Odontogenic keratocysts in a 5-year-old: Initial manifestations of nevoid basal cell carcinoma syndrome

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Abstract

The purpose of this paper is to report the occurrence of odontogenic keratocysts in a young child. Odontogenic keratocysts are one of the principal features of nevoid basal cell carcinoma syndrome. Their occurrence in this syndrome is usually during the second or third decades of life. This report describes the occurrence of odontogenic keratocysts in a 5-year-old, which proved to be the initial presentation of nevoid basal cell carcinoma syndrome and highlights the need to consider this syndrome as a possible diagnosis in all cases of odontogenic keratocysts. (Pediatr Dent 22:53-55, 2000)

The nevoid basal cell carcinoma syndrome is a generalized disorder consisting principally of multiple nevoid basal cell carcinomas, odontogenic keratocysts of the jaws, vertebral and rib anomalies, and intracranial calcification.[1] The skull vault is increased in size due to frontal and parietal bossing and there is usually mild ocular hypertelorism.[2] There were early descriptions of the condition in the literature but the syndrome was clearly delineated by Gorlin and Goltz in 1960.[3] The syndrome has been variously referred to as Gorlin-Goltz syndrome, basal cell nevus syndrome, Gorlin syndrome and nevoid basal cell carcinoma syndrome. There are up to 100 less common features described, including associated endocrinopathies, potential for mental retardation, medulloblastoma, ovarian fibromas and an increased incidence of cleft lip and/or palate.[4]

The nevoid basal cell carcinomas can arise in any region of the skin but they occur especially on the face, neck and upper trunk.[5] Unlike non-syndrome basal cell carcinomas, they occur on both non-exposed and exposed areas of the skin. The facial regions most commonly affected are the periorbital areas, eyelids, nose, malar region and upper lip.[2] Minute epidermal cysts (milia) are frequently intermixed with the facial lesions. The nevoid basal cell carcinomas do not usually appear until after puberty[6,7]—before puberty the lesions are harmless and after this age only a few will become aggressive and locally invasive.[2] Nevoid basal cell carcinomas are present in only 15% of cases before puberty and 90% of people with the syndrome will have basal cell lesions by the age of 30.[6] Evidence of aggressive transformation is heralded by an increase in size of the lesion, ulceration, bleeding, and crusting. Other skin lesions that occur frequently, but rarely, seen in children, are palmar and plantar skin pits.[8]

In this disorder odontogenic keratocysts occur most commonly in the second and third decades of life.[6,9,10] This is approximately 10 years earlier than the much more common isolated keratocyst, not associated with the syndrome.[2] The cysts occur three times more often in the mandible than the maxilla and most frequently occur in the canine to premolar area, in the mandibular retromolar and ramus area, and in the region of the maxillary second permanent molar, in that order.[11] In children and adolescents the cysts may cause displacement of the developing teeth,[2] and delayed dental development has been reported.[12] Following enucleation of these cysts, the recurrence rate is high with an estimated recurrence rate of 30% to 60%.[13]

The most common skeletal anomalies are splayed and/or bifurcated ribs which are seen in approximately 60% of cases. Vertebral anomalies that are frequently manifest are kyphoscoliosis and spina bifida.[8] Intracranial calcification is usually manifest as lamellar calcification of the falx cerebri and/or the diaphragma sellae. Calcification of the falx cerebri is seen in 85% of cases, compared to a normal occurrence of 5%, and calcification of the diaphragma sella occurs in 60-80% of cases (normal 4%).[8] Calcification of the tentorium cerebelli is also common. The paranasal sinuses may be enlarged due to hyperpneumatization and the sella may be small because of hyperpneumatization of the sphenoid.[2]

Inheritance is autosomal dominant with complete penetrance and extreme variable expressivity.[14,15] A defect in the tumor suppressor gene located at chromosome 9q has been identified.[15] Approximately 40% of cases represent new mutations.

Case report

A white male aged 5 years 9 months was referred by his family dentist concerning a symptomless swelling in the mandibular left primary molar region. The child's mother had recently noticed the swelling while cleaning his teeth. There was no medical history of significance. Extraorally it was noted that the child had a large and relatively wide forehead. Intraoral examination revealed a caries-free complete primary dentition

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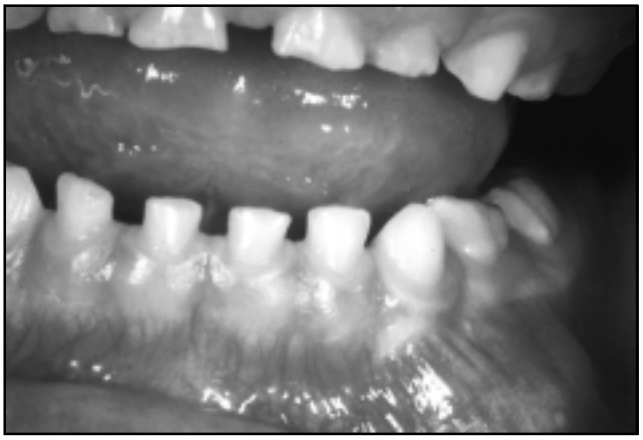

Fig 1. Clinical photograph of swelling buccal to the mandibular left first primary molar.

