CASE REPORT

Progressive Pseudorheumatoid Dysplasia Misdiagnosed as Seronegative Juvenile Idiopathic Arthritis

Ozgur Taspinar[1], Fatih Kelesoglu[2], Yasar Keskin[3], Murat Uludag[4]

ABSTRACT

BACKGROUND: Progressive pseudorheumatoid dysplasia (PPD) is a rare spondylo-epi-metaphyseal dysplasia (SEMD). It can be confused with juvenile idiopathic arthritis (JIA), both clinically and radiologically. Early detection and diagnosis of PPD are important in helping to relieve the pain and disability associated with this disease and in avoiding unnecessary investigations and anti-rheumatic interventions.

CASE DETAILS: We report the case of a 15-year-old girl with PPD who was misdiagnosed with JIA.

CONCLUSION: In conclusion, PPD is a rare SEMD and can be confused with JIA, both clinically and radiologically. Early detection and diagnosis of PPD are important in helping to relieve the pain and disability associated with this disease and in avoiding unnecessary investigations and anti-rheumatic interventions.

KEYWORDS: Progressive pseudorheumatoid dysplasia, juvenile idiopathic arthritis, spondylo-epi-metaphyseal dysplasia

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INTRODUCTION

The spondylo-epi-metaphyseal dysplasias (SEMDs) are a heterogeneous group of disorders comprising more than 20 distinct entities with different modes of inheritance. All are defined by the combination of vertebral, epiphysealand metaphyseal abnormalities. Diagnosis is based on specific skeletal manifestations or the presence of characteristic extraskeletal features (1).

Progressive pseudorheumatoid dysplasia (PPD) is a single-gene disorder and is inherited in an autosomal recessive manner. Other names for this disease are spondyloepiphyseal dysplasia (SED) tarda with progressive arthropathy and progressive pseudorheumatoid arthropathy of childhood (PPAC) (2). Initial reports referred to PPD as progressive pseudorheumatoid chondrodysplasia, being a progressive connective tissue disease with radiological features of Scheuermann's disease and juvenile idiopathic arthritis (JIA) (3). In the 1997 revision of the International Nomenclature and Classification of the Osteochondrodysplasias, PPD was listed as an autosomal recessive disorder in group 10, ''other spondylo-(meta)-physeal dysplasias [SE(M)D]'' (4,5).

The incidence of PPD is approximately 1:1,000,000, with the highest rates occurring in Arabic countries (6). Most PPD cases may remain undiagnosed because of the similar skeletal abnormalities shared with other arthropathies, SEMDs and glycogen storage diseases (7).

The primary site of involvement is the

[1]Department of Pyhisical Therapy and Rehabilitation, Cinarcik State Hospital, Yalova, Turkey
[2]Department of Pediatric Rheumatology, Istanbul University Capa Medical Faculty, Istanbul, Turkey
[3]Department of Pyhisical Therapy and Rehabilitation, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey
Corresponding Author: Özgür Taşpınar, Email: drozgur82@gmail.com

articular cartilage. The first symptoms generally appear between the ages of 3 and 8 years, with progressive joint stiffness that first affects the hips. Further progression to joint contractures is observed. PPD is frequently erroneously diagnosed as JIA, with clinical symptoms of morning stiffness and increasing stiffness of the limb joints and the spine (2). We report the case of a 15-year-old girl with PPD who was misdiagnosed with JIA.

CASE REPORT

A 15-year-old girl was brought with complaints of progressively worsening stiffness and restriction of movements of all joints, associated with increasing difficulty in walking and the inability to form a fist. She is from nation Turkey. She was examined in August 2015. She never reported inflammatory signs in the involved joints. There was a symmetrically impaired range of motion of the elbow, knee, hip, ankle, shoulder, wrist, metacarpophalangeal (MCP), proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints. The patient had no history of fever, joint pain or fractures. Up to the age of 3 years, the patient displayed normal physical and mental development. Three years later, a gradual limitation of joint movement began. The patient complained of difficulties in sitting, standing and climbing. She was the product of a non-consanguineous marriage. There was no history of similar illness in any family member. She was bugh orn by a full term thronormal vaginal delivery. The antenatal, intranatal and neonatal periods were uneventful. Her mother, father and six brothers were healthy. After diagnosis of seronegative JIA, treatment was initiated with a regimen of prednisolone 5 mg once daily, methotrexate 15 mg/week, calcium–vitamin D once daily, and folic acid once daily, twice a week at a second rheumatology clinic for 3 months.

