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Dyggve-Melchior-Clausen Syndrom About A Case

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Abstract

Dyggve-Melchior-Clausen syndrome is a constitutional bone disease with autosomal recessive inheritance. It is characterized by the association of staturo-ponderal retardation, spondylometaphyseal dysplasia and mental retardation. The aim of our work is to describe this pathology clinically, radiologically and biologically. Treatment remains symptomatic, hence the importance of genetic counseling.

Keywords: Dyggve-Melchior-Clausen Syndrome, Osteochondrodysplasia, Staturo-Ponderal Retardation.

Introduction

Dyggve-Melchior-Clausen syndrome (DMC) is a constitutional bone disease with autosomal recessive inheritance. It is classified as an osteochondrodysplasia according to the 1977 Paris nomenclature of the European Society of Pediatric Radiology. The disorder is characterized as progressive spondyloepimetaphyseal dysplasia associated with intellectual disability. Clinically, the syndrome is characterized by osteochondrodysplasia and mental retardation, and radiologically, by specific radiological aspects of the disease that are sufficient to make a positive diagnosis, namely generalized platyspondyly with deformation of the iliac crests.

Biochemically, there is an absence of mucopolysaccharides in the urine. The gene responsible for this syndrome is located on chromosome 18q21.1. In this context, we report a case of DMC syndrome diagnosed in our department on the basis of clinical and radiological data. This patient also presented with an associated pancytopenia which, to our knowledge, has never been described in the literature.

Observation

A boy 7 years old, was admitted to management of staturo-ponderal retardation. He was the 3rd of 5 healthy siblings. His parents are 1st degree consanguines. He was born at term and he was breastfed for 2 months, Dietary diversification began at 6 months. Symptoms began at the age of 8 months, with delayed weight-bearing, worsening with age, delayed walking, which was acquired at the age of 3, delayed language, with first words at only the age of 5, and learning and memory disorders. Clinical examination revealed a child in fairly good general condition, a peculiar facies, delayed staturo-ponderal development with a weight of 14kg (-3DS), a height of 97cm (-3DS) and microcrania with a head circumference of 45cm (-4DS). The neck and trunk were short. Bone age was 7 years according to the Atlas of Greulich and Pyle.

The hands were large with short, pudgy fingers, and the lower limbs were in moderate bilateral genu-valgum. Thorax examination revealed sternal protrusion with thoracic and rib deformity. Neurological examination revealed a waddling gait, with no sensory or motor deficits. The child psychiatric approach revealed a significant psychomotor deficit. Ophthalmological examination was normal. Biologically a urine mucopolysaccharide test was negative. Standard radiographs of the spine from the front and side showed generalized platyspondyly with a "double hump" appearance of the vertebral bodies [fig.1].

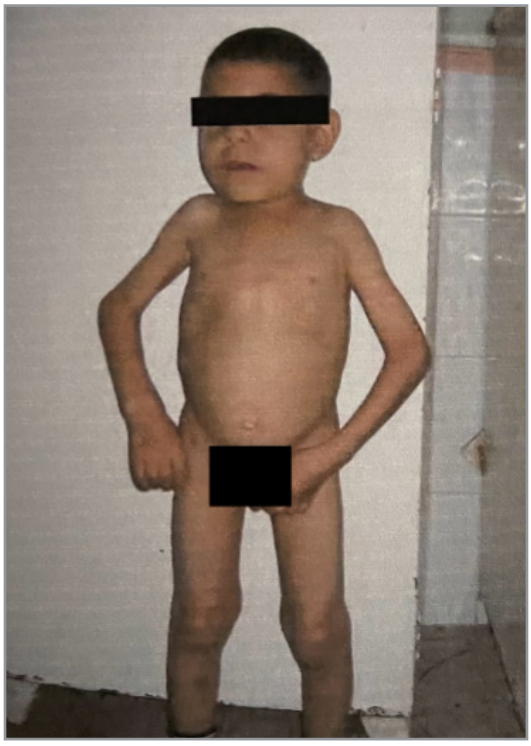

Figure: 1

X-rays of the pelvis revealed a scalloped areolar aspect of the otherwise small "bearded" iliac crests, a coxa-valga, an enlarged pubic symphysis and wide, irregular sacroiliac joints. Femoral necks were short, acetabular cups hypoplastic and femoral heads irregular, hypoplastic with diffuse demineralization [fig.2a and 2b]. The diagnosis of Dyggve-Melchior-Clausen syndrome was made in view of the association of mental retardation, a dysmorphic syndrome and, above all, the specific radiological aspects of this disease. A genetic study is in progress.

