Case study

PYCNODYSOSTOSE ASSOCIÉE AU STRIDOR: CASE REPORT

ABSTRACT

Pycnodysostosis is a rare genetic disease, caused by a mutation of the cathepsin K gene which is involved in bone renewal. It is associated with dwarfism and bone fragility, but the association with a stridor is exceptional. We report the case of a child treated for stridor with sleep apnea syndrome confirmed by sleep recording. His clinical examination showed stridor with laryngomalacia, the characteristic dysmorphism of pycnodysostosis and failure to thrive. The patient was put under non-invasive ventilation during evenings, and underwent ablation of adenoids, which resulted in a stable blood oxygen saturation. A surgery to lengthen the patient's mandibular is being considered, depending on her evolution. Practitioners should overlook this rare disease when faced with atypical stridor associated with high obstruction, failure to thrive and dysmorphism.

Keywords: Pycnodysostosis; Stridor; Sleep Apnea Syndrome;

INTRODUCTION

Pycnodysostosis or Toulouse-Lautrec disease is a rare autosomal recessive disease of unknown exact prevalence (between 1/100,000 and 1/1 million) [1], classified as an osteochondrodysplasia. It affects both sexes equally and is caused by a 1q21 mutation in the cathepsin K gene [2]. The absence of this protein, secreted by the osteoclasts, leads to a defect in the cleavage of the proteins of the bone matrix and the bone becomes abnormally fragile [3]. The arguments allowing the diagnosis to be made are: clinical, with growth retardation predominant in the limbs which are short and massive, fontanelle open or closing late, characteristic facial dysmorphism (macrocephaly, protrusion of frontal and occipital bumps, micrognathia, hypomaxillia with prominent nose, koilonychia, dental implantation defect with double row) [4]. The facial abnormalities of pycnodysostosis, such as micromandibuli or maxillary hypoplasia, are anatomical factors that can reduce the upper airway pathway. However, upper respiratory obstruction, leading to obstructive sleep apnea syndrome (OSAS), is rarely the main symptom of the disease [5–6]. We report a case of pycnodysostosis associated with stridor with OSAS.

CASE REPORT

The patient is a child aged two years and 4 months who was referred to our unit at two months of age for stridor. He is of first degree consanguineous parents. The interrogation revealed that the stridor dates back to birth. The examination found a dysmorphic syndrome made up of frontal hump, persistent anterior fontanelle, micrognathia, short fingers, with curved nails (Figure 1), glossopltosis and elongation of the soft palate. Asymmetrical thorax, scoliotic attitude of the dorsal spine, with significant stature delay (-3 standard deviations), cranial circumference 41 cm (+1 standard deviation). Chest CT angiography did not show any vascular abnormalities. Otorhinolaryngological examination in favor of mild laryngomalacia. The skeletal radiographs showed densification of the bones of the base of the skull, persistence of the anterior fontanelle, diffuse condensation of the rib cage and pelvis with a dense appearance of the spine (Figure 2), diaphyseal densification and metaphyseal long bones and hypoplastic phalanges (Figure 3). A computed tomography of the skull and the facial bone showed mandibular hypoplasia (Figure 4). In view of the clinical signs and radiological manifestations, the diagnosis retained is pycnodysostosis. Consultation with a geneticist subsequently confirmed the diagnosis of pycnodysostosis. Genetic counseling has been proposed for the family and the risk of recurrence, in the patient's couple, during subsequent pregnancies is 25%. The child is regularly taken care of in otolaryngology and orthopedics. Faced with chronic snoring with installation of obstructive sleep apnea syndrome (OSAS), a ventilatory polygraphy was performed and showed that the patient presents with obstructive sleep apnea hypopnea syndrome with a severe snoring index and desaturation index figured at 54.4/h. Our patient then presented the disease of pycnodysostosis with obstruction of the upper airways secondary to mandibular hypoplasia, the patient was then put on non-invasive ventilation during sleep, which made it possible to improve her saturation and reduce sleep apnea pending surgical treatment.

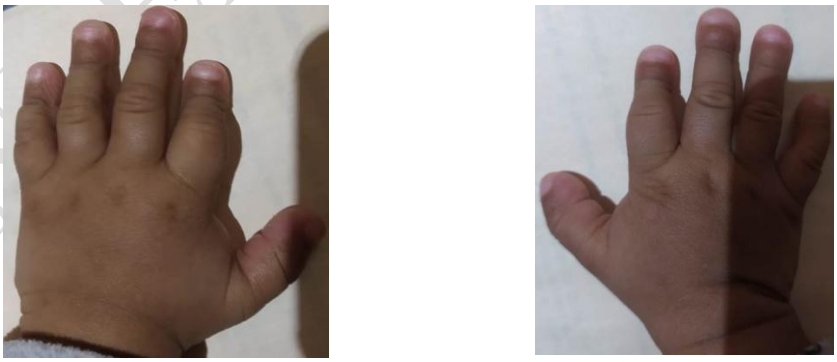

Figure 1 : short fingers, with curved nails

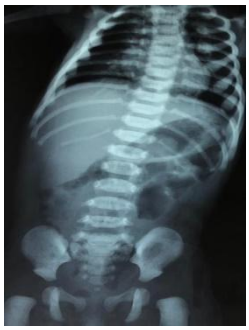

Figure 2 : diffuse condensation of the rib cage and pelvis with a dense appearance of the spine

