Case Report

Nevoid Basal Cell Carcinoma Syndrome: Report of a Case and Review of the Literature

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Multiple odontogenic keratocysts are a characteristic manifestation of the nevoid basal cell carcinoma syndrome (NBCCS). The syndrome is characterized by symptoms primarily involving the skin, central nervous system, and skeletal system. Here we report a case of a young girl suffering from NBCCS and review the current concepts in the understanding and management of this syndrome.

Introduction

The nevoid basal cell carcinoma syndrome (NBCCS), acquired as an autosomal dominant disorder, presents itself as a series of multi organ abnormalities. The syndrome is believed to be a consequence of mutation in the PTCH gene.1 90% of patients suffering from NBCCS report with recurring odontogenic keratocysts (OKCs).2

The triad of multiple odontogenic keratocysts, basal cell carcinomas and vertebral anomalies is well established while other expressions, such as intracranial calcification, hypertelorism, mental retardation, cleft lip and palate, cutaneous cysts, and palmar and plantar hyperkeratosis, are less pronounced and can easily be overlooked.3 The features involving the bone can be imaged easily using conventional and advanced radiology.

Though this condition had previously been described, it was not until 1951 that the broad extent of this altered morphogenesis was set forth by Binkley and Johnson.4

Gorlin and Goltz first described the spectrum of features associated with this syndrome in 1960; hence, it is also called Gorlin-Goltz syndrome.5

Here we discuss a case with an expression of NBCCS and review briefly, latest trends in the treatment of multiple OKCs associated with the syndrome.

Case Report

A 16 year old female presented with discharge from the right maxillary posterior area for the past 10 days. She also complained of swelling in the area but no pain. Her vitals were found to be within normal limits.

Fig 1: Orthopantomogram showing the cystic lesions (Arrows)

Fig 2: CXR-Bifid ribs (3rd bilaterally, 4th on left side)

The patient also gave a history of similar swelling and discharge on at least one previous occasion fifteen months back when she was operated upon in another hospital. Unfortunately no record of her past treatment could be retrieved. Intra-oral
examination revealed teeth numbers 18, 14, 28, 38, 32, 43 and 48 to be completely missing. There was expansion of the buccal cortical plate in the maxillary canine and premolar region on the right side as well as in the anterior mandible.

![Figure 3: Skull CT showing calcification of the falx](image)

Figure 3: Skull CT showing calcification of the falx

Figure 4: Histopathology of odontogenic keratocyst (H&E X 100 Insets X 200) Note the cyst is lined by stratified squamous epithelium. The insets show keratin flakes (A) and granulation tissue with plasma cells (B).

Panoramic radiograph indicated the presence of corticated and scalloped radiolucencies in the maxillary canine and premolar region on the right, anterior mandible as well as surrounding both the unerupted mandibular 3rd molars (Figure 1).

The patient’s chest radiograph showed 3rd rib to be bifid bilaterally while the 4th rib was bifid on the left side (Figure 2). A skull CT was also done which demonstrated calcification of the falx cerebri (Figure 3).

The patient was admitted to hospital; all the cysts were enucleated under general anesthesia with peripheral ostectomy and application of Carnoy’s solution soaked gauze for 3 minutes. The tissue was submitted for microscopic examination. The cysts were lined by stratified squamous epithelium which was several layers thick. There were abundant keratin flakes. No Dysplastic or frankly malignant cells seen. The underlying stroma contained abundant granulation tissue and scattered chronic inflammatory cells mostly plasma cells (Figure 4).

**Discussion**

The odontogenic keratocyst (OKC) was first described in 1876 and named by Phillipsen in 1956. It is one of the most aggressive odontogenic cysts of the oral cavity. OKC is known for its rapid growth and its tendency to invade the adjacent tissues including bone. It has a high recurrence rate and is also associated with the nevoid basal cell carcinoma syndrome.

