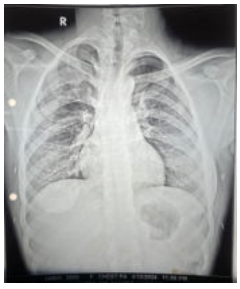

Figure 5- Bifid ribs of the patient

Based on the patient's history, clinical findings, and radiological findings a provisional diagnosis of Gorlin-Goltz syndrome was given. Differential diagnosis of Bazek Syndrome and Torres syndrome was given. The patient underwent sequential enucleation of the cystic lesions of both the maxilla and mandible with the placement of 5FU for 24 hours followed by iodoform dressing. The specimens were sent for histopathological evaluation, confirming the odontogenic keratocyst diagnosis. The final diagnosis of Gorlin-Goltz syndrome was reached. The patient was advised to report in the department at regular intervals of 1 month up to 18 months follow up.

DISCUSSIONS

Gorlin-Goltz Syndrome also known as nevoid basal cell carcinoma (NBCC) is an infrequent autosomal dominant genetic disorder with strong penetrance and extremely variable expressivity.[1] The syndrome affects between 1 in 57,000 to 1 in 256,000 people in the general population, with a male-to-female ratio of 1:1.[1,4,5] It was first reported by Jarisch and White in 1894 and later by Robert J.Gorlin and Robert W. Goltz comprised of multiple nevoid basal cell carcinoma, jaw cyst, and bifid ribs Many Researchers have found that the cause of this syndrome was due loss or mutation of tumour suppressor gene called Patched gene (PTCH1) and abnormality in the long arm of chromosome 9q22.3-q31.[6-8] An autosomal dominant way of Mutation is seen transmitted from the parents to the sibling, but this syndrome can also occur from a spontaneous mutation without any family history in 35% to 50% of the cases. The patient reported in our case has no familial history so the possibility of this syndrome may be because of spontaneous mutation. Diagnosis is based upon established major and minor clinical, and radiological criteria and ideally confirmed by DNA analysis.[9] Early diagnosis and treatment of Gorlin Goltz Syndrome as well as family screening and genetic counseling are essential as it may be associated with 10% of the patients with aggressive basal cell carcinoma and malignant neoplasias.

Evans[10] et al first established major and minor criteria for the diagnosis of the syndrome and later modified by Kimonis[11] et al in 2004.

The presence of two major and one minor or one major and three minor criteria is necessary to establish the diagnosis.

Major and minor criteria consist

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.

Macrocephaly

Congenital malformation Cleft lip or cleft palate, frontal bossing, coarse face moderate or severe hypertelorism Other skeletal abnormalities. Sprengel deformity, marked gestus deformity, marked syndactyly of the digits.

Radiological abnormalities: Bulging of sella turcica, vertebral anomalies such as hemi vertebrae, fusion or elongation of vertebral bodies, modelling defect of the hands, feet or flame-shaped hands or feet.

In our patient diagnosis was made by three major criteria, namely OKC, bifid ribs, and calcifications of falx cerebri and three minor criteria namely macrocephaly, frontal bossing, hypertelorism, pectus deformity. Regarding the site predilection, OKCs which are associated with NBCCS are more common in the mandible with 69% involvement, as compared to 31% in the maxilla, In the mandible, 47% OKC occurs in the molar ramus region, followed by 10% in the incisor canine areas. In the maxilla, 14% of OKCs were found to occur in the incisor canine areas followed by molar tuberosity with 12%, 7% in the mandibular premolar region and 3 % in the maxillary premolar region.[12]

Regarding the male-to-female ratio it was 1:0.62 for OKC which was not associated with NBCCS and 1:1.22 for OKC in NBCCS This shows that simple keratocysts are more common in males, but more females seem to have NBCCS.[13]

Woolgar et al in 1987 concluded that the mean age group for syndromic cases is 10-30 years. The age of our patient is 17 years which supports the study done by Woolgar et al in syndromic cases, more commonly maxillary molar areas are affected, rate of recurrence is higher in syndromic cases that is 63%Woolgar et al have also noted significant differences histologically, OKC associated with Basal Cell Nevus Syndrome showed (i) an Increased number of satellite cyst, (ii) solid islands of epithelial proliferation (iii) odontogenic rests within the capsule, and (iv)increased mitotic figures in the epithelium lining the main cavity.[14] Katase et al analyzed the neoplastic nature and biological potential of sporadic and nevoid basal cell carcinoma syndrome associated KCOT. Heparanase is an endo-d-glucuronidase enzyme that specifically cleaves heparan sulfate and the increase of its level in tumours promotes invasion, angiogenesis, and metastasis. In his study, all odontogenic cysts have shown positive immunoreactions for the heparanase for the heparin protein in various intensities. Intense gene and protein expressions have been observed in KCOT associated with NBCCS, as compared with sporadic ones and dentigerous cysts. So heparanase expression may be correlated with the neoplastic properties of KCOT, particularly in NBCCS-associated cases. The satellite cyst, linear expansion, neoplastic nature, and recurrence rate are high.[15]