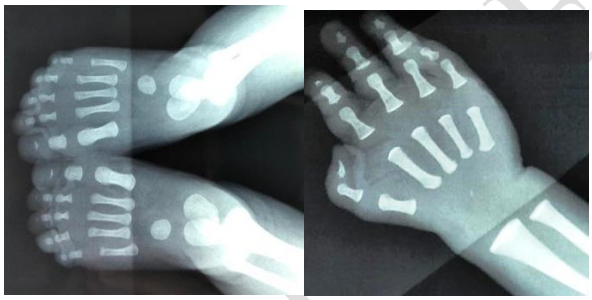

Figure 3 : diaphyseal densification and metaphyseal long bones and hypoplastic phalanges

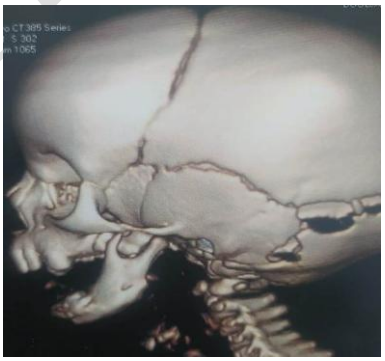

Figure 4 : mandibular hypoplasia

DISCUSSION

Pycnodysostosis is a rare autosomal recessive lysosomal genetic disease [7]. The most common clinical manifestations are dwarfism, acroosteolysis of the distal phalanges, bone fragility with spontaneous fractures and dysplasia of the clavicles. The characteristic cranial malformations are a bulky skull with the presence of wormian bones and persistence of the anterior fontanel, a small mandible, decayed, poorly implanted or abnormally shaped teeth. The nails are sometimes irregular and cracked. Respiratory distress and sleep apnea

are sometimes observed, at any age of life, but stridor is very rare. Diagnosis is clinical and should be confirmed by full skeletal radiographic examination and skull radiographs. A CTSK gene analysis may also be requested. The few respiratory obstructions associated with pycnodysostosis reported in the literature are located at different levels of the upper airways, at any age of life. Thus, in children, narrowing of the pharynx associated with glossoptosis has been described in two boys aged 4 and 5 years with pycnodysostosis [8]. Another case of narrow and obstructive cavum was reported in a 4-year-old boy [5]. Finally, mandibular hypoplasia was also implicated in the genesis of the obstructive syndrome in a 3-year-old boy [6]. In adults, a cephalometric study in two sisters aged 70 and 67 localized the narrowing to the pharynx by the association of maxillary and mandibular hypoplasia, glossoptosis and an excessively long soft palate [9]. The management of respiratory obstructive symptoms in pycnodysostosis depends on the level and severity of the obstruction. Thus, maxillofacial surgery can enlarge the pharyngeal canal in cases of marked bone hypoplasia. Lengthening of the mandibular ramus by bilateral rib graft to propel the base of the tongue forward was performed in a 3-year-old boy [6]. A Lefort I osteotomy with maxillary distraction for 6 weeks was performed on a 15-year-old girl [10]. Non-invasive ventilation is an interesting therapeutic possibility in children with OSAS of multiple etiology, daytime hypercapnia is the most often accepted criterion for initiating non-invasive ventilation (NIV). The occurrence of acute respiratory failure, particularly during superinfection, for example, is also a recognized indication for NIV.

Pycnodysostosis is caused by mutations in the gene for cathepsin K (located in 1q21), a lysosomal enzyme secreted by osteoclasts which allows the cleavage of proteins from the bone matrix (collagen type I, osteonectin or osteopontin).

CONCLUSION

Faced with atypical stridor associated with high obstruction, failure to thrive and dysmorphism, it is important not to overlook a rare disease. Pycnodysostosis is one of them and its early diagnosis makes it possible to detect and prevent its complications, which are bone fractures, head trauma and the consequences on the development of the child of a sleep apnea syndrome. The level of respiratory obstruction is variable and its precise identification allows appropriate treatment, often combining surgery and non-invasive ventilation. As this genetic is autosomal recessive, genetic counseling is important.

CONSENT DISCLAIMER:

We have added the Consent Disclaimer in the revised paper. The revised paper is attached herewith this mail for your kind perusal. Kindly check the revised paper.

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