Pycnodysostosis: orofacial manifestations in two pediatric patients

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Pycnodysostosis (PKND) is a rare autosomal recessive skeletal abnormality acknowledged as a distinct entity by Maroteux and Lamy in 1962. More than 150 cases have been reported from all racial groups and more than 30% of cases are the product of consanguineous parents. A review of 78 cases by Sedona and associates found a 1:1.6 male predilection, while 54 cases reviewed by Muto found a slight 1:1.3 female predominance. Patients with PKND usually have normal intelligence, sexual development, and life spans.

The clinical manifestations of PKND commonly include increased bone density, bone fragility, and short stature. Other clinical features include skull deformities with open cranial sutures, an obtuse gonial angle, hypoplastic paranasal sinuses, dysplastic lateral clavicles, shortened terminal phalanges, proptosis, blue sclera, and frontal/occipital bossing. Oral manifestations include a flattened mandibular angle, grooved palate, anterior crossbite, malpositioned teeth associated with an increased incidence of dental caries and periodontitis, hypoplastic maxilla and chin, delayed eruption of permanent teeth, delayed exfoliation of deciduous teeth, hypoplasia of the roots, and obliterated pulp spaces.

The locus for PKND maps to the human chromosome 1q21.9 The defective gene has been identified recently as that encoding cathepsin K, and PKND is now classified as a lysosomal disorder caused by defective tissue-specific expression of this enzyme.

Cathepsin K is a lysosomal cysteine protease that is highly expressed in osteoclasts. It plays a major role in the process of bone matrix resorption, and the deficiency of this enzyme in individuals with PKND results in the inability to efficiently resorb bone matrix. Therefore, continuous endosteal formation occurs in PKND without resorption and remodelling by osteoclasts, leading to an increased generalized sclerosis of bones. Many of the clinical features result directly from this increase in bone density and fragility.

Diagnosis of PKND is based on the clinical presentation, and medical treatment for the condition is symptomatic. The differential diagnoses of PKND include osteopetrosis, acrosteolysis, mandibuloacral dysplasia, cleidocranial dysplasia, and osteogenesis imperfecta. Unlike osteopetrosis, hepatosplenomegaly and anemia are rare in PKND due to the presence of active medullary hematopoiesis. The primary difference between PKND and cleidocranial dysplasia is that dense and brittle bones are found in PKND, not in cleidocranial dysplasia. Fractures of the extremities in PKND are common in childhood, but the incidence appears to decrease in adulthood, probably because patients have modified their lifestyle to avoid injury. Whether or not bone healing is normal in patients with PKND is controversial. Most fractures heal in these patients, however, a recent radiographic survey of 14 patients indicated a common occurrence of nonunion, stress-fracture lines, and little uptake of technetium in bone scans of recent fractures.

We report on two siblings with PKND, present the maxillofacial clinical features, and discuss management issues for this type of patient. These patients are the only children in the family. A family pedigree was obtained but no other member exhibited any signs of PKND.

Case reports

Case 1

An 8-year, 1-month-old female was diagnosed with PKND at birth, coinciding with the diagnosis of her older brother (Case 2) based on clinical manifestations. The patient reported a history of multiple fractures and presented with a cast on the right leg. The parents reported their daughter had obstructive sleep apnea (OSA). Surgical correction by uvulopalatopharyngoplasty (UPP) and adenoidectomy was attempted at age 4. However, OSA continued to be a problem and was being treated with continuous positive air pressure during sleep. The patient's height was 106.8 cm, well below the third centile for her age.

The patient has frontal bossing with signs of proptosis, apparent midface hypoplasia, and open mouth posture (Fig 1). There is clear evidence of micrognathia with an increased lower face height. A high arched palate with a deep groove was present (Fig 2), with significant dental crowding of the upper arch. An edge-to-edge anterior occlusal relationship was present, with recession of 2 mm on the facial of the
Characteristic oral features include deeply grooved palate and upper anterior crowding.

Anterior edge to edge malocclusion with severe crowding and upper and lower gingival recession.

Profile of patient with PKND demonstrating micrognathia, mild proptosis, and steep mandibular plane.