The physical examination described the patient as slender, height in 75th percentile and weight in 50th percentile. Examinations of the musculoskeletal system found a limited range of movement in all joints. Prominent interphalangeal joints were present in the hands. Fixed flexion deformity of the MCP and PIP joints of the hands resulted in a claw hand appearance. She had coxa vara and genu valgum. No pain or tenderness was experienced in the joints. The ophthalmological, neurological, otorhinolaryngological and cardiological examinations were all normal. Her intelligence was normal. She had normal laboratory findings for erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), hemoglobin, white blood count (WBC), platelets, rheumatoid factor (RF) and antinuclear antibody (ANA). She had fixed finger contractures of the metacarpal and phalange (Figure 1). The radiological findings indicated irregularities of the medial aspect of the epiphyses and the metaphyses of the MCP, distal ulna, and radius (Figure 2). In the spine, radiological findings were universal platyspondyly and kyphosis deformity, with obvious irregularity of the vertebral end plates (Figure 3,4). Radiographs of the extremities showed flattened and enlarged epiphyses at the hips, knees, ankles, shoulders, elbows and wrists, with osteophytic lipping and loss of joint space.

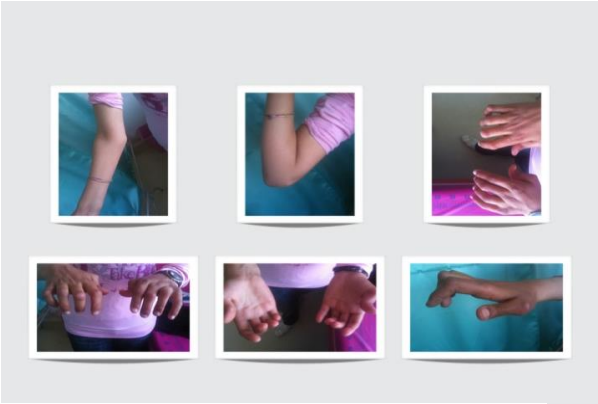

Figure 1: *Fixed flexion deformity of the MCP and PIP joints of the hands*

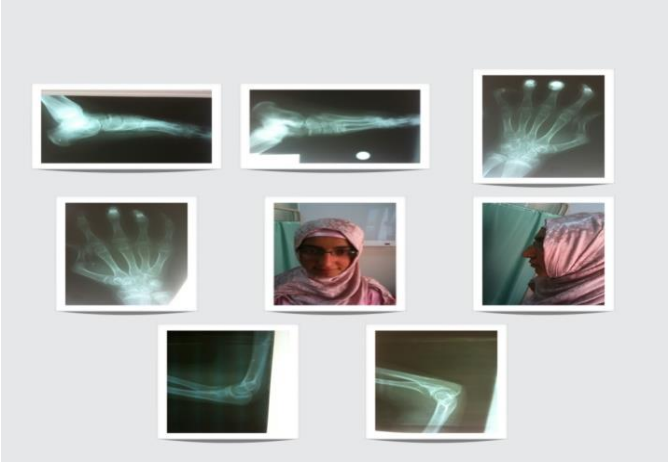

Figure 2: *Irregularity of the medial aspect of the epiphyses and the metaphyses of the MCP, distal ulna, and radius*

