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Case Report

Progressive pseudo rheumatoid dysplasia mimicking juvenile idiopathic arthritis

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Abstract

Progressive pseudo rheumatoid dysplasia (PPRD) is an autosomal recessive skeletal dysplasia with an underlying mutation in WISP 3 gene. Clinical, it is frequently misdiagnosed as juvenile idiopathic arthritis (JIA), particularly the seronegative polyarticular JIA. It is the characteristic radiological feature which helps in the early recognition of this disease. Here, we report a case of PPRD which has been previously diagnosed as JIA and was on antirheumatoid drugs with no improvement rather a progressive course. Because of its resemblance, PPRD should be kept in mind in the differential diagnosis of inflammatory joint diseases and metabolic bone diseases to prevent inappropriate treatment and unnecessary investigation.

Key words: *Epiphyseal, inflammatory, arthritis*

Progressive pseudo rheumatoid dysplasia (PPRD) is an autosomal recessive skeletal dysplasia with radiographic changes in the spine similar to spondyloepiphyseal dysplasia tarda (SEDT) and clinical resemblance to juvenile idiopathic arthritis (JIA). Patients are asymptomatic at birth, however, with the advancement of age, joint swelling with associated pain and limitation of motion without signs of inflammation, with enlarged interphalangeal (IP) and metacarpophalangeal joints, osteoporosis, short stature, platyspondyly become evident [1,2]. The nature of disease is progressive and clinically indifferent from JIA [3]. It differs from the rheumatoid-factor-negative polyarticular form of JIA and other seronegative rheumatoid spondyloarthropathies by the absence of arthritic and inflammatory changes, and radiographically by absence of destructive and presence of dysplastic bone changes [4].

Not so rare, rather less recognized entity; therefore, we should be familiar with radiographic features of the disease to avoid needless investigation and trials of inappropriate treatment. Here, we describe a 10-year-old girl with PPRD.

CASE REPORT

A 10-year-old girl previously diagnosed as JIA presented to us with no improvement of symptoms rather a progressive course despite regular treatment for last 2 years. She was the first child born of non-consanguineous marriage and was asymptomatic until age of 7 years. Then, she developed pain in knee joint with difficulty in walking. There was progression of symptoms with easy fatigability, difficulty in getting up from the squatting posture and climbing stairs. There is increasing restriction of range of movements and pain and swelling at various joints (shoulder, elbow, wrist, hip, knee, ankle, and IP joints). She did not complain of fever. She had been evaluated elsewhere and given a provisional diagnosis of JIA, received treatment with anti-rheumatoid drugs (non-steroidal anti-inflammatory drugs and Disease-modifying anti-rheumatic drugs) and steroids without any significant relief.

On examination, her weight was 20 kg and height was 122 cm (<2 standard deviation for age) with upper and lower segment ratio of 0.9 and arm span of 117 cm. Her intelligence quotient was normal. Her hearing assessment and ophthalmic examination (vision - 6/6) including fundus and slit lamp examination was normal. There was decreased the range of movement at various joints including spine, with enlargement of bilateral knee, ankle, and elbow joints with wrist widening and fusiform enlargement of IP joints (Fig. 1a). Rest of the systemic examination was normal.

Her routine laboratory investigations including complete blood picture, erythrocyte sedimentation rate (ESR), renal and liver function tests were within normal range. Assays for C-reactive protein (CRP), ASO titers, antinuclear antibody (ANA), and rheumatoid arthritis (RA) factor were negative. Her serum calcium, alkaline phosphatase, phosphorus, parathormone, and vitamin D levels were also within normal limits. Urine for mucopolysaccharidosis was also negative.

X-ray spine showed platyspondyly with dysplastic vertebrae with anterior beaking and physeal irregularity, particularly at thoracolumbar vertebrae (Fig. 2). Both the knee showed a flattening of articular surface. In X-ray shoulder, both humeral

epiphyses were dysplastic and widened with decreased joint space (Fig. 3). X-ray pelvis and bilateral hips show widened pelvic symphysis, reduced hip joint space, irregularity of bilateral greater trochanter, and epiphysis of head of femur (Fig. 4). In wrist and hand, there is periarticular osteopenia with decrease joint space and epiphysis and metaphysis of IP joints were enlarged. Radial epiphysis was widened and irregular (Fig. 1b). Radiographs did not show the destructive changes of RA. X-ray skull and chest were normal. Her bone age was 9-10 years.

By radiological findings, she was diagnosed as PPRD. Molecular testing was advised to confirm the diagnosis but could not be done due to non-availability in our setup and parents were non-affording to get it done from outside. The parents were informed about the disease, joint protection and exercise programs.

DISCUSSION

PPRD has been also described as SEDT with progressive arthropathy (SEDT-PA) or progressive pseudo rheumatoid arthropathy of childhood. The International Working Group on Constitutional Diseases of Bone had adopted the term "PPRD" to avoid confusion with other disease entities'[4].

