

## Spondyloepiphyseal dysplasia tarda with progressive arthropathy

Ece Kaptanoğlu<sup>1</sup>, Ferda Perçin<sup>2</sup>, Sıtkı Perçin<sup>3</sup>, Ayça Törel-Ergür<sup>4</sup>

Departments of <sup>1</sup>Rheumatology, <sup>2</sup>Genetics, <sup>3</sup>Orthopedics and Traumatology, and <sup>4</sup>Pediatrics, Cumhuriyet University Faculty of Medicine, Sivas, Turkey

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Spondyloepiphyseal dysplasia tarda with progressive arthropathy (SEDTPA) is a rare autosomal recessive skeletal dysplasia affecting primarily the articular cartilage. Here we present a nine-year-old girl from Middle Anatolia (Sivas) with SEDTPA. Her complaints were pain and progressive deformity of the joints. She had a short stature with increased thoracic kyphosis and lumbar lordosis. The range of motion was limited in the spine and the peripheral joints and she had deformities. Radiologic examination revealed generalized platyspondyly and irregularity of the vertebral endplates. There was minimal joint space narrowing at proximal interphalangeal joints, but there were no bone erosions. Metaphyses were widened and epiphyses were squared in other joints with generalized osteopenia and severe osteoarthritic changes prominent in hips. Laboratory examination revealed a mild increase in acute phase reactants. Genetic disorders like SEDTPA may also have rheumatological involvement, so they should be kept in mind in differential diagnosis of inflammatory joint diseases.

**Key words:** spondyloepiphyseal dysplasia, pseudorheumatoid arthropathy.

Spondyloepiphyseal dysplasia tarda with progressive arthropathy (SEDTPA) is an autosomal recessively inherited skeletal dysplasia, which primarily affects the articular cartilage<sup>1</sup>. The disease begins mostly between the ages of 2-8 years with abnormal gait and fatigability<sup>2</sup>. The nature of the disease is progressive and clinically indifferent from juvenile idiopathic arthritis (JIA)<sup>3</sup>. Though rare, because of this resemblance, diagnosing this entity is important to prevent inappropriate treatment.

Here we describe an Anatolian girl with SEDTPA and discuss the clinical and laboratory features of the case reviewing the literature.

### Case Report

A nine-year-old girl from Middle Anatolia (Sivas) was admitted to our clinic with complaints of pain and progressive deformity of the joints, which were first noticed at three years of age. She was the first child of third-degree consanguineous parents. Family history was unremarkable, and other siblings were healthy. Her first symptoms began as difficulty in walking and genu varum deformity of both

knees at the age of three years. She was diagnosed as Blount's disease, and bilateral tibial osteotomy was performed when she was five years old. However, she suffered progressive stiffness and pain in all joints and a generalized muscle weakness in the following years. She was diagnosed as JIA and started on antirheumatic drug therapy but her condition deteriorated further.

At the age of nine, she was admitted to our clinic. On physical examination, she had an antalgic and stiff gait. She had a striking growth retardation with normal mental and motor development. Her height was 118 cm (below 3<sup>rd</sup> centile), and weight was 22.5 kg (below 3<sup>rd</sup> centile). Her vital signs were stable. Her systemic examination was normal, including the eyes; chest; and cardiovascular, abdomen and genitourinary system examinations.

There was a minimal redness on her cheeks. She had a short stature with increased thoracic kyphosis and lumbar lordosis (Fig. 1). The range of motion (ROM) was limited in the neck, as in the rest of the spine. Shoulders, elbows and wrists were minimally painful and ROM was

limited to 25% in the elbows and wrists, where swelling was observed. Metacarpophalangeal joints and interphalangeal joints were painful. There were bilateral mild flexion deformities in interphalangeal joints where spindle-shaped swelling was also prominent (Fig. 2a, 2b). She

was unable to make a fist. Hips were painful and ROM was severely limited. Bilateral operation scars were noted in the anterior part of the legs. Knees were painful, ROM was limited and there were bilateral genu valgum deformities. There was an increase in warmth in the left knee and



Fig. 1. Photograph of the patient showing the slightly reddened cheeks, generalized atrophy of the body, short stature, swelling in the elbows, knees and ankles, and bilateral pretibial operation scars. There are also flexion contractures in the hands and genu valgum deformity in the knees.



(a)



(b)

Fig. 2. a) Photograph of the hands showing the fusiform deformity and mild flexion deformities of the proximal and distal interphalangeal joints. b) Widened ends of the shafts of the phalanges and abnormally shaped epiphyses are shown. There is also minimal joint space narrowing at proximal interphalangeal joints without bone erosions.

left ankle, but neither redness nor effusion was detected. She had bilateral pes planus deformity. Neurologic examination was normal other than a generalized muscular atrophy and weakness, thought to be due to disuse.

