Syndromic Odontogenic Keratocyst: A Rare Case Report With Review of Literature

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Type of Publication: Case Report

Conflicts of Interest: Nil

Abstract

Syndromic OKCs which is also known as Nevoid basal cell carcinoma syndrome (NBCCS) or Gorlin-Goltz syndrome is an infrequent multisystemic disorder with autosomal dominant mode of inheritance. Multiple odontogenic keratocyst (OKC) occur as one of the common findings of Syndromic OKC associated with other features like basal cell carcinoma, bifid ribs, ocular, skeletal and neurologic abnormalities. We hereby report a rare case of syndromic OKC in a 33 year - old male patient along with complete clinico-pathological details.

Key words: Nevoid basal cell carcinoma syndrome; bifid ribs; autosomal dominant.

Introduction

Odontogenic keratocysts (OKC) are developmental cysts that originate from remnants of dental lamina. They may occur in two different form- either as solitary (non syndromic OKC) or multiple OKCs (syndromic OKC). Nevoid basal cell carcinoma syndrome (NBCCS) also...
known as Gorlin-Goltz syndrome is an infrequent multisystemic disease that is inherited in an autosomal dominant way, which shows the high level of penetrance and variable expressibility.\textsuperscript{[1-3]} Sporadic cases may comprises of 60\% of all affected individuals. The estimated prevalence varies from 1/57000 to 1/2,56000, with a male to female ratio 1:1.\textsuperscript{[4]} Multiple OKCs usually manifest as one of the important findings in Gorlin-Goltz syndrome.

This syndrome has received several names throughout the times such as, Basal cell nevus syndrome, Multiple NBCCS, Multiple basal cell carcinoma syndrome, Multiple basalioma syndrome, Jaw cysts basal cell tumor skeletal anomalies syndrome, Odontogenic keratocysts skeletal anomalies syndrome and fifth phacomatosis.\textsuperscript{[5]} Jarish and White first reported this syndrome in the year 1894\textsuperscript{[6,7]} which was further illustrated by various researchers like Straith in 1939 where he found multiple basocellular carcinoma and cyst appeared together.\textsuperscript{[8]} Gross in 1953 presented a case, suggesting additional sign such as synostosis of first left ribs and bilateral bifurcation of 6\textsuperscript{th} ribs.\textsuperscript{[9]} In 1960 Gorlin- Goltz established a classical triad of basal cell carcinoma, odontogenic keratocysts and bifid ribs that characterizes the diagnosis of this syndrome. According to Rayner \textit{et al}, for giving the diagnosis of syndromic OKC atleast a cyst had to appear in combination with calcification of the falx cerebri or palmer and planter pits.\textsuperscript{[10-11]}

Gorlin-Goltz syndrome or Nevoad basal cell carcinoma syndrome is characterized by the presence of multiple number of OKCs, involving the jaws, frontal bossing, depressed nasal bridge, bifid ribs, ocular hypertelorism, prominent supraorbital ridges and mild mandibular prognathism. This clinical manifestation are catagorized into major and minor diagnostic criteria. Evans \textit{et al} and Kimonas \textit{et al} suggested that to diagnose a patient to have Gorlin-Goltz syndrome, two major or one major and two minor criteria should be present.\textsuperscript{[12]} According to different literature review this syndrome is predominantly seen in younger group ranging in between 10-30 years.

\begin{itemize}
  \item **Major Criteria**
  \begin{enumerate}
    \item Multiple BCCs or one under 20 years.
    \item Odontogenic keratocysts of the jaws proven by histopathology.
    \item Palmar or plantar pits (3 or more).
    \item Bilamellar calcification of the falx cerebri.
    \item Bifid, fused or markedly splayed ribs.
    \item First degree relatives with NBCCS.
  \end{enumerate}

  \item **Minor Criteria**
  \begin{enumerate}
    \item Macrocephaly determined after adjustment for height.
    \item Congenital malformation: cleft lip or palate, frontal bossing, “coarse face”, moderate of severe hypertelorism.
    \item Other skeletal abnormalities: sprengel deformity, marked pectus deformity, marked syndactyly of the digits.
    \item Radiological abnormalities: bridging of the sella turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modeling defects of the hands and feet, or flame-shaped lucencies of the hands or feet.
    \item Ovarian fibroma.
    \item Medulloblastoma.
  \end{enumerate}
\end{itemize}

