Case Report

Non-Syndromic Recurrent Multiple Odontogenic Keratocysts: A Case Report

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Abstract:

Odontogenic keratocysts (OKCs) are one of the most frequent features of nevoid basal cell carcinoma syndrome (NBS). It is linked with mutation in the PTCH gene. Partial expression of the gene may result in occurrence of only multiple recurring OKC. Our patient presented with nine cysts with multiple recurrences over a period of 11 years without any other manifestation of the syndrome.

Key Words: Odontogenic Cysts; Basal Cell Nevus Syndrome; Pathology, Surgical, Jaw Cysts

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INTRODUCTION

Nevoid basal cell carcinoma syndrome (NBS) is associated with a triad of multiple basal nevi, multiple odontogenic keratocysts (OKCs) and skeletal abnormalities [1]. These triad of symptoms may be associated with other manifestations involving skeletal, craniofacial, neurological, skin, sexual, ophthalmic and cardiac anomalies [2]. Multiple OKCs have been known to occur in non-syndromic cases though it is very rare [3]. These multiple lesions may be the first manifestation of the NBS or otherwise it may be because of the multifocal nature of OKCs [4,5].

We present a case of recurrent multiple OKCs which is not associated with any syndrome. We emphasize here that the present case may be because of partial expression of the PTCH gene and long-term follow-up in such cases is mandatory. After a long follow-up, we could not see any recurrence. So probably the importance of this case is just due to the aberrant nature of OKCs rather than being associated with the syndrome.

CASE REPORT

A 20-year-old female, who is a dental student of our institution, reported to the department of oral and maxillofacial surgery with the chief complaint of discharge from the right maxillary posterior region for two years. The patient gave a history of multiple isolated jaw cysts at the age of nine years, all the cysts were enucleated and histopathologically diagnosed as OKCs. She also gave a history of jaw surgery three years before for OKC in association with maxillary right second molar (17) (Table 1).

Intra-oral examination revealed a mild ill-defined swelling in the right maxillary tuberosity region. There was also a spheroidal swelling measured approximately 1×1 cm in the mandibular left lateral incisor (32) region, mild cortical plate expansion was also seen in relation with the right mandibular lateral inci-

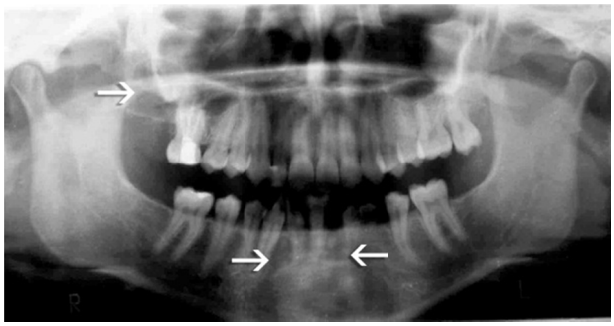

Fig 1. Radiolucencies (arrows) in the first, third and fourth quadrant.

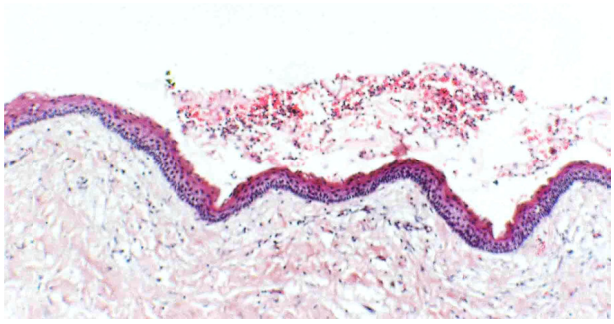

Fig 2. Cystic lining showing parakeratinized stratified squamous epithelium of uniform 6-8 cell thickness with surface corrugation.

sor (42) to the left mandibular central incisor (31) regions.

Radiographically, three separate radiolucencies were seen such as a well-defined 2.5×2.5 cm^2 radiolucency in the right maxillary tuberosity region, a well-defined radiolucency in the mandibular left central incisor (31) area and a well-defined radiolucency in between the roots of the right deciduous mandibular canine (73) and the right mandibular first premolar (44) measured approximately 1×1 cm^2 (Fig 1).

