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Atypical Spondylo-Epiphyseal Dysplasia in an Adult Male Patient

Spondylo-epiphyseal dysplasia is a genetic disorder, resulting in the dysfunction of type II collagen (the major collagen of cartilage).

We present a 17-year-old male with a history of mechanical pain predominantly in the lumbar spine and joints of the lower extremity for one year, who was previously diagnosed with and treated for spondylo-arthropathy, with normal laboratory test results but severe radiographic abnormalities in the form of generalized osteoarthritis of pelvic and knee joints. The patient was a case of late-onset spondylo-epiphyseal dysplasia.

Keywords: epipysial dysplasia, spondylo-epiphyseal dysplasia

Introduction

Osteochondrodysplasia consists of a great variety of dysplasias, characterized by abnormal growth of bone and cartilage.[1,2] The condition is classified as epiphyseal, metaphysical, and diaphysial according to the section of the bone involved. Osteochondrodysplasia is divided into different types according to whether the defect involves the tubular spinal bones or the cartilage. When the vertebrae are involved, the disorder is termed as spondylo-epiphyseal dysplasia (SED).[2, 3]

Chondrodysplasia, or enchondromatosis, results from primary defects in the metaphysis. Metaphysial dysplasia or spondylo-epiphyseal dysplasia can be misdiagnosed for rickets due to their similar radiographic pictures, but unlike rickets, the laboratory findings are normal despite the general demineralization of bones.

Recent advances in DNA regeneration and mapping of the human genome have led to the identification of the genes that cause skeletal dysplasias. The disorder is mainly autosomal dominant; however, some cases have been found to be autosomal recessive.[4,5] Genetic studies on the responsible defective genes suggest that the encoded proteins are crucial for the normal growth and development of the skeleton.[6] Recently, Type II pro-collagen gen (Col2A1) mutation has been reported in patients with mild forms of spinal chondrodysplasia associated with the precocious onset of generalized osteoarthritis.[4,5] A type II procollagen mutant gene has been reported in this group.[7]

Spondylo-epiphyseal dysplasia presents as a wide variety of clinical manifestations, resulting from the dysfunction of collagen type II, which is the chief constituent of cartilage.[2] In severe cases, various cartilages and other tissues containing type II collagen are involved, while in mild cases only articular cartilages are affected. The clinical picture of severe cases is characterized by short trunk, disproportionately long extremities, broad face, cleft palate, short neck, barrel chest and limitation of the range of movement of the joints (reduced extensity and flexibility). As for the linear growth, scoliosis, kyphosis, and lordosis of the spine can occur, which may result in severe respiratory problems.

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Radiologically, peripheral joints show incomplete and abnormal epiphyseal ossification, reduced joint space, sclerosis, and osteophyte, with joint deformity.[6] Radiological examination of the axial joints show reduced vertebral height and increased vertebral length-to-height ratio. In neonatal cases, the vertebrae are pear-shaped, due to growth failure in posterior part of the vertebral body. In young children, anterior wedging and generalized irregularity and flattening of the body of the vertebrae, combined with kypho-scoliosis and lordosis of the spine occur. The interpediculate distance in the lower vertebrae may be narrowed.[6]

Majority of the late-onset spondylo-epiphyseal dysplasia shows X-linked recessive inheritance. The condition is often not diagnosed until degenerative arthritis develops in the shoulders and hips in late childhood or early adulthood. The radiographic findings in the femoral capital epiphyses and proximal humeral epiphyses, which are difficult to distinguish form multiple epiphyseal dysplasia. The spine is not only more severely affected, but also is characteristic.[8,9]

Pelvic radiography reveals delayed ossification of the pubis and proximal femur. Hips are nearly always affected, with abnormal ossification of the capital femoral epiphyses leading to a flattened femoral head, the acetabulum is usually affected; and protrusion of acetabuli is often seen.[7] Developmental coxa vara occurs due to precocious osteoarthritis of the femoral joints. In these patients, the thorax is flattened and bell-shaped, with a reduction in the scapular height (they become short and squared), and flattening of the frontal ends of the ribs due to delayed ossification of sternum. There is also delayed epiphyseal ossification in tubular bones. The epiphyses and diaphyses are flattened and irregular. Bilateral genu valgum and genu varum may also be present.

