CASE REPORT

SURGEONS PERSPECTIVE OF GORLIN GOLTZ SYNDROME -CLINICAL STUDY

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Abstract

Gorlin-Goltz syndrome or nevoid basal cell carcinoma syndrome is a rare hereditary autosomal-dominant disorder characterized by multiple basal cell carcinomas in young patients, keratocystic odontogenic tumours, calcification of the falx cerebri and skeletal malformations. This syndrome is associated with PTCH1 mutation (patched homolog 1 in Drosophila), a tumor suppressor gene. We in our department of OMFS did a clinical study on 5 cases who had all clinical features of Gorlin- Goltz syndrome without an affected first degree relative without basal cell carcinomas, but presented with a plethora of skeletal and CNS anomalies and found the surgical management is very much influenced by other clinical features of the syndrome. Multiple odontogenic keratocysts (KCOTs) are a major feature of nevoid basal cell carcinoma syndrome (NBCCS).1 They are frequently compared with basal cell carcinomas (BCCs), particularly in those case series derived from global communities that are not of European origin. It has been suggested that syndromic patients with darker skin are less susceptible to BCCs.

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INTRODUCTION

Gorlin-Goltz syndrome or nevoid basal cell carcinoma syndrome is a rare hereditary autosomal-dominant disorder characterized by multiple basal cell carcinomas in young patients, keratocystic odontogenic tumours, calcification of the falx cerebri and skeletal malformations. This syndrome is associated with PTCH1 mutation (patched homolog 1 in Drosophila), a tumor suppressor gene.

We in our department of OMFS did a clinical study on 5 cases who had all clinical features of Gorlin- Goltz syndrome without an affected first degree relative without basal cell carcinomas, but presented with a plethora of skeletal and CNS anomalies and found the surgical management is very much influenced by other clinical features of the syndrome.

Multiple odontogenic keratocysts (KCOTs) are a major feature of nevoid basal cell carcinoma syndrome (NBCCS).[1] They are frequently compared with basal cell carcinomas (BCCs), particularly in those case series derived from global communities that are not of European origin. It has been suggested that syndromic patients with darker skin are less susceptible to BCCs.

The main characteristic features of NBCCS are multiple OKC (75%), BCC (50-97%), bifid ribs (40%), Palmar and Planter pits (60-90%) and ectopic calcification of falx cerebri (37-79%) [2]

CASE REPORT 1

A 35 years old female patient presented with the chief complaint of pus discharge from the right lower border mandible for a period of 10 days which started as a small swelling developing into a fluctuant swelling and ultimately draining as a sinus which was treated with an empirical antibiotic therapy targeting the anaerobic and aerobic pathogenic oral microflora. on examination the patient had coarse facial features of frontal bossing, hypertelorism, prognathic mandible, meeting eyebrows, mild heterochromia of the eyes. Intraorally a diffuse swelling extending from the symphysis to the right angle region was evident obliterating the vestibular space. when the hands were examined the palmar pits could be demonstrated on both hands.

