
Unusual feature of pycnodysostosis: Pectus carinatum

Pycnodysostosis (MIM# 265800) is characterized by separated cranial sutures, dysplasia of skull bones, flattened mandibular angle, partial aplasia of the terminal phalanges, and increased bone density as detected radiographically. It is a rare, autosomal recessive trait. The responsible gene CTSK was mapped to the chromosome 1q21 and encodes for cathepsin K, a lysosomal cysteine proteinase critical for bone remodeling and resorption by osteoclasts [1]. Cathepsin K is well known to be highly expressed in osteoclasts, however there is little data about its expression in others cells or tissues. Rantakokko et al used Northern blots and in situ hybridization of mouse tissues to identify the specific cell types expressing cathepsin K. They found the highest levels of expression in musculoskeletal tissues and the strongest in situ signals were seen in osteoclasts and, to a lesser extent, in some hypertrophic chondrocytes [2]. Söderström M et al demonstrated that Cathepsin K mRNAs were predominantly seen in multinucleated chondroclastic and osteoclastic cells at the osteochondral junction of mouse long bones and on the surface of bone spicules [3]. Monko et al observed an up regulation of cathepsin mRNA expression in the knee joints of transgenic Del1 mice at the oncet of cartilage degeneration and cathepsin K was found near sites of matrix destruction in articular chondrocytes, particularly in clusters of proliferating cells, and in calcified cartilaginous matrix [4].
We report here, the first molecular diagnosis of pycnodysosyosis in Tunisia and an unusual feature of this disease: pectus carinatum which is, to the best of our knowledge, never been reported in this disease and we speculate on the pathogenesis of pectus carinatum in pycnodusostosis.

Case report
A 4-year-old boy was referred to our department for the management of a short stature. His parents are first cousins. There were no similar cases in his family. The child had a normal level of social functioning. Physical examination of the patient revealed short stature (- 3 standard deviations), exophtalmia, antimongoloid slant of the palpebral fissures, beaked nose, hypoplasia of the midface, large head, bulging of frontal and parietal areas of skull, open fontanels and separated cranial sutures, short stubby hands and feet and severe pectus curanitum (Figure 1). Intraoral examination revealed macroglossia, poor dental hygiene, dental crowding and dental caries. Plain radiography of the skeleton demonstrated increased bone density and a transverse fracture at the midshaft of the tibia with bone cal. CT scan and X–ray of the skull showed separated sutures, open fontanels, basal sclerosis, opened fontanels, wormian bones and obtuse angle of mandible (Figure 2). X–ray of hand showed tapering phalanges; the terminal phalanges were small. Based on these clinical and radiological features the diagnosis of pycnodysostosis is suggested. Blood investigations showed normal hemoglobin level, serum calcium (Ca), inorganic phosphate (PO4) and Serum alkaline phosphatase (ALP) concentration. This patient did not have a growth hormone (GH) deficiency; he showed a normal response to GH insulin provocation and the MRI of the brain including the hypothalamic-pituitary area showed cortical atrophy with normal anterior pituitary volume. Ophtamological examination revealed myopia. The molecular analysis of the CTSK gene revealed a homozygous missense mutation, a G-to-C transversion at nucleotide 541, predicting a gly146-to-arg (G146R) substitution: (p.G146R). On the follow up, this patient presented a mild head trauma without loss of consciousness. Skull examination showed an hematoma on the right frontoparietal region of scalp. Neurological examination was normal. Brain computed tomography showed a right frontoparietal extradural hematoma with minor compression and without skull fracture; no neurosurgery drainage of the extradural hematoma was performed. The brain CT scan was controlled 24 hour after the trauma and showed no impairment of the hematoma. The outcome was favourable with non operative management.

Figure 1 : craniofacial features, pectus carinatum, short hands and feats

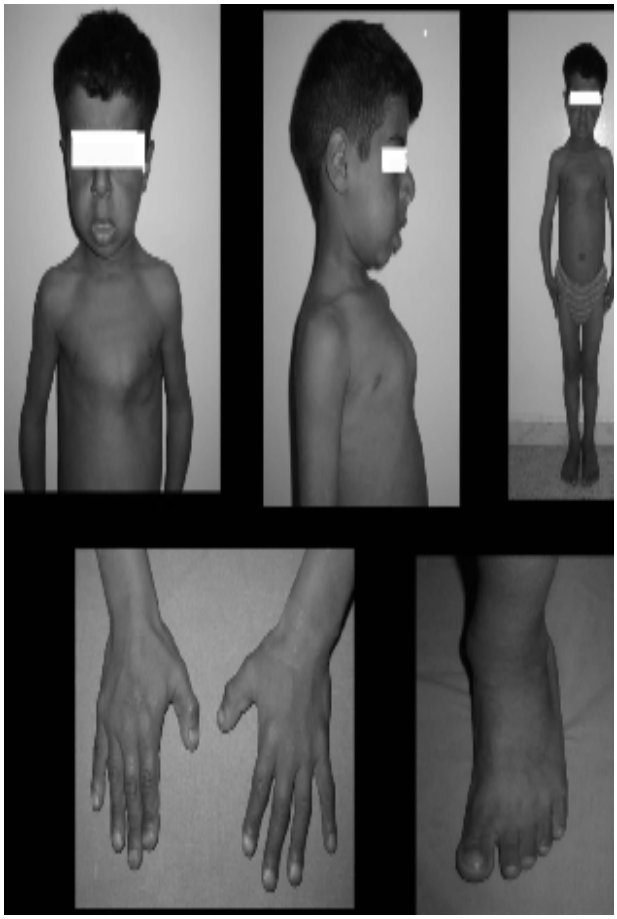
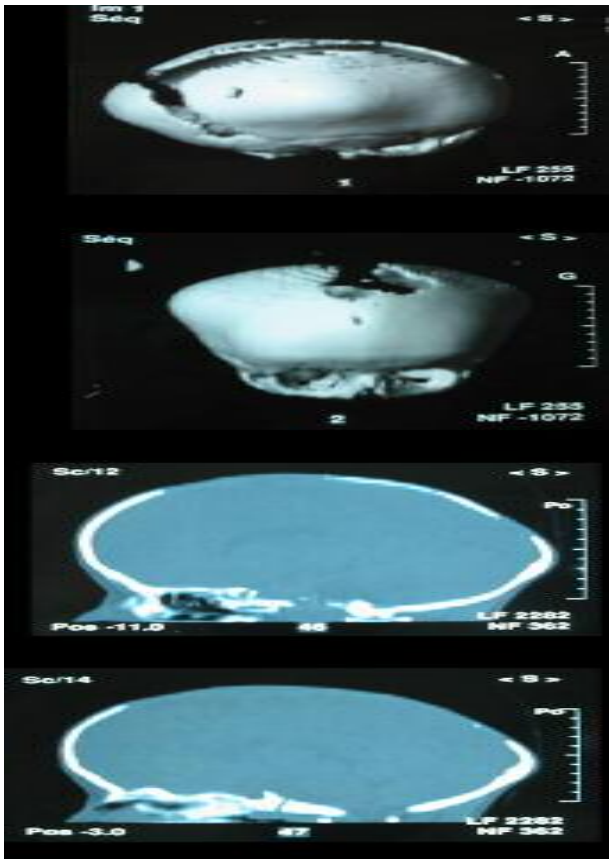