In late-onset spondylo-epiphyseal dysplasia (late-onset SED), which occurs due to mutation in the genes governing the production of type II collagen, the patient manifests precocious osteoarthritis of the weight-bearing joints, with otherwise natural skeletal growth, without other significant skeletal disease ,thus, many of these patients are of normal stature and have no other abnormalities.[2] The term "familial (or autosomal dominant) osteoarthritis" sometimes is used to describe this syndrome. Recurrent mutants of type II collagen gene have been observed in a few instances of familial osteoarthritis. Mutation in an X-linked gene that codes a protein termed sedlin can produce a similar but clinically distinct picture in males, which is called SED tarda.[2]

The case that is introduced here is a rare case of late-onset spondylo-epiphyseal dysplasia.

Case Report

The patient is a 17-year-old male with a history of severe back pain of mechanical type for one year. He reported morning stiffness of 30 minutes in the lumbar spine, which had gradually got worse and longer. He had frequently sought medical care and was prescribed various palliative treatments for mechanical back pain, as well as standard treatments for spondylo-arthropathy, which had made some improvement in his symptoms. The patient experienced severe pain in his right knee following physical activity, which was alleviated with rest and physiotherapy. A few months later, the patient felt pain in his left knee, and on both sides of his neck, with no obvious systemic signs and symptoms (e.g. fever, convulsion, reduced appetite, etc.).

The patient's most recent complaint was persistent intensifying pain, which interfered with his daily activities. He was admitted to hospital for clinical investigation. He had no underlying disease, and took no medication except for some occasional over-the-counter analgesics. He reported no familial disease. The physical examination of head, face, heart and lungs, and abdomen were normal. The thorax showed no sign of deformity and the skin was perfectly normal. Upper extremities were symmetrical without muscular atrophy. The shoulders, elbows, and wrist joints had normal active and passive flexion and extension. The peripheral pulses and the tendon reflexes were symmetrical and normal. The patient was 174 cm tall and had an arm span of 177 cm. At the supine position, the lower extremities were maintained in a flexed antalgic position. He was unable to extend either of his lower extremities. Mild symmetrical atrophy of quadriceps muscles were noted. Hip joints were painful bilaterally and active and passive movements of hips were greatly hindered. Both knees

pheral pulses and the tendon reflexes were symmetrical and normal. Examination of the spine showed no sign of kyphosis, but there was a mild scoliosis. Schober test and thoracic expansion test were normal. Pelvic radiography revealed flattend femoral head. Protrusion of acetabuli was seen too (Figure1).
Radiological examination of the axial joints showed reduced vertebral height and increased vertebral length to height ratio. Anterior wedging and flattening of the body of the vertebrae was seen (Figures 2 and 3). Laboratory test results are showed in table 1.

Table 1. Laboratory Test Results:

WBC	7800 (PMN 85%) /mm^3
Hb	12.7
PLT	315,000 /mm^3
ESR	10 mm/h
CRP	Negative
Latex	Negative
Creatinine	0.8 (0.6-1.2 mg/dL)
Urine analysis	Normal
TSH	2.3 (0.4-4.2 mU/L)
Calcium	9.7 (9-11 mg/dL)
Phospate	4.3 (3-4/5 mg/dL)
Alkaline phosphotase	150 (25-100 U/L)
Wright	Negative
Widal	Negative
HLA B_{27}	Negative

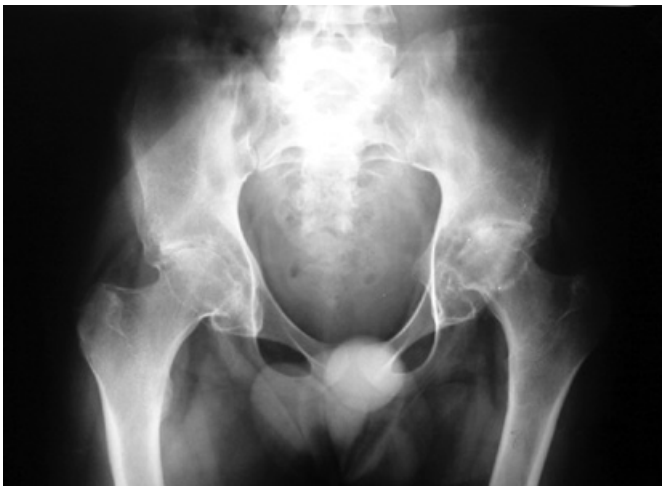

Fig 1. Pelvic x-ray: Note the deep acetabula.