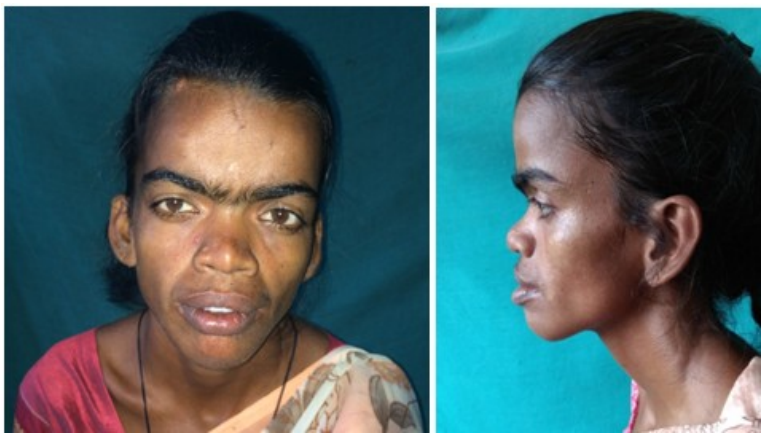

Figure 1: Patient 1-Hypertelorism,frontal bossing and prognathic mandible

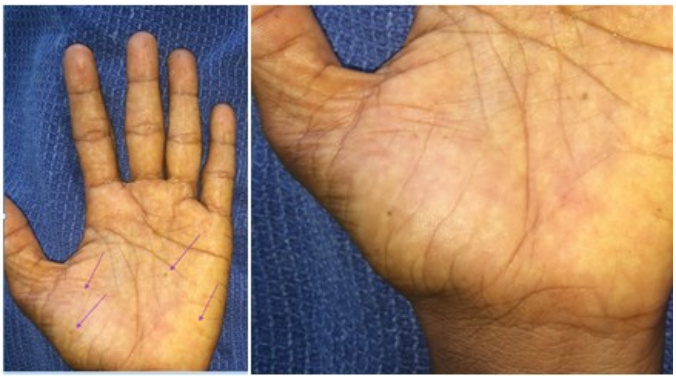

Figure 2: Palmar Pits

CT facial bones and Orthopantomogram revealed multiple lesions involving the mandible with an anteroposterior pattern with minimal cortical expansion, thinning of buccal and lingual cortices and few areas of cortical breaching. 2 separate lesions were present at the left parasymphysis and the right half of mandible obliterating the inferior alveolar nerve on the right side.

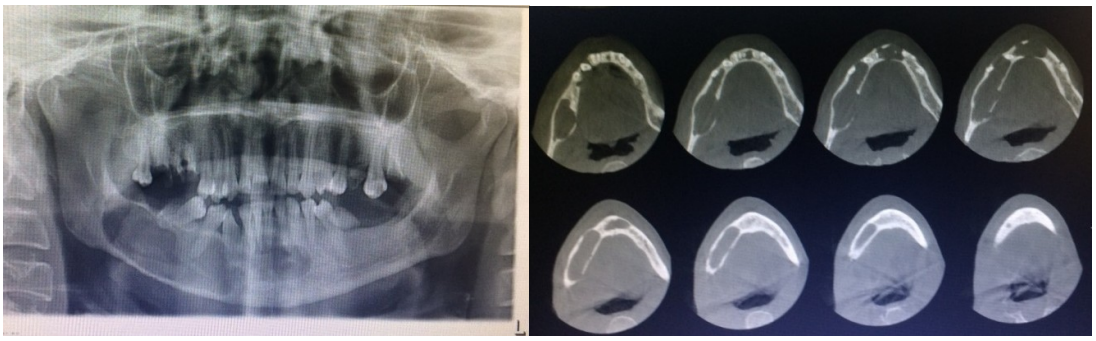

Figure 3: OPG AND CT

Considering the coarse facial features, multiple cysts in the mandible and palmar plantar pits to rule out the CNS features and to arrive at a diagnosis of Gorlin-Goltz syndrome the CT brain was taken. Some of the rare findings of this syndrome could be seen in the CNS in CASE 1. In addition to the calcification of falx cerebri , the communicating hydrocephalus, arachnoid cyst, choroid plexus calcification, spotted meningeal calcification was seen in the CT brain. The patient did not have any focal neurological deficit. An incisional biopsy specimen proved to be an odontogenic keratocyst and it was diagnosed to be a case of gorlin-goltz syndrome. The chest x-ray showed to have bifid ribs and scoliosis of the thoracic vertebrae

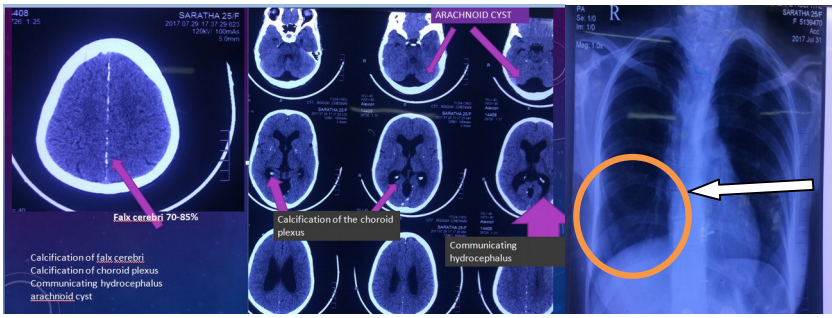

Figure 4: CT BRAIN & CHEST XRAY- bifid ribs & scoliosis

With all the critical neurological findings neurophysicians and neurosurgeons opinion was sought and a high risk consent for surgery was obtained from the patient for surgical enucleation ,peripheral osteotomy and chemical cauterisation with carnoy's solution .The neurological findings deemed the surgical procedure to increase the complications related to increased intracranial pressure (ICP) and epileptic episodes during the surgical procedure and phenytoin was prescribed to the patient as directed by the neurosurgeon. The patient did not need a ventricular shunting as ICP was normal and the patient did not have any focal neurological deficit.