Figure 2 : CT scan and X- Rays of the skull showing open fontanels, separated cranial sutures and bulging of frontal and parietal areas of skull



Conclusion

This is the first molecular diagnosis of pycnodysostosis made in Tunisia and this mutation has been previously reported in 2 pycnodysostosis families, Moroccan Arab and American Hispanic [5]. Our patient had an unusual feature of pycnodysostosis: pectus carinatum and based on some reports in the literature [1-4]. and on our case, we suggest that chondrocytes of costal cartilage may also express cathepsin K and that its deficiency leads to decrease in degradation of the cartilaginous extracellular matrix and the overgrowth of costal cartilage and the development of pectus carinatum. This hypothesis should be confirmed by animal model lacking cathepsin k and the correlation between cathepsin K and pectus carinatum should be established.

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REFERENCES

1. Gelb BD, Shi GP, Chapman HA, Desnick RJ. Pycnodysostosis, a lysosomal disease caused by cathepsin K deficiency. Science 1996; 273:1236-8.

2.Rantakokko J, Aro HT, Savontaus M, Vuorio E. Mouse cathepsin K: cDNA cloning and predominant expression of the gene in osteoclasts, and in some hypertrophying chondrocytes during mouse development. FEBS Lett 1996; 393: 307-313.

3.Söderström M, Salminen H, Glumoff V, Kirschke H, Aro H, Vuorio E. Cathepsin expression during skeletal development. Biochim Biophys Acta 1999;1446:35-46.

4. Morko JP, Söderström M, Säämänen A-M K , Salminen HJ , Vuorio EI. Up regulation of cathepsin K expression in articular chondrocytes in a transgenic mouse model for osteoarthritis. Ann Rheum Dis 2004;63: 649-655.

5.Donnarumma M, Regis S, Tappino B, et al. Molecular Analysis and Characterization of Nine Novel CTSK Mutations in Twelve Patients Affected by Pycnodysostosis. Hum Mutat. 2007;28: 524 , DOI: 10.1002/humu.9490.

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Sarcoïdose systémique révélée par une atteinte naso-sinusienne

La sarcoïdose est une granulomatose chronique diffuse qui touche avec prédilection les poumons et le médiastin. La localisation ORL constitue l'une des atteintes extra thoraciques les plus rares (0,7 à 7%) [1]. Il s'agit habituellement de polyadénopathies cervicales, d'une atteinte parotidienne, laryngée ou pharyngée [2]. Les localisations naso-sinusiennes sont encore plus exceptionnelles. Nous présentons un cas rare d'une sarcoïdose multiviscérale révélée par une atteinte naso-sinusienne.

Observation

Il s'agissait d'une femme âgée de 44 ans**,** non tabagique**,** aux antécédents d'hypertension
artérielle et de tuberculose ganglionnaire correctement traitée il ya 4 ans, qui présentait depuis un an une rhinorrhée chronique avec jetage postérieur associée à une épistaxis et une obstruction nasale droite. Depuis quinze jours, elle rapportait une aggravation de la symptomatologie avec bilatéralisation de l'obstruction nasale devenant gênante et installation d'une dyspnée de repos paroxystique. Par ailleurs, l'interrogatoire retrouvait la notion de paresthésie au niveau du membre supérieur droit évoluant depuis 2 ans.

L'examen somatique trouvait une patiente obèse (BMI = 37 kg/m^2), apyrétique, eupnéique, une auscultation cardio-pulmonaire normale et une tension artérielle à 150/80 mmHg. Il n'y avait pas de douleur à la palpation des sinus ni d'ulcérations nasales évidentes. Les aires ganglionnaires étaient libres et l'abdomen était souple sans viscéromégalie. L'examen neurologique notait une diminution de la sensibilité superficielle au niveau des membres inférieurs.

Il n'y avait pas de syndrome inflammatoire biologique. La numération formule sanguine était sans anomalies. Les bilans rénal, hépatique et phosphocalcique étaient normaux.