Basal cell carcinoma are reported in 90\% of the patients at some stage in their life occasionally proliferate between puberty and 35 years of age. Only about 40\% African-Americans affected by NBCCS develop BCCs, while incidence was shown to be higher in whites approximately 90\%.\textsuperscript{[13]} Recurrent jaw cysts are the one of the important oral sign being present in the 90\% of patients.\textsuperscript{[14]} These cysts appear in the tooth bearing areas of jaws and being most consistent and representative sign of NBCCS in the first and second decades of life.
An abnormal skull configuration characterized by frontal bossing (25%), biparetial or temporal bossing, and large calvaria is frequent. About 70% of patients affected by NBCCS have ocular hypertelorism. Other skeletal signs are scoliosis (40%), and abnormalities such as bifid, wide, fused, partially missing or underdeveloped ribs (30–60%). Ectopic calcifications of the central nervous system have been reported: lamellar calcification of the falx cerebri (70–85%), calcification of the tentorium cerebella (20–40%), the petroclinoid ligament (20%) and the diaphragm sellae (60–80%), and complete or partial bony bridging of the sella turcica (25%) [14]. Cardiac and ovarian fibromas occur in approximately 2% and 20% of individuals respectively. Approximately 5% of children with NBCCS develop medulloblastoma (primitive neuroectodermal tumor [PNET]), generally the desmoplastic subtype. Peak incidence is at age 2 years. Life expectancy in NBCCS is not significantly different from average. Considering the rarity of this disease we present a case of NBCCS.

**Case Report**

A unique case of 33 year old male patient with Gorlin-Goltz syndrome has been discussed herewith brief clinical, radiological and histopathological features.

A 33 year old male patient of average built coming from semi urban area reported to the Department of Oral and Maxillofacial Pathology, GNIDSR, with the chief complain of swelling and purulent discharge at the anterior region of mandible since last three months. The swelling was initially smaller in size and gradually increased in size to attain the present dimension. His past medical history revealed that he was previously treated for the same swelling three years back when surgical intervention was done. But the complaint persisted even after 3 years. The patient did not reveal of any such similar swelling in his parents and siblings.

A thorough clinico-radiological examination was carried out. On clinical examination, extra oral swelling which was non-tender and hard in consistency. There was no sign of extra oral perforation. On physical examination, presence of dysmorphic facial features like relative macrocephaly, frontal bossing, depressed nasal bridge, mild ocular hypertelorism, prominent supra orbital ridge, and mild mandibular prognathism were observed.

![Fig1](image1) Extra-oral photograph showing frontal bossing, prominent supra orbital ridge, mild mandibular prognathism and mild ocular hypertelorism. Fig 1(d &e): Intra oral photograph showing crowding and malalignment of dentition.

On intraoral examination, presence of mild to moderate swelling involving lower anterior region of the jaw crossing the midline extending upto lower left second molar region. On palpation, swelling is hard in consistencey and non tender with no obvious pain or paresthesia present. Clinically there is no significant buccal or lingual cortical plate expansion. There was significant crowding of maxillary and mandibular dentition with very poor oral hygiene.
A radiographic examination was carried out that comprised of a panoramic and periapical films. Pre-operative orthopantomograph (OPG) revealed presence of a multilocular radiolucency extending from right parasymphyseal region of jaw crossing the midline to lower left posterior border of mandible extending upto the lower left second molar with significant thinning of inferior border of mandible.[Figure 1].Presence of bilateral impacted canine and molar in lower right jaw and impacted canine at upper left jaw was also evident. There was significant crowding of teeth in both the jaws and displacement of teeth without any root resorption adjacent to the lesion was observed. Considering the above clinical-radiological features, possibilities of some jaw cyst associated with syndrome was suspected. Further advanced diagnostic modalities like Computed Tomography (CT) scan of brain revealed ectopic calcification of falx cerebri and tenorium cerebri. Antero posterior view of the chest revealed splying of ribs or bifid ribs in relation to 8-9, 9-10, 10-11. CBCT of jaw revealed lytic changes of the body of mandible extending from left molar-ramus region upto the parasymphyseal region of right mandible crossing the midline with thinning of lower border of mandible.[Fig 3; Fig 4]

Routine blood investigations include complete blood count, serology, serum calcium, phosphorous and alkaline phosphatase were within normal limits. With the provisional diagnosis of multiple odontogenic cysts the patient was sent to Department of Oral and Maxillofacial Surgery where complete enucleation along with marsupilization of lesion was performed & the specimen was sent to Department of Oral & Maxillofacial Pathology for histopathological evaluation. Gross examination revealed multiple bits of soft tissue specimen and cystic lining, together measuring about 3.5cm×2.5cm×2 cm.

Histopathologically, Hematoxylin & Eosin stained section revealed the presence of a cystic lining that is thin, folded at places. The cystic lining appeared as parakeratinized stratified squamous epithelium backed by fibrovascular connective tissue stroma. The parakeratinized lining is uniform in thickness with strongly basophilic palisaded basal cell layer & relatively flat epithelio-mesenchymal junction. The stromal connective tissue showed scanty areas of inflammatory cell infiltrate and hemorrhagic areas at places. Based on histopathological findings a diagnosis of Odontogenic keratocyst in relation to lower jaw was made. After relating clinical, radiological and histopathological features a final diagnosis of Gorlin-Goltz syndrome was made. The patient had been on periodic follow up and planned for prosthetic rehabilitation.
Discussion

The Gorlin-Goltz syndrome or Nevoid basal cell carcinoma 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 hereditary cutaneomandibular polioncosis, multiple nevoid basal cell epithelioma-jaw cysts, or bifid rib syndrome. NBCCS was first described by Jarisch and White in 1894 and later established as a unique syndrome by Gorlin and Goltz in 1960.