The surgery was anticipated to cause a pathologic fracture of the right body of the mandible as the lesion was extensive with cortical breaching .there was sufficient bone buttressing the lower border of mandible so a reconstruction plate was avoided in this case. after the enucleation the inferior alveolar artery on the right side had pulsatile spurts of profuse bleeding was encountered which was difficult to control. The artery was later cauterised and bone wax was placed to arrest the bleeding from the cancellous bone. There were multiple areas of cortical breaching which were meticulously curetted, osteotomized and chemically cauterised with excision of the overlying mucosa as advocated by Stoelinga.[4]

The protocol followed i.e. excision of the overlying, attached mucosa and treatment of the bony defect with Carnoy's solution, aims at the elimination of two possible causes for recurrences. First, epithelial rests from the cyst wall may be left behind. This is particularly the case with larger cysts, which are located in anatomically difficult to reach areas. [3] Carnoy's solution is supposed to eliminate these cells. Secondly, clusters of epithelial islands and microcysts are consistently found in a large group of cysts in the overlying mucosa, attached to the cyst through a bony perforation.[4]

The pathophysiology of the bone at the surgical site showed distinct characteristics of absence of cancellous bone, bleeding from vessels which could not be identified to be inferior alveolar vessel ,the inferior alveolar nerve could not be identified to isolate from the application of carnoy's solution for chemical cauterisation and resorption of the bone made the surgery technique sensitive to carefully enucleate the cyst lining ,address the areas of cortical breach to prevent recurrence from satellite cysts and to maintain the osseous integrity to prevent the pathological fracture without a rigid fixation.

However, During the postoperative period, there was exposure of the surgical site which was managed by resuturing and iodoform packing, which healed over a period of 2 weeks.

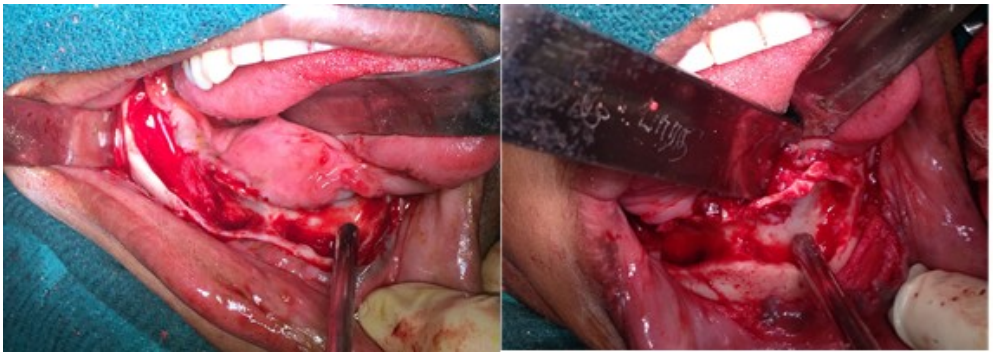

Figure 5:Mmucosal excision in areas of cortical breach

CASE REPORT 2:

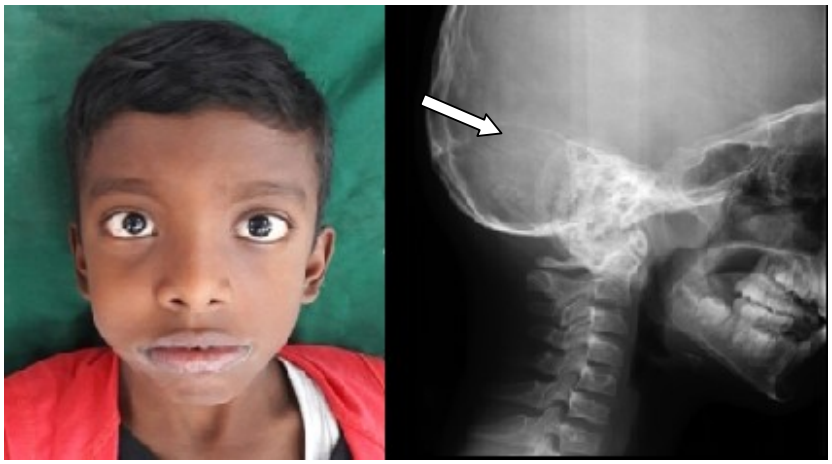

Figure 6:Patient 2-hypertelorism,meeting eyebrows & lateral cephalogram showing bridging sella turcica

