

Abnormal Dentition in an 8 Years Old Female Child

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Patient with shortening distal phalanx 1st finger both hands, from the birth and familiar precedents of similar abnormality. At the age of 8 she presented dental alterations with hipertrofia gingival and dental incorporations, and backaches and pain in femoral region. Radiology: increase of bony widespread density, hypoplasia lower jaw, and acrosteolisis distal phalanxes. The jaw biopsy (dental piece and alveolar surrounding bone): bony fragments are constituted for coarse and irregular trabeculas with importantly bony resorption and newly formed. Bone densitometry: T+5.2 in column lumbar and neck femoral. Gamma scan bone: diffuse captation of the axial skeleton. Diagnosis: picnodisostosis.

Dentición anómala en niña de 8 años

Presentamos el caso de una paciente con acortamiento de la falange distal del primer dedo de ambas manos desde el nacimiento y con antecedentes familiares de similares anomalías. A los 8 años presentó alteraciones dentarias con hipertrofia gingival e inclusiones dentarias, y dolores lumbares y en la región femoral. Las pruebas radiológicas evidenciaron aumento de densidad ósea generalizada, hipoplasia maxilar inferior y acrosteólisis de las falanges distales. Biopsia mandibular (pieza dentaria y hueso alveolar circundante): los fragmentos óseos están constituidos por trabéculas toscas e irregulares con importante resorción y neoformación ósea. Densitometría ósea: T +5,2 en la columna lumbar y el cuello femoral. Gammagrafía ósea: captación difusa del esqueleto axial. Diagnóstico: picnodisostosis.

Introduction

Picnodysostosis is a rare bone dysplasia that is transmitted in an autosomic recessive manner. It is due to a mutation

Figure 1. Orthopantomography: hypoplasia of the jaw. The left half of the jaw is radiolucid from the premolars to the second left molar, and in the region of the second right molar there are multiple radio-opaque inclusions.

in the 21, 1q chromosome, which inactivates cathepsin K, which plays an important role in the degradation of the bone matrix. The disease is characterized by a marked osteosclerosis in all of the axial and peripheral skeleton. The clinical characteristics and the radiologic alterations allow for a diagnosis.

This disease very likely affected the french painter Henri Toulouse-Lautrec (1864-1901).

Clinical Case

We present the case of a 32-year-old woman, who at the age of 8 presented diffuse bone pain in the femoral an lumbar spine area with marked dental alterations, a delay in deciduous and definite dentition, gingival hyperplasia and dental inclusions on the maxillary and jaw bones (Figure 1), requiring a gingivectomy at the age of 11. Her development otherwise had been normal (155 cm, 58 kg), she had a female karyotype 46XX. She presented shortening of all of the fingers on both hands, which was more evident on the first finger (Figure 2A), due to shortening of the distal phalanges (Figure 2B), and nail anomalies characterized by clubbing, hyperpigmentation and parched striae. The patient had required several maxillofacial surgeries up until the age of 18 and is currently asymptomatic.

She did not have any history of interest. Her paternal grandmother and her 5 brothers had hypoplasia of the

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Figure 2. A: current image of the first finger on both hands of the patient. B: x-rays of the hands: hypoplasia or acro-osteolysis of the tip of the distal phalanges.

distal phalanges of the hands and/or similar nail abnormalities than the patient; the family had a history of inbreeding.

The image tests observed a generalized increase in bone density with more trabecular and cortical bone and homogeneous osteosclerosis (Figure 3). Hypoplasia of the

Figure 3. Pelvic and spinal x-ray: generalized increase of the bone density with more cortical and trabecular bone. Homogeneous osteosclerosis.

jaw (Figure 1) with a radiolucid left half from the premolars to the second left molar and multiple inclusions. There was also acroosteolysis and hypoplasia of the distal tip of the distal phalanges (Figures 2A and B).

