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ARE WE IGNORING THE IMPORTANCE OF GENETICS AND FAMILIAL HISTORY IN THE EARLY DIAGNOSIS AND TREATMENT OF ODONTOGENIC KERATOCYST? - A CASE SERIES.

Dental Science

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ABSTRACT

Odontogenic Keratocyst(OKC) is a developmental cyst which is well known for its aggressiveness and high incidence of recurrence. It possesses a unique challenge to the clinician in identifying and managing it. Importance was given for its invasiveness, recurrence and different treatment modalities but not for its potential to inherit in the family. This paper presents a series of 3 cases belonging to same family diagnosed with OKC and impact of familial history and genetic counselling on early diagnosis and treatment planning.

KEYWORDS

Odontogenic Keratocyst, Okc, Genetic Counselling, Gorlin-Goltz Syndrome, NBCCS, Keratocystic Odontogenic Tumor

INTRODUCTION

"An ounce of prevention is worth a pound of cure".

Odontogenic Keratocyst(OKC) is a developmental cyst which arises from the cell rests of dental lamina. It is well known for its aggressiveness and high incidence of recurrence. Despite of many classifications and nomenclature, clinicians are still facing difficulty in understanding its nature[1]. Thus it is considered to be an inexplicable cyst which deserves special attention. Early diagnosis and treatment of OKC prevents the destruction to the maxillofacial skeleton caused due to its aggressive behaviour[2]. Philipsen was the first one to coin the term OKC in 1956. Its typical features were described by Pindborg and Hansen in 1963[1]. Many efforts have been made to classify this cyst since 1876 to 2017 finally. Mikulicz in the year 1876 was the foremost to describe it as a familial condition affecting the jaws, later importance was given for its invasiveness, recurrence and different treatment modalities but not for its potential to inherit in the family. Here we discuss a series of three cases of OKC within the same family and the impact of early diagnosis.

CASE REPORT 1:

A 32 year female patient reported to department of oral and maxillofacial surgery in August 2011 with a complaint of swelling over the lower right back tooth region since 1 month. The swelling was initially smaller and gradually increasing in size. The patient's past medical or family history did not signify any relevance. On clinical examination patient had an obvious facial deformity over the right side of the face. Frontal bossing and mild hypertelorism was noted. Intraoral examination revealed diffused swelling the right mandibular region with mild buccal vestibular obliteration over w.r.t 46 to 48 teeth. On Palpation egg crackling was elicited over the buccal and lingual cortical plates. shell Based on the clinical findings it was provisionally diagnosed as odontogenic Keratocyst. Radiographic examination revealed a multilocular radiolucent lesion extending anterio-posteriorly from 46 to the ramus of the mandible. FNAC and histopathology suggestive of odontogenic Keratocyst. Under general anesthesia segmental resection of the mandible sparing the condyle was done and defect was reconstructed using a 2.5 mm stainless steel recon plate. The gross examination and histopathology of the specimen was reported as OKC. Following surgery patient was kept under follow-up every 6 months and genetic counselling was given.

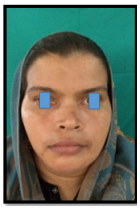

Figure 1 Post operative followup case 1

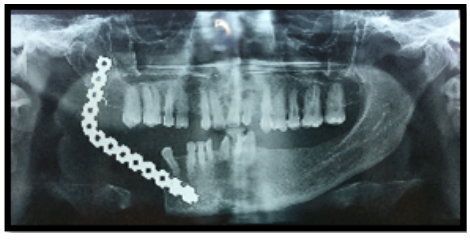

Figure 2 Post operative OPG showing resected mandible which is reconstructed with a reconstruction plate and no recurrence.

CASE REPORT 2:

A 10-year-old boy who is son of the 1st case presented to our department in march 2015 with the complaint of swelling over the anterior mandible since one month. There were no associated symptoms like pain, paraesthesia or discharge into the mouth. On recording the medical history, the patient had difficulty in concentrating and low IQ. On extra oral examination patient had frontal bossing, mild hypertelorism and widened nasal bridge along with an obvious swelling in the lower anterior region with the obliteration of the mento-labial sulcus. On intraoral examination there was an obliteration of buccal and labial vestibule extending from 75 to 85. On palpation egg shell crackling was elicited on buccal cortical plate whereas the lingual cortical plate was found to be intact. Based on clinical findings a provisional diagnosis of odontogenic Keratocyst was arrived upon. Orthopanthomograph was advised which revealed a unilocular radiolucent lesion extending anterioposteriorly from 75 to 46 crossing the midline with thinning of the inferior border of the mandible. Multiple tooth buds are seen floating and displaced within the radiolucency. Inferior alveolar canal is not evident, possibility of displacement to the lower border of the mandible.