Based on the clinical and radiographic findings, a provisional diagnosis of recurrent OKCs was considered. Chest and skull radiograph findings were insignificant. Blood investigation values were in normal limits. Dermatology consultation did not reveal any cutaneous abnormality including palmar and plantar defects.

Table 1. Summary of patient's history for multiple recurring cysts.

Age	Cyst no.	Site	Findings			Recurrence	Follow-up
			Clinical	Radiography	at Surgery		
9 years	3	Right body of mandible	Painful swelling	Well-defined unilocular	Tooth attached to the outer surface of cyst. Necrotic material within the lumen	No	9 years
		Symphysis	Asymptomatic	Well-defined unilocular	Inner surface was smooth	After 9 years, (two separate lesions on either side of midline)	9 years
		Left ramus of mandible	Asymptomatic	Well-defined unilocular	Thin wall	No	9 years
17 years	1	Right maxillary posterior region	Aysmptomatic	Well-defined unilocular	Nothing significant	After 3 years	3 years
20 years	3	Right maxillary posterior region	Discharge (from the posterior maxilla and nasal disc)	Well-defined unilocular	Thin lining	No	3 years
		Right parasymphisis	Swelling	Well-defined (minimal cortical plate expansion)	Smooth and regular margin	No	3 years
		Left parasymphisis	Asymptomatic	Well-defined Unilocular	Nothing significant	No	3 years

no.= number

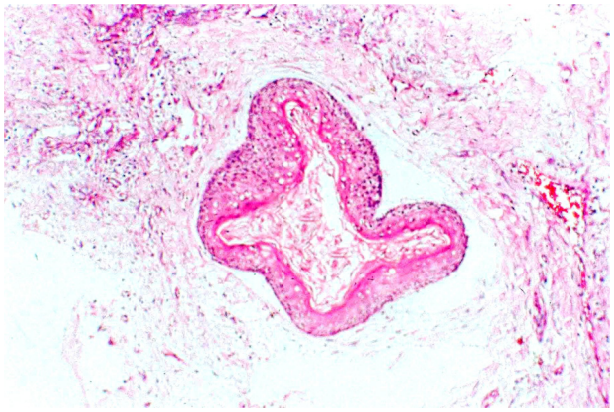

Fig 3. Daughter cyst in the cystic capsule.

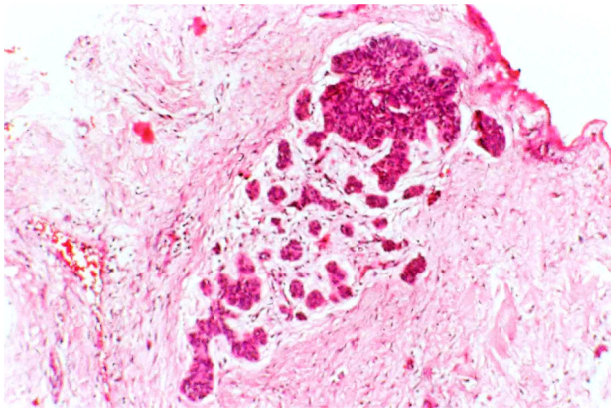

Fig 4. Odontogenic epithelial islands in cystic capsule.

Enucleation of all the three lesions was done separately along with curettage. The specimen from the right tuberosity region was approximately 2×2 cm^2 in size, creamish white in color and containing a yellowish cheesy material within the cystic space. The other two specimens were small roughly 0.5×0.5 cm^2 in size and creamish white in color.

Histopathologically, all the three specimens showed multiple cystic spaces filled with keratin flakes. These cystic spaces were lined by parakeratinized stratified squamous cystic epithelial lining of predominantly even thickness with palisaded basal cells and a corrugated surface (Fig 2).

The capsule was fibrous and occasional chronic inflammatory cells were evident. Daughter cyst (Fig 3) and odontogenic epithelial cells arranged in groups were seen in the stroma (Fig 4). The stroma also showed focal areas of calcifications. The final diagnosis of OKC was confirmed. The patient is being followed up regularly and there has been no evidence of recurrence in the last three years after the last treatment.