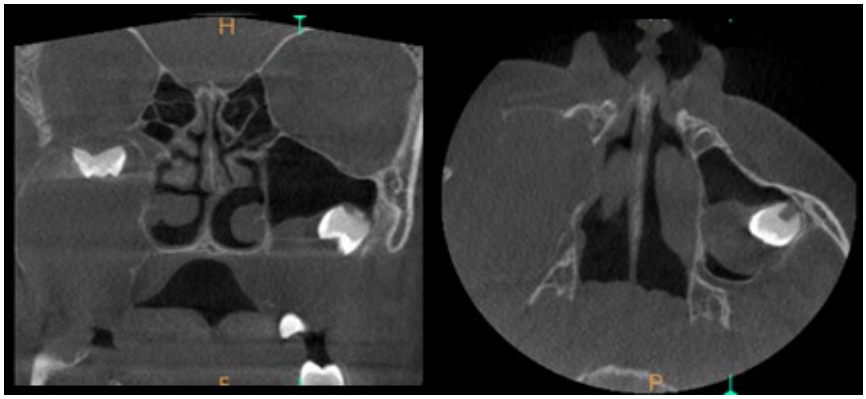

Figure 7:CBCT images showing multiple odontogenic keratocyst in the maxilla and the mandible

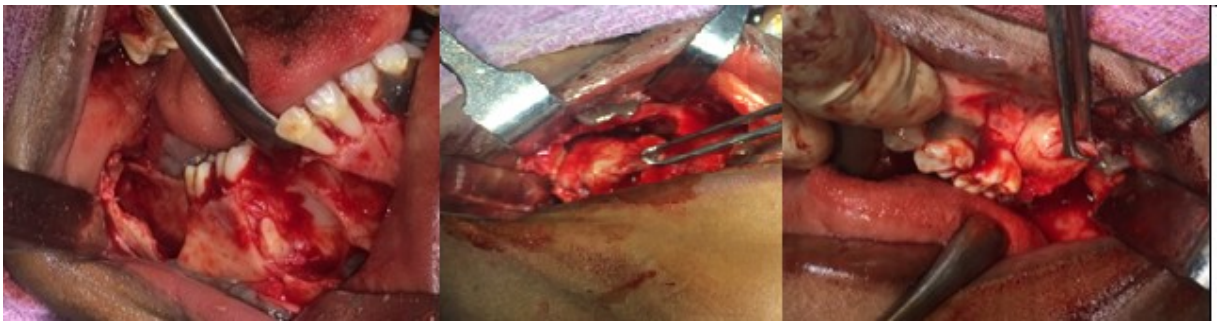

Figure 8: Surgical enucleation

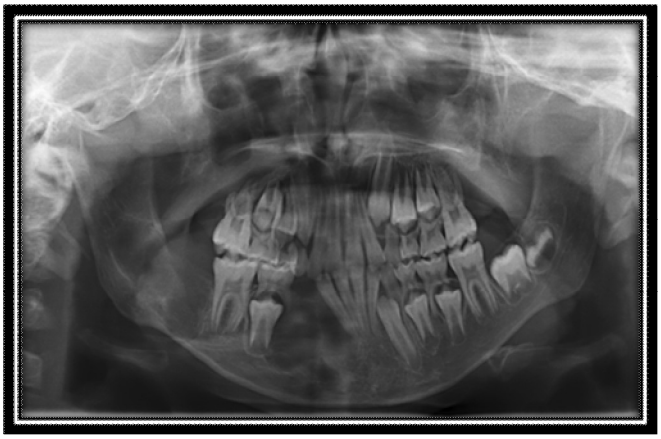

Figure 9: 6th month post operative OPG

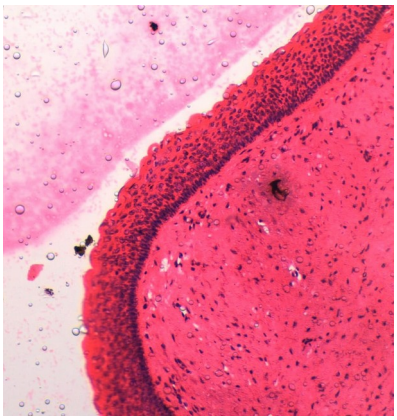

Figure 10: Histopathology suggestive of Odontogenic keratocyst

A total of 5 cases of Gorlin Goltz syndrome were treated for multiple odontogenic keratocysts of the jaws. And the observations are listed in **Table 1**