This patient was the 9-year, 5-month-old brother of Case 1. Medical history was significant for pycnodyostosis and a penicillin allergy. The patient was diagnosed with PKND at 12 months of age, having experienced multiple fractures of the extremities. The patient's height was 117.3 cm, demonstrating the short stature associated with this disease. He had frontal bossing, mild proptosis, and blue sclera. Additionally, the patient exhibited brachydactyly with broad thumbs and spoon-shaped fingernails. Severe dental crowding was present with an anterior edge-to-edge malocclusion, early loss of primary canines, labially positioned lower central incisors, and gingival recession. The patient also had a grooved palate.

Clinically, the teeth appeared normal in morphology and color. Active decay was evident in four teeth, with existing restorations on seven teeth. Generalized gingivitis with moderate plaque was present. Dental maturity was evaluated using the method of Demirjian et al. and was calculated to be 9.2 years compared to the patient's chronological age of 9.5 years. Although the dental age is appropriate, dental eruption was significantly delayed, as both upper permanent first molars had not yet erupted. Radiographically, the lack of the mandibular angle and the exaggerated mandibular notch are evident, the second premolars are absent, and the lower permanent second molars are developing in an abnormal orientation.

Panoramic radiograph shows obtuse gonial angle, elongated coronoid and articular processes, and severe crowding.

Cephalometric radiograph shows micrognathia with straightened mandibular angle, exaggerated mandibular notch, and an open lambdoid suture.

Radiograph shows small mandible, lack of ramus, severe crowding, absence of second premolars, and the lower second molars developing in an abnormal orientation.
Radiographic examination revealed widening of the sagittal suture and lambdoid sutures with wide-open anterior and posterior fontanelles. There was evidence of diffuse sclerosis in both hands. Bone age was estimated to be 9 years, compatible with chronologic age of 9.5 years. Dual X-ray bone densitometry was performed on the lumbar spine and the bone mineral density values were 2.6 standard deviations above the mean of an age-matched control, consistent with the diagnosis of PKND.

The dental treatment plan for these patients is to restore the decayed teeth and enroll the patients in a prevention program. Orthodontic treatment to relieve crowding and impaction of teeth can be accomplished by planned timely extractions, which may also improve the effectiveness of oral hygiene measures. The use of an intraoral appliance to treat the sleep apnea will be considered once oral hygiene can be maintained.

Discussion

A normal life span can be expected in individuals with PKND, however, clinical manifestations in the orofacial region can significantly effect the morbidity and even the mortality from this disease. When faced with the challenge of providing dental care for a patient with PKND, one must be cognizant of factors which may have serious consequences if not properly addressed.

Osteomyelitis is the most serious complication that may arise from the oral manifestations of PKND. As previously mentioned, inappropriate remodeling of bone by dysfunctional osteoclasts is present in these patients, while bone formation continues normally. This leads to brittle bones and decreased vascularization which will continue to worsen with age. The increased susceptibility to osteomyelitis with age can be attributed to the increased endosteal bone production, which gradually eliminates the medullary spaces in the jaws and compromises vascularization and the local immune defences.

Osteomyelitis is a common occurrence in adults with PKND but is uncommon in children. In a review of 54 reported cases in the Japanese literature by Muto and associates, nine cases of osteomyelitis were reported with the youngest case at age 20. Zachariaides and Koundouri reported a case with an osteomyelitis of the mandible developing between the age of 9 and 12. Poor fracture healing may also contribute to the increased incidence of osteomyelitis. Jaw fractures that occur in adult patients with PKND are related to trauma or pathologic fractures associated with osteomyelitis—no jaw fractures have been reported in children. An atraumatic extraction should lead to normal healing in a child with PKND. As osteomyelitis occurs rarely in children, the decision to use antibiotic prophylaxis prior to dental extractions should be made on an individual basis.

Excellent oral hygiene must be stressed in patients with PKND. Pathogens associated with high levels of caries and periodontal disease are a real risk for the development of osteomyelitis in the adult patient. Treatment of osteomyelitis is often very difficult in PKND patients, especially in the mandible. Treatment includes drainage, antibiotic coverage, and sequestrectomy. Due to the frequency of refractory osteomyelitis in sclerosed bone, adjunctive hyperbaric oxygen may also be necessary.