There are different treatment modalities described in the literature to reduce the recurrence rate. The treatment of the Gorlin Goltz syndrome follows the generally accepted rules for the treatment of basal cell carcinomas and keratocyts in other patients. The accepted treatment modality for OKC with Gorlin Goltz syndrome can be categorised into 5 types- (i)Decompression or marsupialization for OKC of large size (ii)Enucleation of OKC followed by mechanical curettage (iii)Enucleation followed by chemical cauterisation with Carnoy's solution (v)Enucleation of cyst followed by liquid nitrogen cryotherapy (v). Block resection with or without preservation of jaw.[16] Voorsmit et al have demonstrated that Carnoy's solution penetrates the bone to a depth of 1.54 mm following a 5 min application without any damage to the inferior alveolar nerve.[17]

Carnoy's solution is composed of 3 ml of chloroform, 6 ml of absolute ethanol, 1 ml of glacial acetic acid, and 1 g of ferric chloride. It is usually in conjunction with surgery to prevent recurrence rates after enucleation of cysts. It promotes chemical necrosis of up to 1.5 mm. It is useful in cases where the cyst is adjacent to the neuro-vascular bundle or the lesion is abutting soft tissue. Moreover, as OKC is associated with satellite and daughter cysts, Carnoy's solution is effective in eliminating these small cysts. Although some paraesthesia is noted by the application of Carnoy's solution, however, it is temporary.[18,19]

Small unilocular cysts are enucleated, whereas in larger cysts, marsupialization followed by enucleation is advised. The percentage of postoperative recurrences with this method of treatment is significantly lower, as demonstrated by Chinese authors in a large group of patients. According to our limited experience, we have noticed marsupialization helps reduce the size of lesions, thus preventing the morbidity associated with surgery if treated without marsupialization. Radiation should be avoided, as it may trigger the development of other tumours in the adjacent skin area. In the treatment of the recurrent OKCs which are associated with NBCCS, the overlying surface epithelium should be excised along with the cystic lining to prevent recurrences from the residual epithelial islands and microcysts.[20]

Consideration is given to en-bloc resection of odontogenic-keratocysts in the following situations: (i) When cysts recur despite previous enucleation with an adjunctive procedure. (ii) When cysts recur despite previous marsupialization and enucleation with an adjunctive procedure. (3) in cases of multilocular (multilobular) aggressive intraosseous cysts. (4) In cases of multiple non-syndromic and syndromic cysts (5) Cysts exhibiting aggressive clinical behaviour that should require resection as the initial surgical treatment. In children, conservative management is considered, because an aggressive operation can affect tooth eruption and development of the involved jaws.[21]

Although benign, the recurrence rate after excision is high 12-62% and multiple recurrences do occur. Due to the recurrences of OKCs, ja deformities may result from multiple surgeries. An annual orthopantogram radiograph is usually suggested between the ages of 8 and 40 years to help monitor the recurrence or development of new

OKC. [22,23]A recurring cyst can be a new cyst that originates from epithelial residue or a microcyst left behind in the overlying mucosa. The aggressive behaviour and high rate of recurrence of OKC are believed to be due to a higher rate of proliferation of the epithelial lining.

CONCLUSION

Gorlin-Goltz syndrome is a well-known Autosomal Dominant disorder. The incidence reported worldwide ranges from 1 in 50,000 to 1 in 150,000. Not many cases have been reported in India, and hence we report here a rare case of Gorlin Goltz syndrome. Thorough extraoral and intraoral examinations along with OPG, CT scan (skull) and chest radiographs help in proper diagnosis of the condition. This investigation prompts an early verification of the disease, which is very important to prevent recurrence and better survival rates from the existing diseases. OKC of the jaws which can cause disfigurement of the face, mobility and even loss of teeth can be avoided by early detection and treatment of the same.

Our case highlights the importance of awareness of this rare syndrome, especially in young patients with skin lesions. It is useful to keep in mind the existence of this syndrome and to recognize the presence of some**.**

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