

Suspected familial odontogenic keratocysts related to Gorlin Goltz syndrome

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ABSTRACT

This report represents the suspected familial case series of odontogenic keratocysts (OKCs) related to Gorlin Goltz syndrome (GGS), a rare genetic disorder characterized mainly by multiple basal cell carcinomas, OKCs and other less frequent skeletal and neurological manifestations. Familial cases included grandmother's father, grandmother, father and son. Although they had all OKCs, father additionally possessed some of the other characteristics of GGS. We described all the patients' diagnoses, treatments and long-term follow-ups under the light of current literature.

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Essential features of odontogenic keratocysts (OKC) were first described in 1963.¹ They differ from those of usual odontogenic cysts with their clinical and histopathological features. They have a tendency for local invasion and recurrence.^{2,3} Gorlin Goltz syndrome (GGS), also known as nevoid basal cell carcinoma syndrome, is an autosomal dominant disorder principally characterized by the features such as multiple OKCs of the jaws, basal cell carcinomas, congenital skeletal deformities, ectopic calcifications, and plantar or palmar pits owing to a mutation in a patched, a tumor suppressor gene that has been mapped to chromosome 9q22.3-q31.^{4,6} Most of the anomalies in GGS are minor and usually not life threatening. Prognosis generally depends on skin tumors.⁶ It is a rare pleiotropic autosomal condition, and a positive family history may be elicited from the patients.⁷ The OKCs may occur as single or multiple lesions with no other overt manifestations of the GGS.⁸ They are present in at least 75% of the patients with the syndrome. Lesions of both upper and lower jaws are encountered earlier particularly in after the

7th year of life without any racial predilection and may be multiple when associated with GGS.^{7,9}

The treatment methods of OKCs vary from enucleation with curettage, enucleation with peripheral osteotomy and en-bloc resection. Lesions associated with GGS are more recurrent and aggressive in behavior than the keratocysts of non-syndrome patients. This is related to some factors such as incomplete removal, retention of epithelial islands or satellite microcysts.⁸⁻¹¹ This report demonstrates the diagnoses, treatments and long-term follow-ups of familial cases with OKCs related to GGS.

Case Report. An 8-year-old boy has been followed clinically and radiologically in Oral and Maxillofacial Department of Gazi University, Faculty of Dentistry since October 2001 due to the suspected familiar history of OKC and GGS. While the autosomal characteristic of GGS is well-known, these close follow-ups have been handled with care. His grandmother and grandmother's father had an enucleation of the "jaw cysts" of the mandibles

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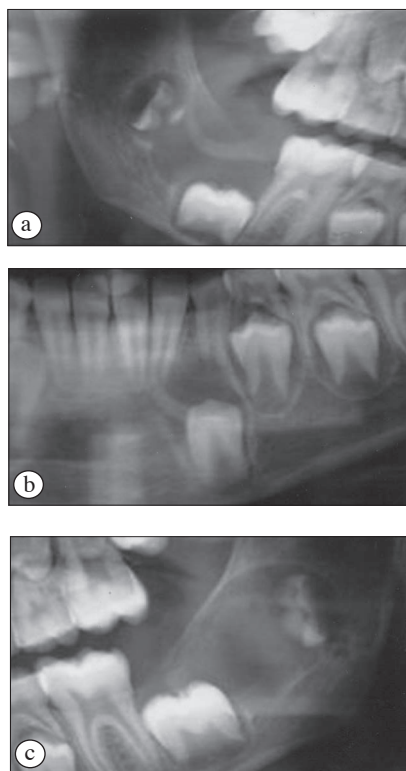


Figure 1 - Panoramic views of the patient scattered cysts through mandible: **a)** right mandibular posterior, **b)** left mandibular canine and **c)** left mandibular posterior regions.

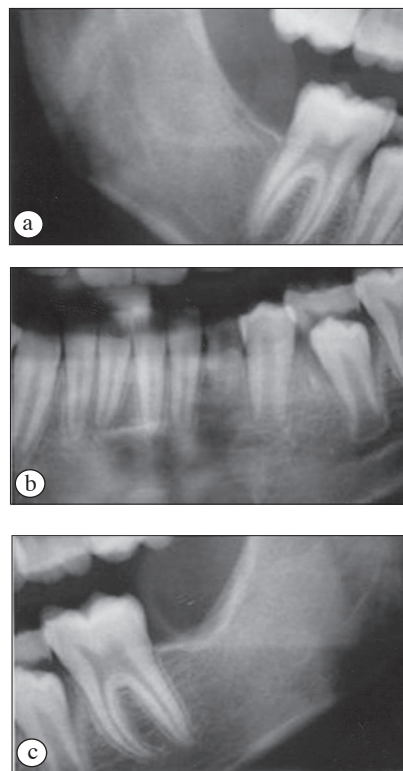


Figure 2 - Panoramic views of the patient postoperative 3rd year follow up without any recurrence: **a)** right mandibular posterior **b)** left mandibular canine and **c)** left mandibular posterior regions.