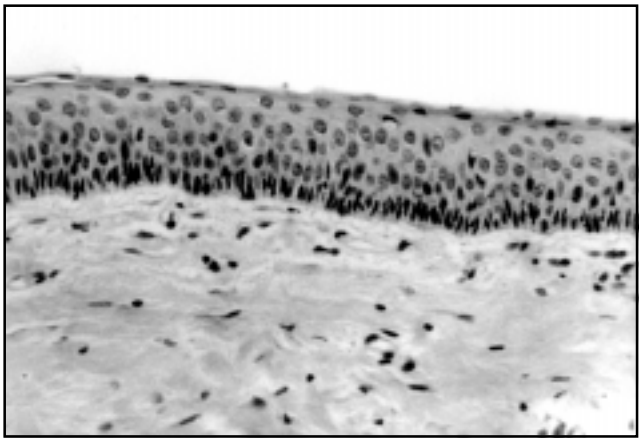

Fig 3. Lining of the first cyst showing typical features of an odontogenic keratocyst–a thin regular parakeratotic stratified squamous epithelium with a prominent palisaded basal layer supported by a thin fibrous wall (H&E, orig. mag x250).

and a 2 cm diameter swelling buccal to the mandibular left first primary molar which was mobile (Fig 1). The upper aspect of the swelling was soft and the lower aspect was firm and clinically represented bony expansion. Radiographically, the lesion had a cystic appearance and there was resorption of the roots of the mandibular left first primary molar (Fig 2). A provisional diagnosis of dental cyst of unknown etiology was made.

Under general anesthesia, the cyst was enucleated and the associated first primary molar was extracted. At operation the cystic contents were noted to be like "thick, inspissated pus." Histopathological examination of the cyst revealed a lining of uniformly thin parakeratinized epithelium with a prominent palisaded basal cell layer. The cyst was filled with keratin. There were very few inflammatory cells in the thin fibrous wall, although a small number of isolated epithelial islands were noted. However, there was no evidence of satellite "daughter" cysts, areas of basal epithelial budding or elongated epithelial cords, features seen frequently but not exclusively in syndrome-associated keratocysts (Fig 3). The associated mandibular left first primary molar had a vital pulp and showed root resorption. The patient was kept under review because odontogenic keratocysts frequently recur following enucleation.

Two years following enucleation of the keratocyst in the mandibular left first primary molar area, mesial displacement of the mandibular right permanent lateral incisor was noted. Radiographic examination revealed the presence of another cystic lesion between the roots of the mandibular right permanent central and lateral incisors (Fig 4). Also revealed was the presence of an unerupted midline maxillary supernumerary tooth. Under general anesthesia the maxillary supernumerary tooth was surgically removed and the cyst in the mandibular incisor area was enucleated. Histopathological examination of the enucleated cyst presented findings very similar to those of the first lesion. The diagnosis was confirmed histologically as that of an odontogenic keratocyst. In view of the occurrence of two odontogenic keratocysts within a two-year period in a young child, the possibility that the cysts might be a sign of nevoid basal cell carcinoma syndrome was investigated.

Dermatologic examination revealed normal skin, and no nevoid basal cell carcinomas, epidermal cysts, or skin pits were present. Medical examination revealed that the child had an asymmetric rib cage. The radiology report determined that there was a relatively tall and broad skull vault with orbital hypertelorism, a small sella with calcification of the diaphragma sellae and asymmetry of the rib cage with bifid anterior right second and sixth ribs. There were no vertebral anomalies. A

