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Pycnodysostosis. A report of 3 clinical cases

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Abstract
Pycnodysostosis is a rare clinical entity, first described in 1962 by Maroteaux and Lamy. It is a genetic disorder, usually diagnosed at an early age. However, the diagnosis is sometimes late, made as a result of bone fracture, given the severe bone fragility resulting from increased bone density. Oral and maxillofacial manifestations of this disease are very clear. The head is usually large, the nose beaked, the mandibular angle obtuse, and both maxilla and mandible hypoplastic. Dental abnormalities and impaction are observed, as well as alterations in eruption and frequent dental crowding. The differential diagnosis is established with osteopetrosis, cleidocranial dysplasia and idiopathic acro-osteolysis.
This article reviews the clinical and radiographic characteristics of pycnodysostosis based on three clinical cases of patients with this disease.

Key words: *Pycnodysostosis, bone dysplasia, maxillofacial alterations.*

Introduction
Pycnodysostosis is an autosomal recessive disorder, described in 1962 by Maroteaux and Lamy. These same authors speculated that the famous French painter, Toulouse-Lautrec (1864-1901), may have suffered from this disease (1, 2).
The principal characteristics of this syndrome are short stature, cranial dysplasia, obtuse angle of mandible, clavicular dysplasia, total or partial dysplasia of the terminal phalanges and generally increased bone density (1). The exfoliation of deciduous teeth is usually altered, as well as the eruption of the permanent dentition (3). The disease is usually diagnosed at an early age; the main reasons for consultation are usually short stature and open anterior fontanelles. In later ages, consultation is usually for fracture resulting from slight or moderate trauma, given the severe bone fragility (3, 4).
This review of the radiographic and clinical characteristics of pycnodysostosis allows the professional to make an early diagnosis and establish the differential diagnosis with other clinically similar conditions.

Clinical Cases
We present three clinical cases of patients attending the Oral Surgery Service of the Odontology Clinic, University of Barcelona who presented clinical and radiographic characteristics typical of pycnodysostosis.
- *Case 1* – Female patient, short stature (1.58 m), diagnosed with pycnodysostosis at the age of 38. No history of systemic pathology. Presented at the oral surgery service

with a pathologic bilateral fracture at the angle of mandible caused by mastication. Examination revealed facial asymmetry, limited mouth opening (20 mm) and pain at the points of fracture. The orthopantomograph (Figure 1) revealed non-pneumatized maxillary sinus, thin mandible, obtuse angle of mandible, malposed teeth and various radicular remains. The treatment involved bilateral mandibular setting and osteosynthesis after extracting a tooth located at one of the points of fracture.

- *Case 2* – Male patient with no medical history of interest. Pycnodysostosis had been diagnosed at the age of 45. Height 1.72 m, and presenting facial dysmorphia. The reason for the visit was edentulous and hypomobile mandible (10 mm maximum opening) with notable masticatory alteration. In addition to mandibular edentulism, the patient presented chronic periodontitis, obtuse mandibular angles and elongation of the condyle and coronoid apophyses (Figure 2).

- *Case 3* – Male patient who recently attended the Oral Surgery Service for the extraction of asymptomatic impacted teeth in preparation for prosthetic rehabilitation. Age 46, height 1.65 m, and with no pathologic history of interest. The examination revealed facial dysmorphia, impacted and malposed teeth, obtuse angle of mandible and chronic periodontitis. The maxillary sinuses were non-pneumatized and both the mandibular condyles and coronoid apophyses were elongated (Figure 3).

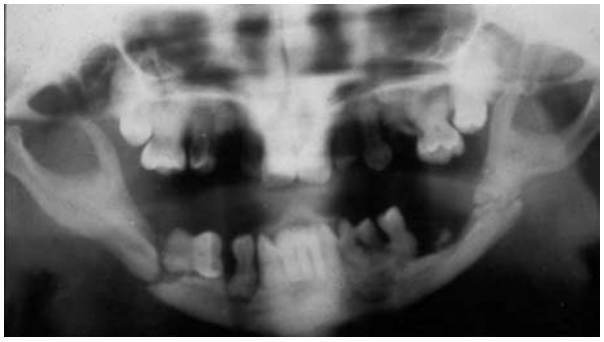

Fig. 1. Orthopantomograph Patient 1.

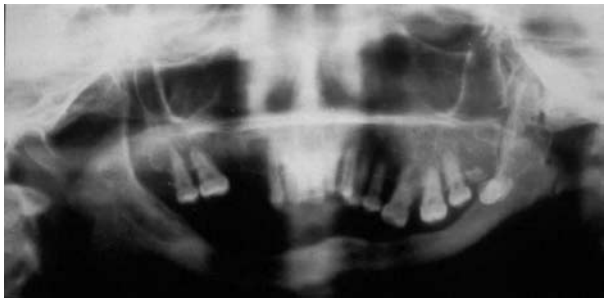

Fig. 2. Orthopantomograph Patient 2.