Deficiencies of the maxilla and mandible and insufficient growth of the arches do not permit normal tooth alignment. Subsequent dental crowding makes oral hygiene more difficult for PKND patients. Inability to maintain good oral hygiene may explain the reported increased incidence of caries and periodontitis in this population. Early intervention to relieve dental crowding may be indicated in the pediatric patient to allow better alignment of the primary and erupting permanent teeth. Such treatment would make maintenance of excellent oral hygiene more attainable, reduce the chances of impaction of permanent teeth, and reduce the need for surgical intervention in early adulthood when osteomyelitis becomes a significant risk for these patients. Malposition of teeth due to retained deciduous teeth and hypoplastic facial bones may best be managed by early planned extractions of selected crowded teeth. The one case of reported osteomyelitis in a child arose from complications of an abscessed tooth, which is a different situation compared to a planned extraction of a malpositioned noninfected tooth.

Movement of the teeth into an ideal alignment will make teeth more cleansable and possibly avoid the common sequel of osteomyelitis due to extraction of teeth compromised by caries and periodontal disease in later life. However, no recommendation or information is available in the literature regarding the efficacy and safety of orthodontics in children with PKND. Given that the underlying defect is due to a lack of remodelling and resorption of bone, an orthodontic approach does not appear promising. Therefore, planned extractions seem to be the principal option to relieve crowding in pediatric patients.

Surgical methods to correct maxillofacial deficiencies have been described in adults, however the risk of osteomyelitis may deter patients from electively choosing this option.

OSA has been reported in young children with PKND, often with fatal outcomes. OSA is defined as the cessation of respiratory air flow for longer than 10 s more than 30 times in a 7-h period. The craniofacial abnormalities in PKND reduce the upper airway space and increase the risk of respiratory insufficiency. Nielsen has reported the presence of a long soft palate in PKND patients who experience
respiratory insufficiency in addition to the usual facial anomalies. If not treated, hypoxemia may result in clinical manifestations ranging from cor-pulmonale to cardiac failure. Treatments for this condition include adenoidectomy, uvulopalatopharyngoplasty, tracheostomy, or any surgical procedure that increases the upper airway space.

It is not surprising, therefore, that our patient, who exhibits micrognathia, also has OSA. Our patient underwent a uvulopalatopharyngoplasty and adenoidectomy at age 4 to increase the upper airway space. However, this proved insufficient, and the patient now uses a home positive-airway-pressure device. The parents and patient find the use of this device restrictive and are exploring other possibilities. Many intraoral appliances are currently used to treat OSA. They work by increasing the upper airway space by opening the vertical dimension, posturing the mandible forward, advancing the tongue, or elevating the soft palate. There are no reports of the success of any such appliance in patients with PKND, however positioning the mandible forward should prevent obstruction of the oropharyngeal airway. Use of an intraoral appliance should be considered for PKND patients with respiratory insufficiency. Surgical correction of maxillofacial abnormalities by osteotomies has been successful in young adults, although there are no reports of this approach in PKND patients. If surgical manipulation is necessary, treatment at a young age and appropriate postoperative use of antibiotics is recommended due to decreased incidence of osteomyelitis in childhood.

Currently, patients diagnosed with PKND are treated symptomatically with emphasis on prevention of fractures. The recent location of the gene defect and the abnormal expression of cathepsin K will hopefully lead to new treatment possibilities for patients with PKND. Bone marrow transplant or gene therapy have been suggested as possibilities to replace the abnormal expression of cathepsin K will hopefully lead to new treatment possibilities for patients with PKND. Bone marrow transplant or gene therapy have been suggested as possibilities to replace the abnormal lysosomal protease expressed on osteoclasts. Until new treatment protocols are devised, education of these patients is essential to avoid the more serious complications of PKND. Because of the morbidity associated with orodontal findings, it is essential that these patients are enrolled in a dental prevention program from an early age. Stressing the importance of exceptional oral hygiene practices and early and frequent visits to the dentist is advised to allow early intervention to alleviate many of the serious complications previously described in the literature.

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References