<table>
<thead>
<tr>
<th>Table 1: Diagnostic criteria for nevoid basal cell carcinoma syndrome</th>
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<tr>
<td><strong>Major criteria</strong></td>
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<tr>
<td>More than 2 basal cell carcinomas (BCCs), 1 BCC</td>
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<td>before 30 years of age, or more than 10 basal cell nevi</td>
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<td>Any odontogenic keratocyst (proven on histology)</td>
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<tr>
<td>or polyostotic bone cyst</td>
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<tr>
<td>3 or more palmar or plantar pits</td>
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<tr>
<td>Ectopic calcification; lamellar or early (&lt; 20 years</td>
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<tr>
<td>of age) falx calcification</td>
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<td>Family history of nevoid basal cell carcinoma syndrome</td>
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| **Minor criteria**                                           |
| Congenital skeletal anomaly (e.g., bifid rib, fused,         |
| splayed or missing rib, wedged or fused vertebrae)           |
| Occipital–frontal circumference higher than the 97th percentile, with frontal bossing |
| Cardiac or ovarian fibroma                                    |
| Medulloblastoma                                               |
| Lymphomesenteric cysts                                        |
| Congenital malformations, such as cleft lip or palate, polydactylism or eye anomaly (cataract, coloboma, microphthalmos) |

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NBCCS can also include concomitant skeletal features, such as bifid rib, frontal and parietal bossing, mandibular prognathism and cutaneous abnormalities, such as multiple basal cell carcinomas and palmar and/or plantar hyperkeratosis. Hypertelorism, mental retardation, strabismus, calcification of the falx cerebri, bridging of sella turcica and medulloblastoma have also been reported.10 In our patient, two ribs were found to be bifid and calcification of the falx cerebri was also noted.

The biologic behaviour of OKCs associated with NBCCS is more aggressive and these cysts have higher recurrence rates (82%) compared with solitary keratocysts (61%).11 The higher recurrence rates are attributed to epithelial remnants of the cystic lining or satellite cysts left behind following surgery,12 therefore a recurring OKC can be a new cyst that originates from epithelial residue or a microcyst left behind in the overlying muco
cosa.

There are no specific laboratory tests to diagnose NBCCS, although affected patients may have high levels of cyclic adenosine monophosphate.13 Diagnosis is made clinically based on the criteria suggested by Evans and others (Table 1). Two major or one major and two minor criteria need to be satisfied for a positive diagnosis.14 In our patient two major and one minor criterion were affirmative suggesting a strong possibility of it being a case of NBCCS.

More recently, molecular testing has also become available to confirm the diagnosis in patients with atypical findings or possibly for prenatal diagnosis. Molecular testing may be useful for infants of an affected patient who is too young to have developed diagnostic clinical findings. Because of imperfect sensitivity and specificity, genetic testing should be performed in conjunction with a genetic counselor.15

While treating OKCs associated with NBCCS, overlying surface epithelium should be excised along with the cystic lining to prevent recurrence.5 In addition the use of Carnoy's solution following cyst enucleation; applied only over areas where the cyst is attached to the mucosa12 and cryosurgery (because of the unique ability of liquid nitrogen to devitalize bone in situ while leaving the inorganic framework untouched) is advocated to kill epithelial remnants and dental lamina within the osseous margin thus preventing recurrences.16

Other surgical procedures such as curettage of bony margin following enucleation, peripheral ostectomy with a bone bur and even partial jaw resection have also been documented as possible treatment options for recurrent OKCs.17

All the four cysts in our patient were enucleated under general anesthesia with peripheral ostectomy and car
yo's solution was applied to the mucosa overlying the cysts as well as the walls of the cystic cavities.

Our patient did not show any other signs of NBCCS and parents and all other siblings were normal. In conclusion, all patients with multiple OKCs should be meticulously evaluated for other signs of NBCCS.

References
7. Philipson HP. Om keratocysten (kolesteotom) i kaekberne. Tandlaegegebladet 1956; 60: 963-81.
12. Steolinga PJ. Excision of the overlying, attached mucosa, in conjunction with cyst enucleation and treatment of the bony defect with car