Laboratory Analysis

Hemogram: 3 series of normal characteristics. Serum chemistry: calcium, 9.5 mg/dL; phosphorus, 2.8 mg/dL; alkaline phosphatase (AP) of up to 1477 U/L at age 14, and still elevated (AP, 393 U/L). Twenty-four-hour urine: urine calcium, 178 mg/24 h; urine phosphate, 603 mg/24 h; tubular phosphate reabsorption (TPR), 87%; hydroxiprolinone, 65 (interval, 5-40) mg/24 h; hydroxiprolinone/creatinine, 45 (5-40) mg/1 g creatinine; desoxypyridinoline/creatinine, 80 (3-18) nmol/1 mmol creatinine; erythrocyte sedimentation rate (ESR), 6 mm/h; CRP <3.9 mg/dL; 25-OH-vitamin D, 66.7 (6-98) ng/mL; parathyroid hormone (PTH), 35 pg/mL.

Pathology

Jaw biopsy (tooth and surrounding alveolar bone): the bone fragments are constituted by gross and irregular trabeculae with an important resorption and neoformation of bone; with polarized light microscopy there is an evident absence of the brush-shaped border. In the interior of the wider trabeculae there are apposition lines forming a mosaic. There is also parched areas in which the stroma is more densely cellular and contains mineralized elements with the appearance of cementiculae.

Complementary Testing

Bone scan: diffuse uptake in all of the axial and appendicular skeleton. Bone densitometry: lumbar spine: 1617 g/cm² T +5.2 SD, Z +5.2 SD and femoral neck: 1769 g/cm² T +6.8 SD, Z +6.8 SD.

Analysis of the Complementary Tests

Laboratory findings reflected an increase in bone turnover, with an elevation of bone remodeling biomarkers, AP and hydroxiprolin in urine, as well as an elevation of the hydroxiprolin/creatinine ration and the desoxipiridinoline/creatinine ratio. The increased axial uptake of radioisotope reflected great bone metabolic activity with respect to the zones where uptake was normal. Bone densitometry showed an increased bone mineral density secondary to bone sclerosis.

Diagnosis

Picnodysostosis (Henri Toulouse-Lautrec's disease).¹

Discussion

The term is derived from the greek *pycnos*, dense; *dys*, defective; *osteos*, bone. Picnodysostosis is a rare disease with a prevalence of 1:1 000 000 inhabitants.¹ It is transmitted in an autosomic recessive manner, and is found more frequently in inbred families. It is due to a mutation that inactivates the K² cathepsin, an important protease in the degradation of collagen from the bone matrix, localized on chromosome 21, 1q. Osteoclasts, although quantitatively normal, a qualitatively deficient, leading to alterations in bone remodeling,^{3,4} with conserved bone demineralization but without achieving an adequate exchange of organic matrix. These alterations also lead to a reduction in bone reabsorption without completely abolishing it, with a net increase in the bone density and excessive formation of trabeculae.⁴

Picnodysostosis is a bone dysplasia clinically characterized by low stature with short extremities; micrognathia with an obtuse angle of the jaw, delay, or absence in the closure

of the cranial sutures and alterations in dentition with a retention of deciduous teeth and dental malocclusion, as well as enamel hypoplasia. In addition, hypoplasia or absence of the distal phalanges and nail dysplasia are characteristic of this disease.⁵ There can also be eye proptosis and clavicle hypoplasia with a lack of development of the acromial tip as well as aplasia of the ribs and defects of the hyoid bone.

X-rays show generalized osteosclerosis with a permeable marrow cavity. Cranial x-rays gives the impression of a mask due to the sclerosis of the bones of the nose and the lack of air in the paranasal sinuses. Fontanelles remain open without alterations in the foramina of the base of the cranium. Acro-osteolysis is frequently seen in the distal phalanges of the hands and feet.⁶ The spinal column can present a lack of atlanto-axial segmentation and spondylolistesis of the lumbosacral region.

Regarding the histologic appearance, it is characterized by an increase in the width of the cortical bone with bands of demineralized matrix on the surface of the bone due to a deficit of proteolysis, as well as large calcified inclusions in the cartilage.⁷ Defective osteoclasts with large undigested-collagen filled vacuoles can be seen. Electronic microscopy shows a larger number of mineral particles and a chaotic alignment as a result of the altered orientation of the collagen fibers.⁸ All of these changes lead to a considerable increase in bone frailty in these patients.⁹

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