nearly 40-60 years ago. Since the entity of OKC was described late on this date,¹ whether the lesions were OKCs could not be determined. In addition, the details could not be uncertain regarding to the other characteristics of the GGS as the syndrome was first reviewed in 1951.¹ However, his father's first OKC of the mandible was initially detected in 1976, when he was a 13-year-old boy. After the enucleation of the lesion, routine controls were followed. These controls obviously did not cover the standards of Gorlin,⁹ concerning the syndrome as it was documented approximately 20 years later. Some exophytic nevi were noted on his face and shoulder in 1984, 8 years after the enucleation of the cyst. The GGS was suspected and the diagnosis was made by falx-cerebri calcifications, osteoarthritic changes and minimal scoliosis. Any other characteristics of the syndrome could not be detected at that time. The number of exophytic nevi reached 33 in 6 years period, 3 of them were excised and the case was reported as basal cell carcinoma by Gokler et al.¹² The OKC were again detected in different location of the mandible in 1994 and the right maxilla obliterating the maxillary sinus in 2002. All the lesions were enucleated with the

removal of supra-adjacent soft tissues, and they healed uneventfully without any recurrence. Yearly follow-ups are continuous according to the management of the patients with GGS protocol.⁵

Although, any detectable findings had not been noted related to the features of GGS in the patient in routine examinations previously, in October 2001, bilateral asymptomatic radiolucencies adjacent to the 2nd molars and 3rd molars' crypts, and a big folliculi around left mandibular canine tooth were observed in a panoramic radiograph (**Figures 1a, 1b, & 1c**). Lesions were all enucleated, and the histopathological diagnoses for them were reported as OKC. Yearly follow-ups are continuing without any evidence of recurrence (**Figures 2a, 2b, & 2c**). Any other features of GGS were not noted since his last control in March 2005. In addition, both father and son were sent to the Genetic Unit for study.

Discussion. The frequency of the GGS is variously estimated. Minimal prevalence is between 1 per 57,000 to 1 per 164,000.⁵ Familial long-term follow-up of OKCs related to GGS like these present case series is exceptionally rare in the literature.

However, limited reports of familial cases,^{1,13,14} and some reports of non-familial cases^{3,6} have been documented. The OKCs were first described in 1963,¹ after the diagnosis of the grand parents' cystic lesions in this present report. Therefore, exact diagnosis whether the lesions were OKCs could not be confirmed and any other features of GGS could not be reached as they were treated approximately 50 years ago. However, since only the occurrences of OKCs are sufficient for the diagnosis of the syndrome, it might be speculated that they were OKCs by means of familiar aspect. Characteristically, cysts of both the upper and lower jaws may appear after the 7th years of life in GGS. Therefore in suspected GGS patients, a panoramic radiograph of the jaws once a year from the age of 8 years is suggested.⁵ In this present report, while the father's diagnosis was exacted, son's clinical and radiological controls have been managed regularly according to this suggestion, and 3 lesions were identified in his first radiological control. If the father's controls had been carried out in the same way, the keratocyst located in the mandible might not have been occurred in such a destructive pattern. However, son's lesions and the father's lesion located in the maxilla were identified earlier without a dramatic destruction and their treatments were managed easier. Although a more recent protocol, which has described the treatment of the OKCs, it has not included the lesions related to GGS.¹⁵ Another crucial point of the need of the regular controls of these patients is the occurrence of a squamous cell carcinoma arising from OKCs with GGS. This rare condition has been reported by Ramsden and Barret.¹⁶ Moos et al,¹⁷ have showed another case of malign transformation of OKC with GGS who had a history of previous radiotherapy.

Recurrence of the OKCs following surgery may be a major problem. However, the necessity of radical surgery such as en-bloc resection for these lesions remains controversial even in syndrome patients. Attempts have been made to reduce the recurrence rate such as removal of supra-adjacent soft tissue, smoothing of the osseous walls of the cavity, tanning epithelial lining of the cyst with Carnoy's solution and marsupialisation.^{10,18} The patient and his father's OKCs were enucleated with the removal of supra-adjacent soft tissues and any recurrences were not observed in this present report.

Most often the basal cell carcinomas involve the face, back and chest in GGS. Although new lesions appear from time to time, most of them remain static in growth. It is only after puberty that they can become aggressive. Regular visits (every 2-3 months)

to dermatologists are recommended by means of basal cell carcinoma, especially children at risk during adolescence.⁹ The most crucial point regarding these lesions is metastasis and invasion. Death from the invasion and metastasis has been documented.^{19,20} Therefore, we managed the patients regularly in these present cases.

For infants at risk, medulloblastoma should be eliminated by annual magnetic resonance imaging until 8 years of age and cardiac fibroma by chest radiography in GGS suspected patients. Diagnosis may also be achieved imaging the structures by radiographic means for infants such as falx cerebri calcifications and rib anomalies.⁹ Any of these further symptoms have not been detected to the patient presented in this report. However, multiple keratocysts may be sufficient for the diagnosis of GGS with familiar history.^{8,10} Whenever a diagnosis of OKC is received, presence of GGS must be certain to ruled out due to the many associated problems may be faced. If other symptoms are detected, a multidisciplinary approach in diagnostic and treatment of the disease is required.^{1,8,10,13}

In conclusion, this report attempt to assess how the OKCs may become aggressive in GGS regarding to the suspected familial cases. The follow-ups of these patients should be managed regularly according to the scientific protocols.

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