Bilateral Perthes Masking Morquio Disease

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Learning Point of the Article:
Perthes is a biological disease, its manifestations can mimic other conditions and it’s necessary to consider rare and treatable diseases in a child with limp or hip pain.

Abstract

Introduction: Perthes disease radiography can mask other diseases. Properly observing the X-ray and changes in other joints helps to discard Perthes-like conditions. Association with changes in other systems, as well as the pathological history and even the examination of family members can help diagnose early attenuated cases of rare diseases.

Case Presentation: The case of a girl with hip pain, limp and doubtful radiographs is presented. Perthes disease was diagnosed elsewhere and physical therapy and analgesics were prescribed. As a second opinion, family look for another orthopedic physician, who looks beyond hip pain and limp. Full body X-rays are suggestive of skeletal dysplasia. Metabolic disease diagnosis is suspected with pathological history of the younger brother, with repetitive respiratory infections, as well as abnormal X-ray panel. Multiple dysostoses in both patients are demonstrated. The above findings help to diagnose Morquio disease in an attenuated variant after molecular examinations.

Conclusion: Early diagnosis in progressive diseases is essential to avoid progression to multi-organ deterioration. It is important that physician become familiar with habitual characteristics of Perthes disease on the pelvis radiograph, in order to unsure the error in the diagnosis.

Keywords: Perthes, skeletal dysplasia, attenuated morquio, pelvis, mucopolysaccharidoses.

Introduction

Pelvis X-rays are a common study in the pediatric orthopedics’ practice. Of the changes observed in this study, they may suggest different diseases. Perthes disease shows changes secondary to necrosis in the femoral epiphysis, acetabular changes are rare, and other joint changes, null [1]; in skeletal dysplasia instead, bone changes are observed all over different joints. In metabolic diseases, bone skeletal changes are seen in conjunction with other non-skeletal manifestations [2].

Mucopolysaccharidosis IV A (MPS IV) also called Morquio syndrome, is a rare genetic disorder with autosomal recessive inheritance, is caused by total or partial deficiency of N-acetylgalactosamine-6-sulfate sulfatase enzyme. Consequently, an accumulation of glycosaminoglycans occurs in the lysosomes, interfering with the function of the cell. Its frequency is difficult to calculate due to high variability in the way it is reported in different countries or by different sources [3]. At birth, it ranges from 1/71,000 to 1/179,000 live borns (3, 4). It has been described as a disease with a broad spectrum of phenotypes, diagnosed in all ethnic groups. Its early detection is often hampered by broad variability in its manifestations. Typical cases usually take about 2 years to make the diagnosis after the onset of symptoms, but mild cases may be undiagnosed until adult age [4, 5, 6, 7].

Morquio’s disease manifests as a progressive skeletal dysplasia with disproportionate growth-producing multiple bone and joint deformities, airway obstruction, pulmonary restriction, and multiple damages in other systems. Without adequate treatment, these alterations have a negative impact on patients’
Case Presentation

It is a couple of brothers, male and female, 7 and 8 years old, respectively.

The 7-year-old female starts 3 months before her assessment with a right hip limp and mild pain worsened with physical activity (3/10 in a visual analogous scale of pain). There was no trauma history. Previously examined elsewhere, she is diagnosed as suffering from bilateral Perthes. Physical therapy, analgesics, and activity restrictions are prescribed (Fig. 1).

Consanguinity, family history of orthopedic or deposit diseases are denied. She is the third and last pregnancy of a 35-year-old mother, with a normal course and full-term regular delivery. No perinatal considerations are reported. Surgery at 1 month of life because of urachal canal persistency.

At physical examination, she is a patient weighing 24.3 kg (50th percentile, using the World Health Organization standards, 2006), size 116 cm (10th percentile). Length of arm stroke is 116 cm and height in sitting position of 63 cm, with a sitting size/standing size ratio corresponding to the average for his age. Facies with mild depressed nasal bridge, wide mouth, and thick lips. Complete mobility for the cervical spine. Apparent increase in lumbar lordosis. When flexing the trunk there is dorso-lumbar kyphosis (triangular), which is corrected in standing. In the upper extremities, there is a slight widening of wrists and interphalangeal joints, without any deformities in elbows or wrists. Joint mobility is normal and complete for hips,
Diagnosis of specific skeletal dysplasia is a real challenge. Few consider lysosomal storage diseases as differential diagnoses. Physicians involved in children management should Perthes, there is a need to purposely seek changes in other joints may coincide with localized bone diseases such as bilateral differential diagnostic’s exercise. When skeletal changes that reason for consultation, should alert the physician to expand Presentation of a child who has “bilateral Perthes disease” as a Antecedents on her brother were clue for suspicion. Perthes disease, based on pelvic radiographic findings. Cases shown warn us about wide and subtle variation in clinical Presentation of a child who has “bilateral Perthes disease” as a Antecedents on her brother were clue for suspicion. Perthes disease, based on pelvic radiographic findings. Cases shown warn us about wide and subtle variation in clinical...
for control group [1]. In these two studies, a great difference can be identified comparing acetabular index of 33° in patients with MPS IV versus 12° for severe Perthes group. Our two cases reported had acetabular dysplasia in both hips (20 degrees for male and 25 in girl, who’s initial consultation was intermittent hip pain).