FNAC and incisional biopsy was performed and the histopathology confirmed Odontogenic Keratocyst. Taking into account the extent of the lesion and the patient factors such as age, low IQ and possible non-cooperation from the patient, enucleation with peripheral ostectomy and chemical cauterization of the lesion was done under general anaesthesia.

Based on the clinical radiological and histopathological findings a final diagnosis was given as odontogenic Keratocyst and suspected association with Gorlin-Goltz syndrome hence the patient is kept und er long term follow up.

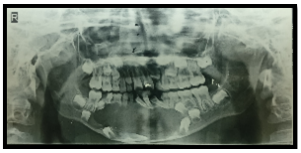

Figure 3Pre operative OPG CASE 2 showing cystic lesion extending anterioposteriorly crossing the midline in the lower border of mandible

Three years later during follow-up, radiographic examination revealed bilateral impacted maxillary canines with a well defined cystic radiololucency irt 23 and increased follicular space irt 13. Patient was asymptomatic but on clinical examination patient had mild tenderness in 23 region over the buccal vestibule. on FNAC cheesy white fluid was obtained. Considering the previous history, clinical and radiographic findings diagnosis of OKC was made and Under general anesthesia enucleation followed by peripheral ostectomy with chemical cauterization was done. The histopathological report suggested as odontogenic Keratocyst. Patient was kept under observation.

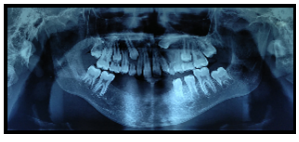

Figure 4 Post operative follow-up OPG case 2 showing OKC associated with impacted maxillary canines

CASE REPORT 3:

An 18-Year-old male, nephew of 1st case (sister's son) reported with the chief complaint of swelling over the left middle third of the face since five weeks which was associated with mild tenderness and paresthesia over the lower eyelid and cheek. on extra oral examination patient had hypertelorism and diffuse swelling was present over the left middle third of face with obliteration of the left nasolabial fold. on palpation it was hard in consistency. On intra oral examination retained 63 and missing 23 was noted with obliteration of the left buccal vestibule extending from mesial aspect of 22 to distal aspect of 26.it was soft in consistency and tender on palpation. 11,21,22, 63 , 24,25,26 & 27 were non vital. On FNAC cheesy white fluid was obtained. CBCT revealed well defined homogenous radiolucency associated with the impacted 23 was noted measuring 4*3 cms, extending from 11 to 27 with loss of buccal cortical plate and extreme thinning of the palatal cortical plate. Based on the results of FNAC and CBCT scan a provisional diagnosis of odontogenic Keratocyst and dentigerous cyst was given. Endodontic restoration was done irt 11 to 27. Enucleation of the cyst followed by peripheral ostectomy and chemical cauterization was done. The histopathology conformed as OKC. Patient was advised for long term follow up.

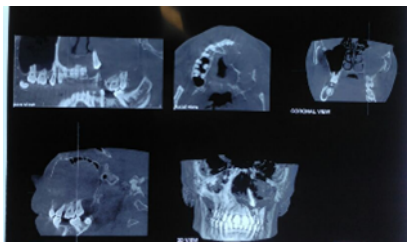

Figure 5 Pre operative CBCT Showing the extent of the lesion

Figure 6 Showing hypertelorism

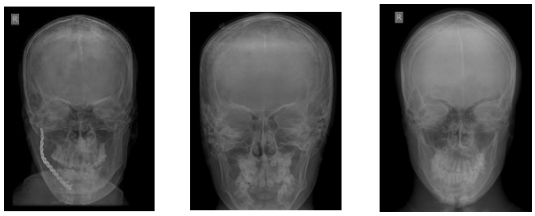

Figure 7 Radiographs showing calcification of flax ceribri

As these patients are suspected to be associated with Gorlin-Goltz syndrome further investigations which included chest x-rays, lateral ceph and PA views were taken to rule out bifid ribs, bridging of the sella tursica and calcification of the falx cerebri respectively. All the three showed falx cerebri calcification. Case 3 showed bridging of sella tursica.

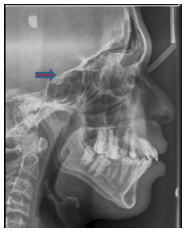

Figure 8 Bridging of sella tursica in case 3

DISCUSSION

Odontogenic Keratocyst (OKC) have been the bone of contention for many a studies and researches[3,4,7]. The aggressive clinical nature coupled with unnaturally high recurrence rate for a cyst made many authors question this lesions' place among odontogenic cysts. Taking this into consideration in 2005 WHO proposed the name Keratocystic odontogenic tumor (KCOT).