CLINICAL FEATURE / PATIENT	Multiple OKC	Falx cerebri calcification	Bcc	Palmar plantar pits	Bifid ribs	Hypertelorism	Meeting eyebrows	CNS calcification	Other vertebral anomalies
1.	+	+	-	+	+	+	+	+	+
2.	+	+	-	+	+	+	+	+	+
3.	+	+	-	+	+	+	-	+	_
4.	+	+	-	+	+	+	_	+	_
5.	+	+	-	+	-	+	+	+	+

UNCOMMON CLINICAL FINDINGS IN STUDY

Congenital hydrocephalus is a common finding gorlin goltz syndrome but Gorlin and Sedanol [3] finally de-emphasized the significant association in 1971. communicating hydrocephalus involving the 4 ventricles is a rare clinical finding presented in the case 1 along with multicentric choroid plexus calcifications, arachnoid cyst along the occipital lobe . The presented case did not have focal neurological deficit and had normal milestones of development. The other cases had bridging sella. None of the studied subjects in this case series have basal cell carcinoma.

FOLLOW UP

All the cases were followed up over a period of 2 years and among 5 no recurrence was reported. 2 cases had delayed healing in the areas of mucosal excision around cortical breached area was managed by iodoform packing and healing by secondary intention.

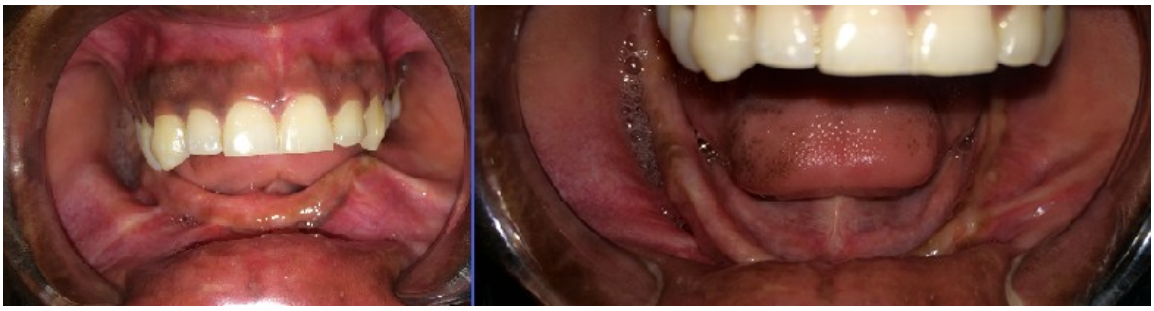

Figure 11: 1 year follow up case 1

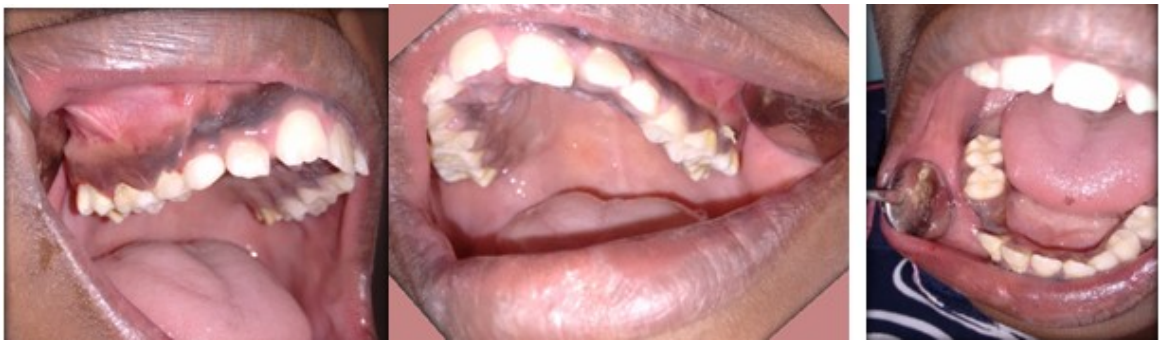

Figure 12- one year follow-up case 2

DISCUSSION

The Gorlin-Goltz syndrome is an autosomal dominant inherited syndrome manifested by multiple defects involving the skin, nervous system, eyes, endocrine system, and bones. It is also known as basal cell nevus syndrome, multiple basal cell carcinoma syndrome, Gorlin syndrome, or multiple nevoid basal cell epethelioma-jaw cysts or bifid rib syndrome.