There are few reports of late diagnosed MPS IV patients (even in adulthood) initially treated as localized orthopedic problems. Fang-Kircher reported a 51-year-old male with hip osteoarthritis, initially diagnosed as Perthes disease at 13 years of age; hip articular replacement was planned when diagnosis of MPS IV was confirmed [10]. Prat describes a French woman, who from childhood was diagnosed with multiple skeletal alterations, and despite not having a definitive diagnosis, was operated throughout her life by alterations in the cervical spine, hips, knees and before confirming the enzymatic deficiency at age 38. In addition, they report her brother of 35 years with a similar phenotype [14]. Mendelsohn reports three cases of late diagnosed mucopolysaccharidosis, one MPS VI patient and one of the two MPS IV patients were initially diagnosed as bilateral Perthes disease. In all three cases, confirmation diagnosis was delayed because normal urinary glycosaminoglycans levels (uGAGs). Due to the lack of consistency to find high urinary levels of GAGs in the MPS, the authors suggest maintaining a high index of suspicion despite normal urinary levels of GAGs and underline the importance of molecular diagnosis [8, 15]. Rush reported a 15-year-old adolescent, with low back and right hip pain, initially diagnosed as avascular necrosis of the hip. He had a decrease in bone mineral density and vertebral changes initially considered as probable compression fractures. Later, platispondilia was confirmed. As in the previous report, uGAGs were normal. Diagnosis of MPS IV was made by sequencing exome due to the non-specificity mutation after he was approached as a probable spondyloepiphyseal dysplasia [7, 9].

More than 180 different mutations have been identified in the GALNS gene responsible to MPS IV. As an example, in genetic study for 163 MPS IV patients, Morrone, reported in 2014 a total of 39 “new” mutations not previously described [15]. Many mutations identified have been associated with attenuated variant of the disease. In 2007 Montaño recognize as many of 25% of their patients might be classified as attenuated phenotype. These patients are often diagnosed after 10 years of age; several years after the onset of symptoms (average 2.1 and 4.1 years of age) [3, 4]. Among the 326 participants on the International Registry of Morquio A in 2007, the diagnosis was made average at 4.7 years of age, while symptoms were initially recognized between 1 and 3 years (average of 2.1 years); In addition, 16% of cases were diagnosed between 5 and 10 years and 8% after 10 years (4). On the other hand, variability in phenotypic expression of the disease has been directly associated to residual enzymatic activity, especially in attenuated phenotype [2]. In addition to specific mutations, clinical factors have been associated with the classification of attenuated phenotype, particularly height and severity of symptoms; however, there are no unified criteria for categorization. Availability of clinical criteria for the early diagnosis of the disease could influence earlier identification in attenuated cases, which could help earlier treatment and prevent cumulative damage at older ages [6].

**Conclusion**

There are many factors that may delay early diagnosis in MPS IV. Children with disease appear healthy at birth. Subsequently, initial clinical manifestations vary due to great heterogeneity of mutations in GALNS gene, some of which have correlation between genotype-phenotype [6]. In Morquio’s disease, skeletal features are first clinical manifestations before diagnosis [4, 5]. Although phenotype is variable, multiple dysostosis is a constant finding on these patients. The X-ray of “bilateral Perthes disease at the same stage” should be an alert for a detailed patient study before planning any therapeutic intervention.

**Clinical Message**

Clinical and radiographic assessment in children is not always easy. Minimal not characteristic changes of a disease should alert the physician to look for other causes of disease, which will improve patient’s prognosis at an early age.

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**Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient’s parents have given their consent for patient images and other clinical information to be reported in the journal. The patient’s parents understand that his names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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