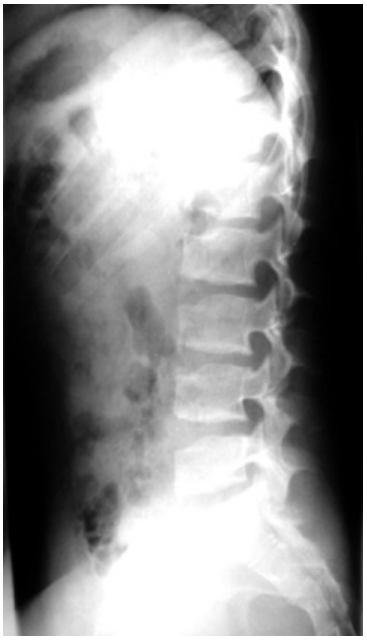

Fig 2. Spine radiographic changes in the spine are progressive; heaping up of the posterior portion of the superior vertebral plate is evident, is particularly distinctive, at first glance, the late changes.

Discussion

Epiphyseal dysplasia is an autosomal dominant disorder, which, can vary in clinical picture, depending on the degree of the underlying dysfunction of type II collagen, as mild spondylo-epiphyseal dysplasia combined with precocious generalized osteoarthritis. It is classified as the late-onset type of the disorder. Spondyloepiphyseal dysplasia tarda (SEDT) is a genetically heterogenous disorder often associated with the early-onset osteoarthrosis. The X-linked recessive form (SEDL) affects men and is characterized by short stature, arm span exceeding total height, and barrel chest deformity. The radiographic phenotype comprises a hump-shaped deformity of vertebral bodies and mild epiphyeal dysplasia of the femoral head associated with early signs of hip arthrosis, the disorders is caused by mutations in the SEDL gene on Xp22.12–p22.31.[10] The distinctive radiological signs and the X-linked mode of in heritance make it easy to diagnose.[11] The differential diagnosis includes Legg-Perthes disease, which is distinguished by being asymmetric, involving the metaphysis, sparing the acetabulum, and usually improving spontaneously.

Our patient was diagnosed as SEDT according to the typical radiographic features. We could not perform genetic tests, since the tests were not available. All laboratory tests for inflammatory diseases, such as ESR and CRP were normal, and HLA B27 was negative. The patient had a negative family history of this disease. So, we report this patient as a rare form of SED in a young male patients, and hence called spondylo-epiphyseal dysplasia tarda (SEDT).

In regard with the rarity of the disorder, no clear-cut epidemiological pattern has been defined. Moreover, in its early stages, there are no characteristic

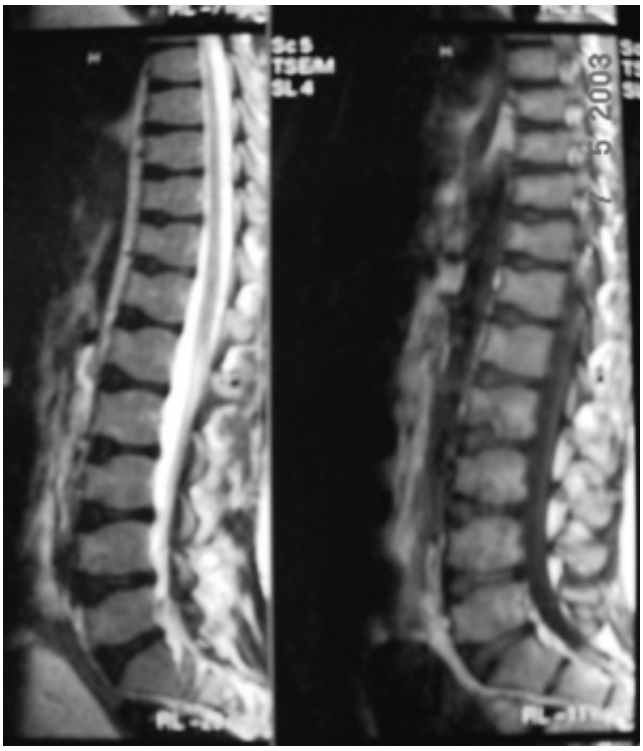

Fig 3. Anterior wedging and flattening of the body of the vertebrae are seen.

over, in its early stages, there are no characteristic clinical or other diagnostic features of the disorder. It is therefore highly recommended that in young adult and adolescent patients presenting with atypical musculoskeletal pains, the possibility of SED should be kept in mind. The patient is to be advised to change his lifestyle and start an appropriate exercise regimen in order to slow down the degenerative and destructive progress of disease, which otherwise can entail enormous diagnostic and therapeutic costs.

Spondylo-epiphyseal dysphasia tarda (SEDT) should be kept in mind as a differential diagnosis in men with an early onset of back pain and radiological abnormalities of the vertebral bodies such as platyspondyly.

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