DISCUSSION

Multiple OKCs usually occur as a component of syndromes such as NBS, orofacial digital syndrome, Noonan syndrome, Ehler-Danlos syndrome and Simpson-Golabi-Behmel syndrome [3,6-8]. In a study by Brannon [9], 5.1% of 312 cases were associated with NBS and 5.8% were accompanied by multiple keratocysts, but without any other features of the syndrome. However, 8.1% of the total 83 cases were associated with NBS and 7.6% of them showed recurrence; none of these cases with multiple OKCs were non-syndromic in a study on the Iranian population [10].

The present case showed only multiple recurrent OKCs without any other notable deformities such as basal cell carcinoma, skeletal defects, orofacial defects, stunted growth, bleeding diathesis and hyperextensible skin and hypermobile joints.

NBS involves various skeletal, craniofacial, neurological, oro-pharyngeal, cutaneous, sexual, ophthalmic and cardiac anomalies [3]. In our patient, none of these features indicative of NBS was present.

NBS is associated with mutation in the PTCH gene [9q (22.3-q31)]. Mutation within PTCH occurs in sporadic OKCs as well as those associated with NBS. It is suggested that a "two-hit" mechanism may underlie the variable expression of NBS and sporadic OKCs. In NBS, the basal cell carcinomas and keratocysts arise as a consequence of a "first hit" of allelic loss of PTCH within the precursor cell. The development of basal cell carcinoma and keratocysts in the absence of NBS reflects two somatic hits in which there are mutations of PTCH within locally susceptible cells that ul-

timately result in allelic loss. The absence of all the manifestation of NBS may be due to variability of the PTCH gene expression as mentioned by Auluck et al [3].

The results of the study by Dominguez and Keszler [11] showed, NBS keratocysts were frequently associated with parakeratinization, intramural epithelial remnants and satellite cysts compared to that of solirary keratocysts. In the present case, cysts showed parakeratinisation, daughter cysts and intra-mural epithelial rests. Immunohistochemical expression of cytokeratin 17 and 19 are considered as better indicators of OKCs when it is distinguished from other odontogenic cysts such as dentigerous and radicular cyst [12] and also over expression of PCNA and Ki-67 proves its highly aggressive behavior and recurrence [13]. However, in the present case, diagnosis was not a problem as it showed characteristic histopathological features of OKC and its aggressive nature is a well-known fact. The correlation between the proliferative markers and its recurrence is still debated [14].

Recently, a similar case report of multiple non-syndromic OKC has been reported in a young adult in the maxillary canine and mandibular third molar region [15]. Multiple non-syndromic OKCs have been reported by Auluck et al [3]. However, there are no surgical details, proper follow up and recurrence details for these, as our case showed multiple recurrences in different regions of the jaws for a follow-up period of nearly 14 years. In addition to that, the case was histopathologically diagnosed as a dentigerous cyst once previously [3].

OKCs associated with NBS have higher recurrence rates compared to solitary OKCs. It is believed that the aggressive behavior and high rate of recurrence of OKCs associated with NBS is due to a higher rate of proliferation of the epithelial lining [2]. In the present case, the lesion has recurred in the symphysis and posterior maxillary region. No family history of OKCs was seen here as there were cases of multiple OKCs with familial history [16]. It is said that multiple OKCs seen in the early age may be considered as a first manifestation of NBS which was proposed by a study [4]. However, in the present case, there has been no recurrence in the last three years and no other sign of NBS syndrome is evident even after 14 years, first time the lesion appeared. Thus, this case may be because of the multifocal nature of OKCs rather than the NBS as discussed in a previous article [5].

The patient was followed regularly and after three years of treatment had no symptoms of recurrence of cysts and no other features associated with NBS was seen. It has been reported that multiple OKCs may occur a decade before other symptoms associated with NBS [17]. However, the present case never showed any other symptoms even after 14 years of follow-up after the appearance of these lesions for the first time.

CONCLUSION

This case shows multiple OKC with frequent recurrences without any other notable features which are indicative of Gorlin Goltz Syndrome. As such the occurrence of multiple recurrent OKC's may be the first and only manifestation of GGS indicating partial expression of the PTCH gene. Thus, it is imperative that patients having multiple OKC's should be screened for the presence of syndromes. However, multiple OKCs may occur without the syndrome and need not be because of gene defect and probably as a result of the multifocal nature of OKCs. Due to the high rate of recurrences associate with such cases, careful follow-up is mandatory.

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