Clinically this condition is characterized by different signs and symptoms. Diagnosis is based on the most frequent and specific features of the syndrome as given by Evans *et al* in 1993.[5] Diagnosis of Gorlin-Goltz syndrome can be established when two major or one major and two minor criterias are present.

Less than 10% of the patients with multiple OKCs have other manifestations of this syndrome. It has therefore been suggested that multiple OKCs alone may be confirmatory of the syndrome. [6] Our case series presented with multiple cystic lesions involving the mandible and maxilla, which were histopathologically proven to be an odontogenic keratocyst. Ahn SG, Lim YS et al [6] in their study have shown 90% of the patients had odontogenic keratocysts and only 15 percent of the patient had nevoid basal cell carcinoma. our study was consistent with the finding in the south Indian cases with 100% of the patients in our study having multiple odontogenic keratocysts leading to our diagnosis of gorlin goltz syndrome. MacDonald DS [7] in a systematic review of 251 east Asian patients and 406 north European patients have shown that 90% of the east Asian and 70% of the north European patients had odontogenic keratocysts of the jaws and 31 percent of the east Asian patients and 71% of the north European patients had a basal cells carcinoma. There are various other literature reviews showing a similar result of lower incidence of basal cell carcinoma in the African and Asian population which makes the name nevoid basal cell carcinoma syndrome for gorlin goltz syndrome as a misnomer on the basis of ethinic segregation of clinical findings. And the same review by macdonald[7] showed the predilection for BCC was for the north European population. In all the studies reported, the consistent findings are the odontogenic keratocysts and palmar plantar pits which are seen in either of the population so an appropriate name with the common clinical finding should be assigned to the syndrome. The OKCs can be the first features of the syndrome and usually during the first decade of life. [9,10,11]

Multiple odontogenic keratocysts pose great challenge to an oral and maxillofacial surgeon from preventing disfiguring facial surgeries keeping in mind the high recurrence rates of such cysts. Enucleation, peripheral ostectomy and carnoy's application have given promising results in maintaining the osseous integrity. The thin cortical plates seen in such cysts after enucleation may cause the pathologic fractures so a rigid osteosynthesis should always be considered when treating patients with lesions involving the mandibular corpus. The technique of advocated by stoelinga[4,9] has been a phenomenal concept in treating areas of cortical breaching, which were previously treated with carnoys alone, to prevent recurrence. our cases did not have any recurrence in the period of review

The associated neurological findings like the hycdrocephalus and ventricular cysts in a symptomatic patients should be considered as high risk for general anaesthesia and our cases were operated under ASA III. So suitable measures and choice of anesthetic agents should be considered before treating patients of this syndrome as they represent as a multisystem disorder and pose multiple risks unrelated to oral and maxillofacial surgery.

CONCLUSION

The pathological bone at the surgical site showed distinct clinical features compared to nonsyndromic patients like communicating cysts with thin bone cortices separating them, the neuro-vascular bundle around the pathological tissues were significantly deformed and could not be delineated anatomically which made the surgical procedure technique sensitive.These patients present with a plethora of neurological features like communicating hydrocephalus pose a higher risk to the patient and the operating surgeon when preoperative assessment and informed consent for the surgical procedure is not obtained Another aspect of the study was that the nutritional supplementation and the postoperative care required extra attention. In the postoperative period we encountered delayed but uneventful healing.

The ethinicity of the study population plays a major role in the population studied and diagnosed .the prevalence of the disease varies in accordance with the ethnicity making the nomenclature of the syndrome questionable and should be considered as a basis for a more appropriate designation in defining the syndrome with a more common clinical feature which is the odontogenic keratocyst seen universally and first to be identified as a pathology [10] [11] irrespective of the ethnicity. The present study of 5 cases proves the same.The manifestations in the central nervous system like the hydrocephalus, arachnoid cysts, medulloblastoma, should be assessed for better surgical outcomes when treating a totally different entity like the odontogenic keratocyst or an ovarian fibroma.

In our surgical experience the excision of the overlying mucosa associated with the cortical breach by the odontogenic keratocyst [4,9] has proved to be a fundamental concept to prevent recurrence. However multicentre studies with bigger sample number may be required to substantiate the concept.

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