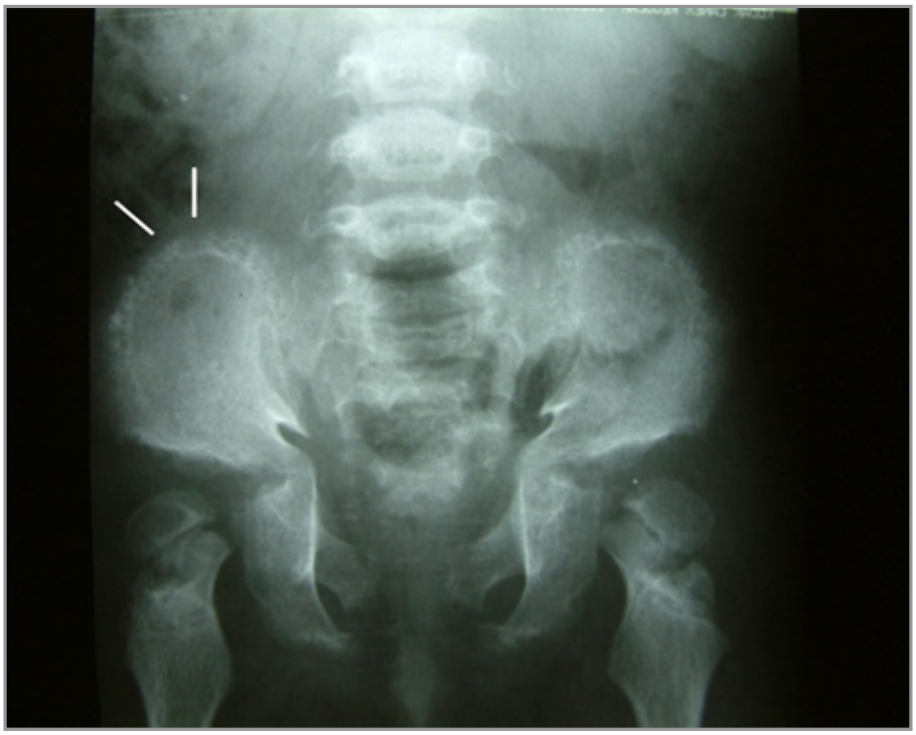

Figure: 2a

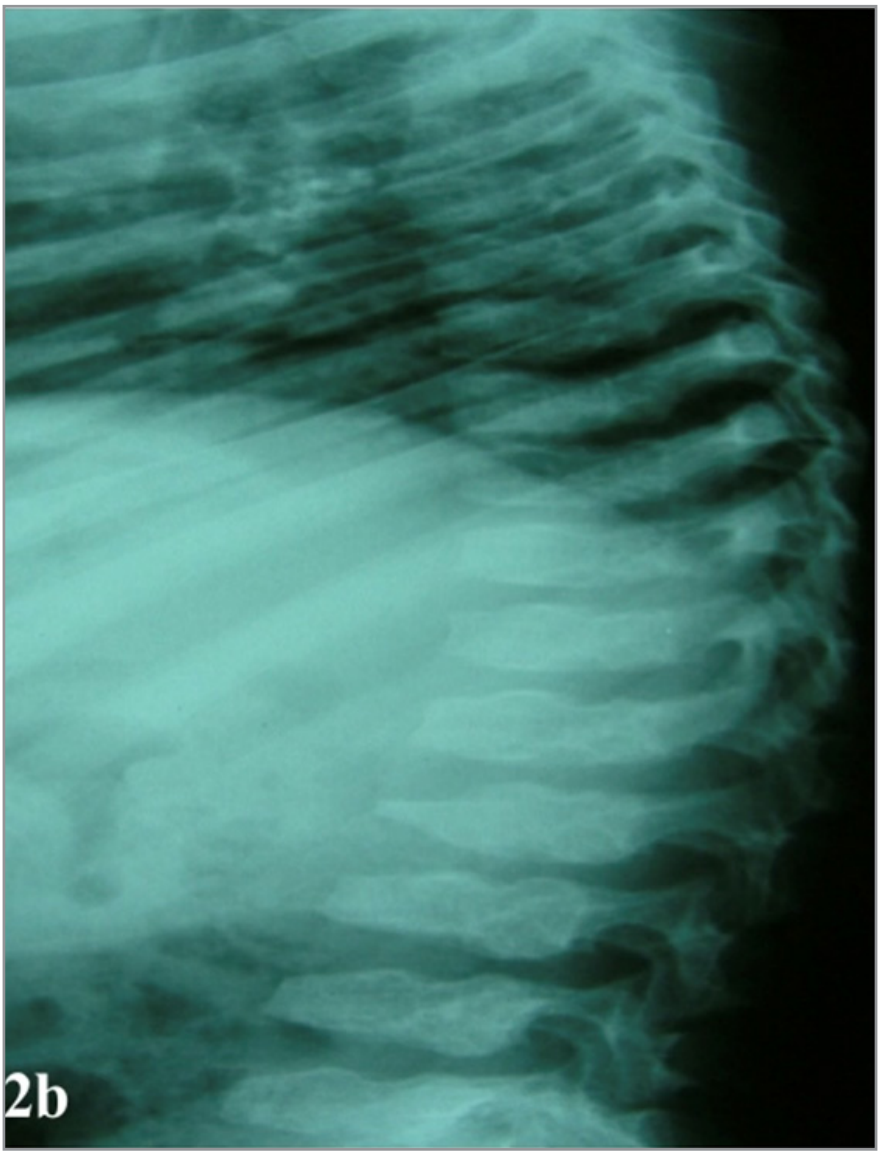

Figure: 2b

Discussion

DMC dysplasia is rare. It was first described en 1962 by Dyggve et al. And then en 1975 by Spranger et al. who completed the description of its clinical and radiological features Some sixty cases have been described in the literature to date [1, 2]. From an etiopathogenic point of view, a metabolic disorder secondary to a genetic anomaly has been evoked in DMC syndrome [3, 4]. The incriminating gene isthought to be located on chromosome 18q.21.1. In one study, the authors described 7 deletion-type mutations in this gene in the 10 families studied with the disease [5].

