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Multiple Odontogenic Keratocysts as Initial Manifestation of Gorlin-Goltz Syndrome: A Case Report

ABSTRACT

Objective: To present a rare case of a 17-year-old girl with multiple odontogenic keratocysts, skeletal abnormalities, central nervous system and cutaneous anomalies.

Methods:

Design: Case Report
Setting: Tertiary Government Training Hospital
Patient: One

Results: A 17-year-old Filipino girl presented with a one-year history of progressive left mandibular swelling. Orthopantomography revealed multiple cysts involving the mandible and maxillae. Histopathologic examination of incision biopsy specimens confirmed odontogenic keratocysts. Other physical examination findings included coarse face and multiple palmar and plantar pits. Radiologic investigations demonstrated calcification of the falx cerebri and tentorium cerebelli, bifid rib and cervicothoracic scoliosis. Based on clinical, radiological, and histopathological findings, a diagnosis of Gorlin-Goltz syndrome was established. The patient underwent enucleation and curettage of the cysts with peripheral ostectomy, and there was no recurrence on repeat orthopantomography at six months and two years post-operatively. However, on the fourth year, the patient claimed there was a mandibular cyst which was not verified as she was lost to follow-up.

Conclusion: This case highlights the importance of recognizing multiple odontogenic keratocysts as a potential manifestation of Gorlin-Goltz Syndrome. Early diagnosis enables appropriate management and long term surveillance to monitor for other manifestations of this syndrome that may occur later in life.

Keywords: *odontogenic keratocyst; Gorlin-Goltz Syndrome; nevoid basal cell carcinoma syndrome; jaw-cyst bifid rib syndrome*

Gorlin-Goltz Syndrome (GGS), first comprehensively described by Gorlin and Goltz in 1960, is a rare autosomal dominant disorder with an estimated prevalence of 1:60,000 to 1:256,000 based on different populations.¹ The syndrome results from gene mutations in patched-1 (PTCH1) and patched-2 (PTCH2)¹⁻³ with 20-40% of cases arising from de novo mutations of the PTCH1 [9q22.3] gene.¹ Recent studies mention mutations of suppressor of fused homolog (SUFU) gene.^{2,3} The classical triad consists of multiple basal cell carcinoma, keratocysts in the jaw, and bifid ribs, but is currently known with various range of clinical manifestations.^{1,2} Early recognition is crucial as patients require lifelong surveillance for malignant transformation of multiple nevi to basal cell carcinoma.^{2,3} In the Philippines, only five cases of GGS have been documented in the literature, with most presenting primarily with basal cell carcinomas rather than odontogenic manifestations.⁴⁻⁸ We present a unique case where multiple odontogenic keratocysts (OKC) served as the initial presenting feature.

CASE REPORT

A 17-year-old girl from Samar Province consulted with a chief complaint of left mandibular swelling for one year, with no associated toothache, fever, dental trauma, erythema, discharge, numbness, or pain, nor was there a history of any dental consult or procedure. Over the preceding months, the swelling gradually enlarged, causing obvious facial asymmetry, now associated with growth of an extraoral fleshy mass measuring approximately 1 cm without any associated discharge.

External physical examination revealed a 4 x 4 x 2 cm firm, fixed, non-tender, non-erythematous extraoral mass over the body of the left mandible (*Figure 1A*) with a 1 x 1 cm granulation tissue, without discharge. (*Figure 1B*) Intraoral examination revealed a bulge in the buccal vestibule adjacent to teeth # 18, 19, and 20, without mucosal changes, discharge or ulceration. Intraoral aspiration yielded straw-colored cystic fluid. There were no carious teeth but missing mandibular canines were noted bilaterally. Otolaryngologic examination (otoscopy, rhinoscopy, laryngoscopy) was unremarkable. No neck masses or cervical lymphadenopathies were appreciated.

Our initial impression of a single odontogenic cyst for the left mandibular mass was corrected when a panoramic radiograph of the jaw revealed five unilocular radiolucencies in the maxillae and mandible with four of them associated with unerupted teeth. (*Figure 2*) Unerupted mandibular canines were also seen. We revised our diagnosis to multiple dentigerous cysts of the maxilla and mandible but considered an underlying syndrome. A review of history was obtained, and a more thorough physical examination and further investigations were performed.

The review of her past medical history revealed surgical excision of an epidermal inclusion cyst in the buttocks. She was a Grade 10 student and denied smoking or drinking alcoholic beverages. There was no known family history of any odontogenic cysts or cancer.