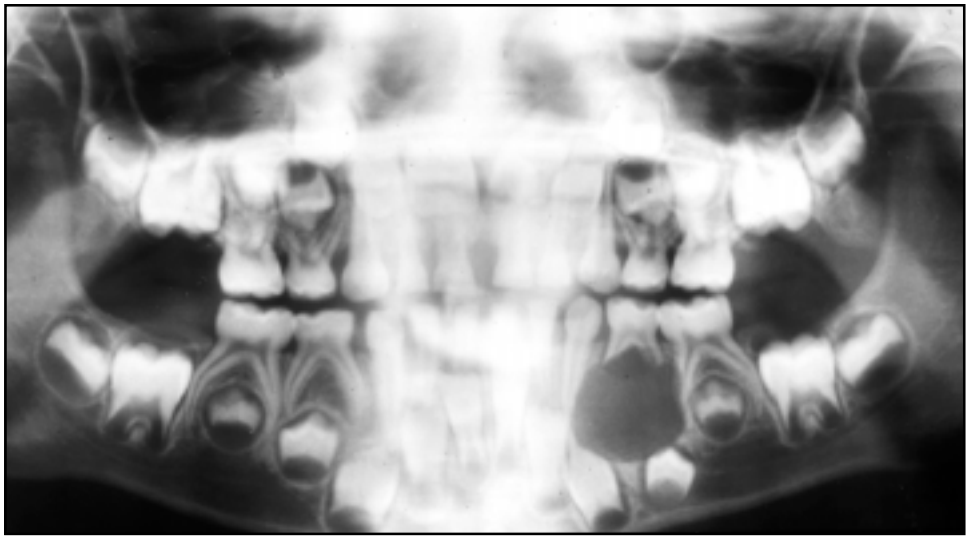

Fig 2. Radiograph showing radiolucent lesion associated with the roots of the mandibular left first primary molar.

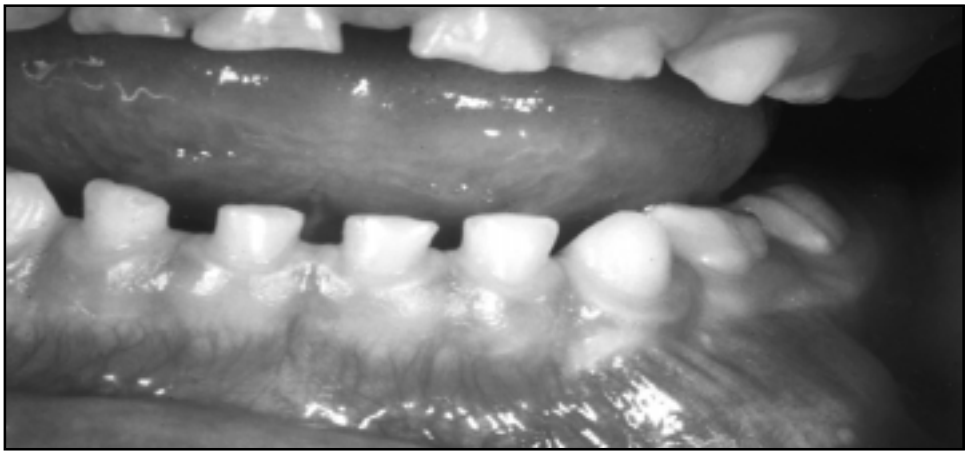

Fig 4. Radiograph showing radiolucent lesion between the roots of the mandibular right permanent central and lateral incisors.

diagnosis of nevoid basal cell carcinoma syndrome was made based on the occurrence of three of the four cardinal signs of the syndrome—namely odontogenic keratocysts, intracranial calcification, and bifid ribs.

The family was then investigated because the syndrome has autosomal dominant inheritance. There was no family history of the syndrome, keratocysts, or nevoid basal cell carcinomas. The parents had no clear signs or symptoms of the syndrome, and the other child in the family, a girl, was not affected.

Discussion

The child in this report presented with an intraoral swelling. The diagnosis of an odontogenic keratocyst and the subsequent occurrence of another cyst led us to suspect the possibility of nevoid basal cell carcinoma syndrome, even though there was no apparent family history of the syndrome. Further medical and radiological investigations confirmed the diagnosis of nevoid basal cell carcinoma syndrome in the child based on the presence of odontogenic keratocysts, intracranial calcification, and bifid ribs. The dental findings were therefore significant in leading to the diagnosis of nevoid basal cell carcinoma syndrome in the child.

The child demonstrated many features of nevoid basal cell carcinoma syndrome. In this disorder odontogenic keratocysts most commonly present during the second and third decades of life[6,9] although they have been reported to occur in the first decade, but only after the seventh year.[2] The presentation of an odontogenic keratocyst at 5 years 9 months is, to our knowledge, and following a search of the literature, the earliest age that an odontogenic keratocyst has been reported to occur in this syndrome.

The importance of early diagnosis of nevoid basal cell carcinoma syndrome is that one can inform the patient and parents of the likely later development of multiple odontogenic keratocysts and multiple basal cell carcinomas. Careful dental follow-up and treatment is required for the odontogenic keratocysts, which are continuous in their development and have a recurrence rate of 30-60%.[13] Specialist dermatologic follow-up is required to assess and treat as necessary the many nevoid basal cell carcinomas that may develop after puberty. Family members should also be investigated because the syndrome has autosomal dominant inheritance. The patient and parents may also be referred, when appropriate, for genetic counseling because an affected individual has a 50% chance of transmitting the disorder.

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