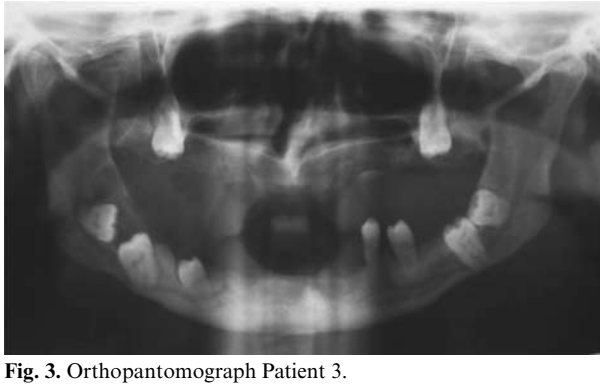

Fig. 3. Orthopantomograph Patient 3.

Discussion

The sclerosing activity of pycnodysostosis is due to a genetic defect located on chromosome 1q21. This anomaly consists of 12 different mutations (5) that produce mutational changes in a lysosomal cystine protease, cathepsin K, the expression of which is reduced in the osteoclasts of these patients (5, 6, 7). This protease is responsible for degrading collagen type 1, that constitutes 95% of the organic bone matrix.

When not diagnosed in infancy, fractures resulting from trauma usually lead to the diagnosis of this disease, as in the first clinical case presented. Mandibular fractures have been described in adults following extractions (8). This is a potential risk in the third clinical case. None of the clinical cases presented referred history of bone fracture, which would explain the late diagnosis of the disease in all these cases. The fractures occur due to the bone fragility, arising as a consequence of the high bone density (9).

A recent study (9) classified the various metabolic bone diseases according to the component of the affected bone matrix. Pycnodysostosis is included in those caused by low bone remodeling. Schilling et al. (10) in a study of cases and controls determined a volumetric bone density of 686 mg/cm in the group of patients with pycnodysostosis versus 290 mg/cm in the control group.

As with the cases herein presented, multiple orofacial manifestations have been described in the literature. We coincide in the facial dysmorphia, occipital and frontal bossing, long wide-based nose, receding chin and increased angle of mandible. This increase can be so exaggerated (almost 180°) that some authors define it as lost or straightened (1,3). This aspect is found in the three cases presented. The maxillofacial features described create a characteristic facial appearance, we therefore believe that the treatment of these patients at an early age may be beneficial, thus avoiding psychological trauma or inferiority complex. Norholt et al. (11) affirmed that due to the maxillary hypoplasia, these patients often present a Class III dentition. These authors defend the orthognathic correction by osteogenic distraction.

Other characteristics typical of pycnodysostosis are: dysplastic claviculae, dysplasia of the terminal phalanges,

elongation of the coronoid apophyses and the mandibular condyles, hypoplasia of the paranasal sinus and high-arched palate. Occasionally exophthalmos and blue sclera coexist (12).

Helfrich (13) asserts that in diseases where the formation and function of the osteoclasts is reduced, as is the case with pycnodysostosis, dental eruption is affected. This situation is confirmed in the third clinical case.

There may be dental abnormalities, with hypoplasia of the enamel, obliterated pulp chambers and hypercementosis. Protrusion of the incisors with anterior open bite may be found, and dental crowding associated with extensive caries and periodontitis is frequent. These conditions cause the premature loss of dentition that may already be complete by the fourth decade of life (3), a situation verified in all three clinical cases. Given that dental crowding impedes correct oral hygiene for the patient, some authors propose early treatment using orthodontic methods, although others argue that the lack of bone remodeling would impede satisfactory results, therefore planned and sequenced extractions would be more recommendable (12). Tooth extraction in patients who suffer from pycnodysostosis demands certain special care, such as carrying out the surgery as atraumatically as possible and with proper asepsis, due to the risk of fracture, especially in the mandible (3). In addition, the greater bone density increases the probability of developing post extraction osteomyelitis (8).

Another fact, verified in the three clinical cases studied, and usually a constant characteristic, is the short stature of the patients. For Soliman et al. (7) this is caused by the increased bone volume of the sella turcica that, on compressing the pituitary gland, causes its hypoplasia and a deficient production of the growth hormone.

Exceptionally, hepatosplenomegaly and hematologic alterations have been observed (7).

Another of the important alterations that usually affect these patients are respiratory problems. This was not seen in any of our cases. These conditions are due, above all, to a very long soft palate that may even come into contact with the base of the tongue (14).

The differential diagnosis of pycnodysostosis is established with osteopetrosis, cleidocranial dysplasia and idiopathic acroosteolysis. In osteopetrosis the bone marrow may be absent; it is therefore frequent for hematopoietic alterations to appear. Signs of compression of the cranial nerves exist such as facial paralysis, deafness or pain. Cranial dysplasia may seem like pycnodysostosis for presentation of agenesis or clavicular aplasia, as well as alterations of the skeletal bone membranes, however, bone density is not increased. In idiopathic acroosteolysis, the appearance of the patients is typical, with hypotelorism, exophthalmos and an upturned nose. The angle of mandible is acute and increased bone density is not present (3).

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