General physical examination revealed coarse facial features with frontal bossing, (*Figure 3A*) café-au-lait spots on the neck, trunk and extremities, (*Figure 3B*) multiple palmar pits, (*Figure 3C*) plantar pits with a 3 x 2 x 2 cm nodular mass on the sole of the right foot, (*Figure 3D*) and a 6 x 3 x 1 mm slightly elevated black nevus over the abdomen. (*Figure 3E*)

A chest radiograph revealed a bifid left 3rd rib (*Figure 4*) while the skull radiograph showed calcification of the falx cerebri. (*Figure 5*) Contrast-enhanced CT scans of the cranium confirmed calcifications of the falx cerebri and bilateral tentorium cerebelli. (*Figure 6*) Contrast-enhanced CT scans of the jaws revealed multiple unilocular cysts in both maxillae (*Figure 7A*) measuring 2.3 x 2.8 x 2.14 cm on the left and 3.2 x 2.4 x 1.9 cm on the right, and in the mandibular body and rami (*Figure 7B*) measuring 6.1 x 3.1 x 2.9 cm on the left and 5 x 2.5 x 2.7 cm on the right. Cervicothoracic scoliosis was also noted. (*Figure 8*) The abdomino-pelvic ultrasonogram and blood exams (complete blood count and comprehensive metabolic panel) showed normal results.



Figure 1A. Left mandibular swelling; **B.** with granulation tissue at left mandibular area a month after. Photos published with permission.



Figure 2. Orthopantomogram showing 5 unilocular lucencies with unerupted teeth



Figure 3. Other pertinent PE findings included **A.** coarse facial features; **B.** café-au-lait spots on the neck, trunk and extremities; **C.** palmar pits identified with ink; **D.** plantar pits with mass on the sole of the right foot; and **E.** elevated black nevus over the abdomen. Photos published with permission.

Histopathologic analysis of the incision biopsy of the left mandibular cyst was consistent with a keratocyst.

Based on the constellation of clinical, radiological, and histopathological findings, a diagnosis of Gorlin-Goltz Syndrome was established. The patient underwent enucleation and curettage of the cysts with peripheral ostectomy under general anesthesia. The extraoral granulation tissue was excised simultaneously. Intraoperatively, well-encapsulated cystic masses were identified in bilateral mandibular and maxillary regions, containing fleshy curd-like materials and unerupted teeth. The suspicious abdominal lesion was also excised to rule out basal cell carcinoma.

She was discharged without complications two days after surgery. Final histopathology confirmed odontogenic keratocysts in three of the four excised cysts, while the right mandibular cyst showed only inflammatory changes. The cutaneous abdominal lesion was negative

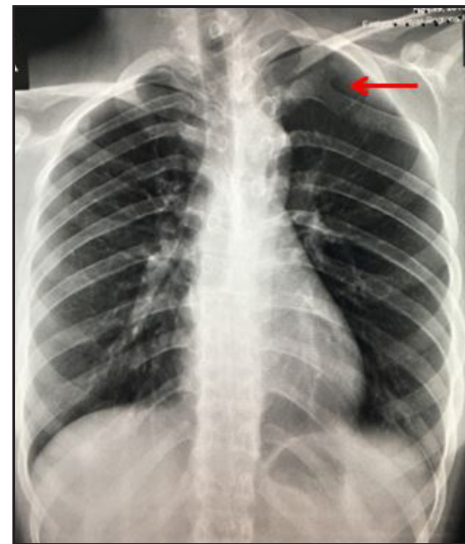


Figure 4. Chest radiograph showing a bifid left third rib (arrow)



Figure 5. Skull X-ray, AP view, showing calcification of the falx cerebri (arrow)

for malignancy. Follow-up orthopantomograms at six months and two years showed no new or recurrent lesions and good healing of the mandibular and maxillary enucleation sites. However, the patient claimed there was a mandibular mass on the fourth year which was not verified as she could not follow-up due to financial constraints, representing a significant limitation in ongoing surveillance.



Figure 6. Contrast enhanced Cranial CT scan, axial view, showing calcified falx cerebri and tentorium cerebelli (arrows)



Figure 8. CT scan of the cervicothoracic spine, coronal view showing cervicothoracic scoliosis

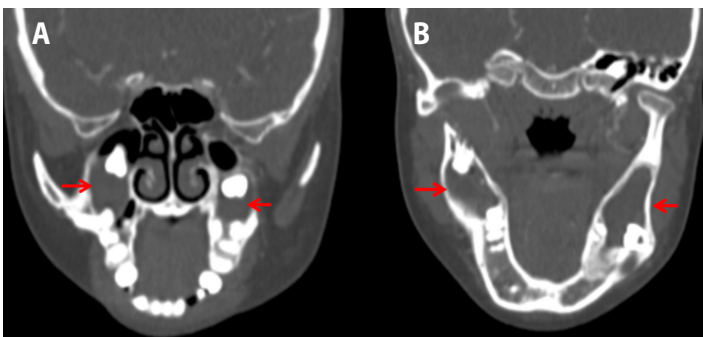


Figure 7. Contrast enhanced CT scans of the oral cavity, coronal views, showing: A. maxillary and B. mandibular cysts

DISCUSSION

This case represents a rare presentation of Gorlin-Goltz Syndrome where multiple odontogenic keratocysts served as the initial manifestation, contrasting with previously reported Filipino cases that primarily presented with basal cell carcinomas.^{4,8} This highlights the variable phenotypic expression of the syndrome and emphasizes the importance of recognizing odontogenic manifestations.