Syndromic OKCs normally occurred in a age range 10-30 years of age. The case under discussion was a 33 year old male patient presenting with cyst involving the lower jaw extending from lower left second molar to lower right premolar region crossing the midline associated with bilateral impacted canines. Several studies have presented multiple OKCs, basal cell nevi and skeletal abnormalities as the principal clinical features of Gorlin-Goltz syndrome. Multiple OKC of mandible may have a close relationship with Gorlin-Goltz syndrome. [12]

Studies have shown that it has an incidence of 1 in 50000-1,50000 cases [13] Apart from Gorlin Goltz syndrome, multiple OKC may also seen in other syndromes such as Ehlar’s-Danlos syndrome and Noonan syndrome.

The lesion is inherited as an autosomal dominant pattern. A thorough review of literature about its pathogenesis revealed mutation of protein patched homolog (PTCH) gene which is mapped to 9q21-23 chromosomes. These genetic studies suggest that in this syndrome there is an abnormal hedgehog signaling pathway. According to Daramola et al chromosomal studies indicated that syndrome is familial, however, sporadic cases also do occur in syndromic OKCs.
In our present case, there was no family history of such syndrome among his parents and siblings, so we may consider it as a sporadic case. But further genetic counselling do require for entire family to rule out any abnormalities.

According to Rayner CR et al. NBCCS is essentially a clinical and radiological diagnosis. The diagnostic criteria for nevoid BCC was established by Evans et al. and modified by Kimonis et al. in 1973. According to them diagnosis of Gorlin-Goltz syndrome can be established when two major or one major and two minor are present.

The syndrome initially consisted of the triad of basal cell carcinoma, jaw cysts and skeletal anomalies. Basal cell carcinoma usually appears between puberty and 35 years of age. According to Goldstein AM et al. the incidence varies widely among ethnic groups, studies have shown that only about 40% of black patients affected by NBCCS manifest basal cell carcinoma, while in whites they are reported in up to 90% of cases. In our present case features of basal cell carcinoma is absent.

Jaw cysts are the second most constant features of syndromic OKCs and present about 50-75% cases. About 1/3 of the patient with NBCCS have only a solitary cyst at the time of initial presentation but most of cases additional cysts will develop over a period range of 1-20 years. According to Voorsmit et al. 1981 recurrent jaw cysts are the main oral sign, being present in 90% of patients. In our present case also revealed presence of multiple OKCs with history of recurrence after 3 years.

Histopathological features of syndromic OKCs are invariably similar to that of conventional OKCs. Woolgar et al. and Dominiguez et al. found significant differences between syndromic OKC and single keratocyst. Syndromic OKC were found to have a markedly increase in number of satellite cyst, solid islands of epithelial proliferation, odontogenic rests within the capsule and mitotic figures in the epithelial lining of the main cavity. Although histopathologically other features are similar to conventional OKCs but satellite cysts are not evident in our present case. According to Rai.s et al. (2007) parakeratotic odontogenic keratocysts is a part of syndromic OKCs with high recurrence rate ranging from 12%-62.5%.

Along with that, partially or completely impacted tooth which are also a features of syndromic OKCs were found in our case too.

In our case three major manifestations such as odontogenic keratocysts, bifid rib, ectopic calcifications of the falx cerebri were identified. Along with that six minor manifestations such as frontal bossing, ocular hypertelorism, macrocephaly, depressed nasal bridges prominent supraorbital ridges and mild mandibular prognathism were identified.

Considering all the features the case was established as OKC in relation to lower jaw and after assessing clinical, radiological features final diagnosis of Gorlin-Goltz syndrome was made.

**Conclusion**

The present case highlights a rare case of syndromic OKCs of a 33 year old male patient who was clinico-pathologically diagnosed as having OKCs with other skeletal and ocular manifestations. Early clinico-radiological diagnosis of this syndrome is of supreme importance along with genetic counselling of the patient and his family as the syndrome have an autosomal dominant trait with good penetrance and variable expressibility. Current guideline for followup a case of syndromic OKC include- neurological examination twice yearly, cerebral MRI once in a year for 1-7 years of age, Orthopantogram every 12-18 month starting at the age of
eight years, yearly skin examination and cardiologic examination according to sign and symptoms.

Acknowledgment
We gratefully acknowledge the contributions made by Professor (Dr.) R. R. Paul, Deputy Director cum-in-charge, Research and Development, Guru Nanak Institute of Dental Sciences and Research (GNIDSR), Kolkata, Professor (Dr.) S. Kundu, Department of Oral and Maxillofacial Pathology, GNIDSR, Professor (Dr.) Amit Roy, HOD, Department of Oral and Maxillofacial Surgery, Kolkata, Dr. Kaushik Dutta, Department of Oral Medicine and Radiology, GNIDSR, Kolkata for their valuable guidance and support in every step. Words are inadequate to express our gratitude towards Dr. R.P. Chatterjee (Reader), Dr. N. Shah (Reader) for providing their insight and expertise. Our sincere thanks to all the technical staff without whose constant assistance and technical inputs it would not have been possible to complete our work.

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