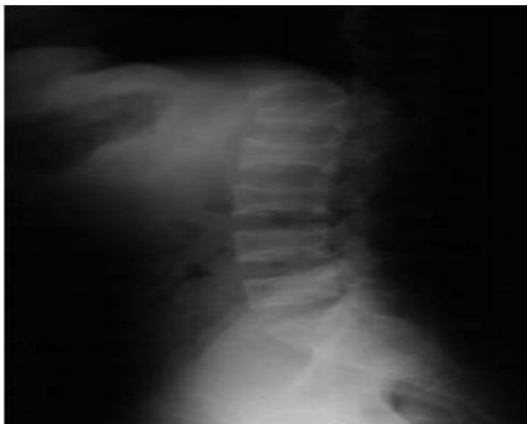

Figure 3: *Universal platyspondyly and irregularity of the vertebral end plates*

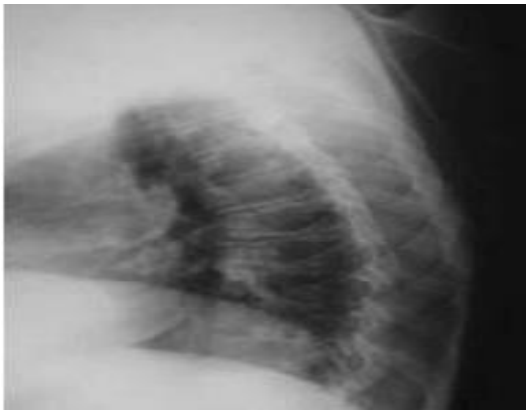

Figure 4*: Kyphosis deformity, with obvious irregularity of the vertebral end plates*

DISCUSSION

The incidence of the chronic childhood arthritis JIA is 10 to 15 per 100,000 children. According to the proposed classification criteria of the ILAR/WHO, JIA is divided into the following seven subtypes: (1) systemic arthritis; (2) oligoarthritis (a: persistent form; b: extended form); (3) RF-negative polyarthritis; (4) RF-positive polyarthritis; (5) psoriatic arthritis; (6) enthesitis-related arthritis; and others (9). Hereditary diseases relevant for the differential diagnosis of JIA include Stickler's syndrome, Kniest syndrome, SED tarda, and PPD (4).

PPD is defined as a potentially disabling, progressive, hereditary arthropathy characterized by platyspondyly, shortening of the pedicles, irregularities of the vertebral bodies, narrowing of the intervertebral discs and joint spaces, widening of the metaphyses, early osteoarthritis, osseous swelling of the peripheral joints without signs of systemic or synovial inflammation, polyarthralgia, multiple joint contractures and short stature (4,9,10).

The presenting complaints in PPD normally include walking difficulties, muscle weakness, easily fatigued, pain and swelling in the joints, especially in the hands and deformities of the knee, genu valgus or varus (11). The forms presenting after infancy are the most relevant for the differential diagnosis of JIA (12). Our patient had symmetrically restricted range of motion of the hip, knee, shoulder, wrist, MCP, PIP and DIP joints. She also had genu valgus and coxa vara deformities.

Joint pain in children can have multiple causes, ranging from a reaction to a minor intercurrent infection that rapidly improves to the presence of severe skeletal lesions resulting from malignancy or skeletal dysplasia (13). Thus, a large range of both synovial and non-synovial conditions can mimic JIA. A careful history (including family history), a full physical examination combined with a careful review of imaging studies and basic blood tests, including ESR, CRP, hemoglobin, WBC, platelets, RF and ANA should help distinguish these conditions from JIA (13,14). Despite the normal values for laboratory blood tests in the patient, her condition was probably misdiagnosed as seronegative JIA because of the widespread involvement of the joints.

Stickler's syndrome is an autosomal dominant form of spondyloepiphyseal dysplasia with variable expression, which can include multiple joint arthropathy. However, ophthalmic abnormalities, particularly progressive myopia, are usually associated with this disorder. Other disorders with platyspondyly such as mucopolysaccharidosis, spondylometaphyseal dysplasia and rare forms of SEMD, have relatively characteristic features. These disorders are not confused with PPD because the small joints of the hand and larger joints such as the knee are normal (15). The involvement of early, progressive, multiple-joint changes differentiate PPD from other bony dysplasias (11).

Spinal abnormalities in PPD mimic those of Scheuermann's disease. However, Scheuermann's disease presents at puberty, whereas spinal

abnormalities in PPD appear prior to 10 years of age (15).

In conclusion, PPD is a rare SEMD and can be confused with JIA, both clinically and radiologically. Early detection and diagnosis of PPD are important in helping to easy the pain and disability associated with this disease and in avoiding unnecessary investigations and anti-rheumatic interventions.

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