Radiologic examination of the spine revealed osteopenia, generalized platyspondyly and irregularity of the vertebral endplates (Fig. 3). Phalangeal metaphyses were enlarged and epiphyses were irregular and flattened. Minimal joint space narrowing was observed at proximal interphalangeal joints, but there were no bone erosions (Fig. 2b). Metaphyses were widened and epiphyses were squared in other joints with generalized osteopenia and severe osteoarthritic changes especially prominent in hips.



Fig. 3. Lateral thoracolumbar graph showing platyspondyly, anterior wedging of the vertebrae and irregularity of the endplates prominent at the dorsolumbar junction.

Laboratory data were as follows: complete blood count, anti-streptolysin O titer, serum electrolytes, liver and kidney function tests, and muscle enzymes were within normal limits. Erythrocyte sedimentation rate (ESR) was

17 mm/hr and 35 mm/hr on two different occasions, and C-reactive protein (CRP) was 12.8 mg/L (N: 0-6 mg/L). Rheumatoid factor, antinuclear antibody, and anti-dsDNA were negative. C3, C4, immunoglobulins and thyroid function tests, and parathyroid hormone level were normal. Hepatitis markers and group agglutination tests (*Salmonella*, *Shigella*) were negative. All cultures were negative, including throat, stool, urine and blood cultures. Electromyogram (EMG) and muscle biopsy were evaluated as normal and mucopolysaccharides were negative in the urine. Her karyotype was 46, XX.

She was diagnosed as SEDT-PA and was started on ibuprofen 100 mg tid, and her pain diminished to a significant degree. The family and the patient were informed about the disease, joint protection and exercise programs.

### Discussion

Spondyloepiphyseal dysplasia tarda with progressive arthropathy is a generalized bone and cartilage dysplasia; however, it differs from other spondyloepiphyseal dysplasia syndromes in the severity of the disease<sup>4</sup>. The presenting complaints may be walking difficulties, muscle weakness, pain and swelling in the joints (especially in the hands), and deformities of the knee in the form of either genu valgum or varum. Involvement of the spine and epiphyses of bones, leading to short stature and thoracic kyphoscoliosis, and pain, swelling, stiffness and contracture of the hands, hips, elbows and feet are specific. Because of this clinical involvement, diseases like JIA, Scheuermann's disease, mucopolysaccharidoses, and hypothyroidism should be ruled out<sup>5</sup>. However, the differentiation between JIA and SEDT-PA is challenging, and most cases are misdiagnosed in the beginning as JIA, as with our patient.

Characteristic radiologic findings of the disease were platyspondyly, enlargement of the epiphyses and both ends of the short tubular bones of the hands, generalized osteopenia and secondary osteoarthritis, and the absence of erosive changes<sup>6</sup>. The absence of systemic signs, history of consanguinity of the parents and a poor response to antirheumatoid treatment were among the other important features which guided us in diagnosis of SEDT-PA in our case<sup>7</sup>. Despite all the well-known features of the disease, there are still some complicated aspects. Inflammatory laboratory findings and



clinical signs of synovitis are known to be unusual in SEDT-PA<sup>8</sup>. However, one of the striking features of the disease is the accompanying secondary osteoarthritis, which seems to be the real reason for the functional deterioration and disability. Though a non-inflammatory disease, osteoarthritis is sometimes characterized by variable degrees of joint inflammation, which correlates with acute phase reactants<sup>19</sup>. Our patient also suffered an increased pain in her joints, signs of inflammation and a minimal increase in the acute phase reactants, which were thought to be relevant to secondary osteoarthritis.

To date, extraskeletal manifestations have not been reported in SEDT-PA, and cartilage appears to be the primarily affected tissue. Since patients continue to have cartilage loss and destructive bone changes during their growth period, in some cases joint replacement surgery is necessary by the third decade of life. When our patient was five years old, bilateral tibial osteotomy was performed. This operation was necessary for the patient's normal development although she was misdiagnosed as Blount's disease.

About two-thirds of the reported patients are of Arabic and Mediterranean origin, which reflects the relative high incidence in this population. To the best of our knowledge there are five reported cases from Turkey, which supports this observation<sup>1,4,7,8,10</sup>. After mapping of SEDT-PA locus to 6q22 region, Hurvitz et al.<sup>13</sup> identified nine different WISP3 gene mutations, which map to same region of 6q, in unrelated affected individuals, indicating that the gene is essential for normal postnatal skeletal growth and cartilage homeostasis<sup>11-13</sup>.

In conclusion, disorders primarily of genetic origin should be remembered among childhood rheumatic diseases, so that inappropriate therapy can be prevented and genetic counseling can be offered to the family for the next generations. We believe that it is necessary to perform molecular analysis for the cases in order to give

effective genetic counseling. For this purpose, we have already obtained blood samples from all family members to conduct molecular analyses.

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