However, as most cases of KCOT behave as a non-neoplastic lesions, in 2017 WHO in its 4th edition reclassified it under cysts as OKC until there is more evidence to label it as a tumor.

Available literature on the treatment modalities and prognosis have been reviewed[3,5,7] by various authors. The most common treatment is enucleation followed by an adjunctive treatment like the application of carnoy's solution will effectively reduce the recurrence rate anywhere between 1 % and 8.7%. Resection which is also an alternative has a reported recurrence rate of 0%[5]. This is an aggressive modality and may not be used in all the clinical situations.

In the reported cases 2 and 3 we did a radical enucleation followed by peripheral ostectomy as well as application of the Carnoy's solution for 2 minutes in the bony cavity. For case 1 we had done segmental resection of the mandible as the lesion was extensive. The aggressive treatment approaches were warranted in these cases as it was reported that conservative treatments would result in a higher recurrence rate in patients suspected of Gorlin-Goltz syndrome[7].

Gorlin- Goltz syndrome has an autosomal dominant inheritance with variable expressivity. About 35 % - 50% represent new mutations. The mutation in tumour suppressor gene PCTH 1 which modifies the Hedgehog signalling pathway causes the various symptoms of this syndrome. This gene is muted not only in this syndrome but also in sporadic basal cell carcinoma[6]. The diagnostic criteria of the Gorlin-Goltz syndrome is said to be based on the presence of two major or one major and two minor criteria. The major and minor criteria are as follows[8]

Major Criteria	Minor Criteria
1. More than 2 BCCs or one under the age of 20	Macrocephaly adjusted for height
2. Odontogenic keratocyst	Frontal bossing, cleft lip/palate, hypertelorism
3. Three or more palmar pits	Sprengel deformity, pectus, syndactyly of digits
4. Bilamellar calcifications of falx cerebri	Bridging of sella tursica, hemivertebrae, flame shaped radiolucencies
5. Bifid, fused or splayed ribs	Ovarian fibroma

This may not be a representative set of criteria because as mentioned earlier the mutation has variable expressivity. In the cases we treated the case 1, other than the KCOT had frontal bossing, strabismus and mild hypertelorism. While case 2 had mild hypertelorism , high arched palate, prognathism, low pitched voice and low IQ and in case 3 hypertelorism, low pitched voice was present.

In a review and case series of NBCCS in Indian patients[9] it was found that the symptoms exhibited by the patients differ from other ethnic groups. There are no reported cases of basal cell carcinoma in association with NBCCS in India. This may be due to the predominant skin type of Indians. In whites, basal cell carcinoma is reported in 100% of the cases while only 38% of the black patients and 30% of Italian patients manifest BCCs, probably owing to the protective skin pigmentation[9,10].

In the management of a suspected case of Gorlin-Goltz syndrome priority should be given to identifying the specific anomalies among the plethora of features attributed to this syndrome. A complete physical examination complimented with various radiographs. An orthopantomography, a frontal-back thorax radiography and a craniofacial CT must be taken in order to detect osseous morphology aspects that cannot be seen in simple radiographies, and also a MR of the cranium and pelvic ultrasonographies in women[10]. A thorough family history also should be taken. Genetic counselling is also warranted for the patient and his/her first relatives for helping them understand and adapt to the medical, psychological, familial associations and genetic influences of the disease[13]. In our case series, case 1 received genetic counselling by the treating doctor as she is a mother of three children and strongly associated with Gorlin-Goltz syndrome, this helped her to recognise and report case 2 and case 3 for further investigations and were treated successfully. The patients have to be kept under regular follow up and they have to undergo a check-up at least every six months in a growing child and at least once a year in adult. In our series of cases the follow-up prevented extensive progression of OKC in case 2 as it was identified and treated early.

CONCLUSION

Gorlin-Goltz syndrome and Odontogenic Keratocyst is an exceptional in the variable phenotypes expressed. This possesses a unique challenge to the clinician in identifying and managing the various symptoms. More emphasis should be given to diagnosis via genetic counselling since the genetic basis of the syndrome and the cyst is established. The genetic defect may predispose the individual to various disorders in the body which occurs only with the right stimulus. Identifying these factors and preventing the exposure by consistent follow-up would be the first step in managing a patient with Gorlin-Goltz syndrome and non- syndromic OKC.

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