This gene encodes a protein called (Dyggve-Melchior-Clausen syndrome protein) or DYMECLIN, which is thought to play a role in the intracellular process of protein digestion [6]. Importantly, the transcribed product of this gene is abundant in chondrocytes, osteoblasts and nerve cells. In addition, biochemical analyses of cartilage fibres in carriers of the syndrome have shown elevated levels of keratan sulphate, and the presence of numerous vacuoles and cytoplasmic inclusions in chondrocytes [7]. Electron microscopy reveals large rough endoplasmic reticulum (RER) cisternae. Finally, clinical data and progressive evolution suggest that Dyggve-Melchior-Clausen syndrome is the result of the accumulation of an unidentified abnormal component [8-10].

Taken together, these findings suggest that Dyggve-Melchior-Clausen syndrome is due to the loss of function of a protein (DYMECLIN) involved in the intracellular digestion process and necessary for normal skeletal development and brain function. Clinical signs are evident before the age of 18 months, and include short-trunked staturo-ponderal retardation, poly- malformative syndrome and mental retardation. The absence of corneal opacity is highly suggestive of this dysplasia.

Staturo-ponderal retardation is present in all patients described in the literature and varies between -3 and -4 DS. The polymalformative syndrome may involve the skull, spine, thorax and

limbs. Cranial microcephaly is frequently described by authors [11-13]. Facial features are coarse, with prognathism. Protrusion of the tongue and protrusion of the superciliary arches can be observed. In the spine, there is generalized plathyspondyly with double hump vertebral bodies including central constriction, posterior protrusion of the intervertebral disc in the lumbar spine and widening of the posterior common vertebral ligament [14].

All curvature anomalies can be found and even associated with each other in the same patient. Dorsal kyphosis is the most frequently described deformity in the literature, followed by dorsal scoliosis and hyperlordosis. Odotoid hypoplasia confers instability on the atlantoaxial joint, which can lead to spinal cord compression, a preventable complication of the disease [15]. In the thorax, the most common feature is sternal protrusion, which can range from moderate to severe. The sternum protrudes like a barrel.

With regard to the limbs, the waddling and shuffling gait is noted by many authors. Other anomalies most frequently described in the literature include shortening of the proximal segments of the upper and lower limbs. Hands and feet are wide, with short fingers and toes, particularly the thumb. In the knees, a more or less severe genu-varum or valgum may be present. Limitation of joint mobility can affect both large and small joints, leading to more or less severe disability. Mental retardation varies from moderate to severe and worsens with age. This distinguishes CMD from another similar dysplasia, isolated by Spranger et al. En 1976, and referred to as Smith McCort syndrome (CMD syndrome without mental retardation or microcephaly).

In fact, both diseases are allelic expressions of the same mutated gene. In most people with CMD, MRI scans of the brain have been normal [16]. However, one observation of cortical atrophy has been reported. And another with atrophy of the corpus callosum [17]. Morquio disease is often confused with CMD, but differs in the presence of mucopolysaccharides in the urine, the presence of corneal opacity and distinct radiological signs. These radiological signs vary with age, but the most typical abnormalities appear between the ages of 8 and 12. Biologically, most biological tests are normal, including urine mucopolysaccharide tests. Other extremely rare manifestations, represented by 1 case of mania and 1 case of schizophrenia described en 2 separate observations [18].

From an evolutionary point of view, survival appears to be better than in mucopolysaccharidosis, but limb deformities increase with age, leading to motor disability, while mental retardation remains highly disabling and a source of great socioeconomic dependence.Treatment is essentially symptomatic, aimed at correcting skeletal deformities through orthopedic measures, and should also include psychomotor rehabilitation. When there is hypoplasia of the odontoid process with partial dislocation of the cervical vertebrae, stabilization by spinal fusion is recommended to prevent spinal cord-related paralysis. Surgery is also indicated to correct other skeletal anomalies such as subluxation or dislocation of the shoulder and hip joints, or to perform a hip prosthèses [19].

Conclusion

DMC is a rare osteochondroplasia. Diagnosis is based on clinical and, above all, radiological signs specific to this disease. We have attempted, through this new case diagnosed in our department, to bring together all the data specific to this disease. Advances in recent years have enabled us to identify the gene and coded protein involved in the genesis of this disease.This opens up new possibilities for optimizing prenatal diagnosis and finding a treatment for this disease, which remains essentially symptomatic actually.

Conflicts of Interest

The authors declare no conflicts of interest.

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