Other differential diagnoses in patients presenting with multiple odontogenic tumors include Noonan Syndrome,⁹ but this was ruled out as it is usually associated with webbed neck, short stature, congenital cardiac defects and bleeding diathesis;¹⁰ oro-facial-digital syndrome,⁹

but this was ruled out because the classic congenital anomalies such as micrognathia, cleft lip or palate, and extra or fused fingers¹¹ were not present; Ehler-Danlos Syndrome,⁹ which was ruled out due to absence of skin hyperelasticity, articular hypermobility, and tissue fragility;¹² and Simpson-Golabi-Behmel Syndrome,⁹ also ruled out due to absence of the characteristic features such as macrocephaly, midline defects, and organomegaly; and non-syndromic familial keratocystic odontogenic tumors (KCOT)⁹ which was also not considered because none of the family members presented with such tumors.

Gorlin Goltz Syndrome is diagnosed through clinical examination and imaging. The diagnostic criteria were first established by Evans *et al.* in 1993, subsequently modified by Kimonis *et al.* in 1997, and finally revised by Bree *et al.* in 2011.³ Recent recommendations on the diagnostic criteria were made during the first International Colloquium on Nevoid Basal Cell Carcinoma Syndrome (NBCCS), changing rib anomalies as minor criterion and medulloblastoma as major criterion.² Diagnosis requires one major criterion and molecular confirmation, or two major criteria, or one major and two minor criteria.^{2,3} Our patient presented with three major criteria: odontogenic keratocysts, palmar and plantar pits, and calcification of the falx and tentorium cerebelli; and three minor criteria: coarse facial features, scoliosis, and bifid rib, establishing the diagnosis of Gorlin-Goltz Syndrome.

Molecular-genetic confirmation is considered the gold standard, but the clinical criteria is enough to establish a diagnosis.^{2,3} However, genetic testing for PTCH1 can be utilized during prenatal testing when a familial mutation has been identified, in confirming diagnosis in individuals who exhibit certain clinical manifestations but do not fully meet the established criteria, and as a predictive testing tool for those with an affected family member and are at risk, yet do not fulfill the clinical criteria.²

Odontogenic keratocysts associated with Gorlin Goltz Syndrome occurs in 44 to 92% of cases with a recurrence rate of 15.4 to 50%.³ Another author documented recurrence rates of as high as 63%, compared to 37% for isolated odontogenic keratocysts.¹⁴ Various theories for recurrence include retention of satellite or daughter cysts, the intrinsic growth potential of the epithelial lining, incomplete removal of the cyst lining, dependence on the site involved with the mandibular molar region significantly having higher recurrence, and operative factors playing a major influence on the likelihood of recurrence.¹⁴

According to Chrcanovic and Gomez, recurrence rates for conservative management of OKCs in general with enucleation and curettage were 22.5% compared to 18.6% for enucleation with peripheral ostectomy, and 2.2% for radical interventions like marginal/segmental resection.¹⁵ To the best of our knowledge, there are currently no randomized controlled trials for the treatment of keratocysts in NBCCS. But considering the age of our patient, radical intervention for complete eradication of the cyst was quite extreme, not to mention the high post-operative morbidity, facial disfigurement, and quality of life thereafter. With this dilemma, the consensus among us physicians and the patient's family was to opt for conservative management by way of enucleation and curettage with peripheral ostectomy using a drill.

Another concern for this syndrome which may contribute to an

additional morbidity in our patient is the worrisome propensity of developing basal cell carcinoma of the skin in about 90% of cases in whites and 40% in blacks.¹ Areas involved may not be limited to sun-exposed areas.^{1,3} Hence, a thorough examination is needed in search for suspicious lesions that may range from minute skin tags to ulcerating plaques.

Thus, regular consults with a dermatologist and/or otorhinolaryngologist every 3-6 months with excision of any basal cell nevus showing evidence of growth, bleeding, and ulceration is recommended.³ An annual panoramic radiograph is also warranted for surveillance of new or recurrent lesions until 22 years of age, then as needed when pain is present or if there is an unexplained change in teeth formation.³ Genetic counselling holds great importance due to its high rate of inheritance. Although this surveillance protocol is ideal, its implementation is challenging in the Philippines and in most low-middle income resource-constrained countries. This makes it difficult to monitor for new or recurrent odontogenic lesions and to assess for any suspicious cutaneous malignancies. Our patient has only had two surveillance orthopantomograms at six months and two years, and has been unable to follow up since, despite reporting a mandibular mass on the fourth year after surgery.

This case demonstrates that multiple odontogenic keratocysts may serve as the initial and primary manifestation of Gorlin-Goltz Syndrome, hence, recognition of this presentation pattern is crucial for early diagnosis and appropriate management. The case underscores the importance of comprehensive physical examination and systematic evaluation when encountering multiple odontogenic lesions, as they may represent "the tip of the iceberg" of a complex genetic syndrome requiring lifelong surveillance and multidisciplinary care. Early diagnosis enables implementation of appropriate surveillance protocols and genetic counseling, ultimately improving patient outcomes and quality of life.

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