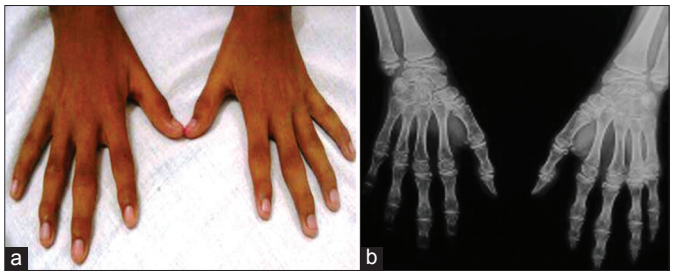

Figure 1: (a) Spindle shaped distal and proximal interphalangeal joints. (b) X-ray hand showing periarticular osteopenia, decrease joint space at interphalangeal (IP) joints, epiphysis and metaphysis of IP joints are enlarged, radial epiphysis is widened and irregular

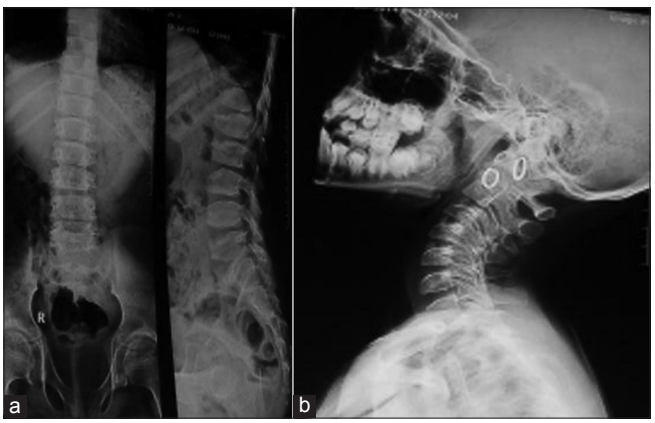

Figure 2: (a and b) X-ray spine showing platyspondyly with dysplastic vertebrae with physeal irregularity particularly thoracolumbar vertebrae

Genetic alterations in the WISP3 (Wnt1-inducible signaling pathway protein 3) gene, located in 6q22 have been implicated in the pathogenesis of PPRD [5]. WISP3 has a main function in maintaining cartilage integrity by regulating the synthesis of type II collagen and aggrecan, and mutations in WISP3 result in continuous degeneration and loss of articular cartilage, which is one of the major complications associated with PPRD [6].

The first case of PPRD was described by Spranger et al. in 1983 [3]. Onset is usually between 3 and 11 years with majority presenting before 8 years with joint pain, kyphoscoliosis, easy fatigability, muscular weakness, progressive restriction of joint movement and swelling at several joints especially in hands. Joint stiffness usually first affects the hips, and progressively involves the other joints, including the proximal and distal IP joints. Overall adult height is reduced and upper and lower segment ratio <1 [1,3].

The characteristic radiographical features of PPRD include narrow joint space with wide metaphyses and flat epiphyses with periarticular osteoporosis and irregular articular surface.

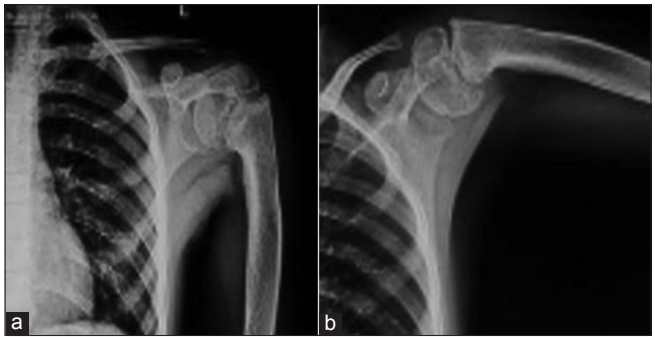

Figure 3: (a and b) X-ray shoulder showing decrease joint space with humeral epiphysis dysplastic and widened with medial breaking of proximal humeral shaft and bowing of humerus

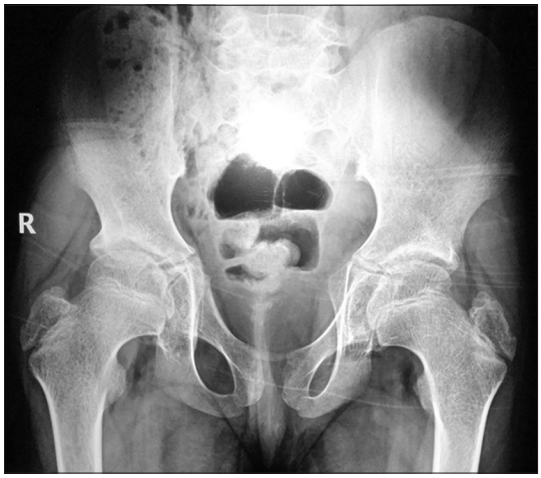

Figure 4: X-ray pelvis showing widened pelvic symphysis, reduced hip joint space, irregularity of bilateral greater trochanter and widened epiphysis of head of femur

Pelvis shows enlarged femoral heads with irregular acetabular margins. Spinal abnormalities include platyspondyly with dysplastic vertebrae [7]. Nature of the disease is progressive, leads to severe difficulties in ambulation and activities of daily living. Various treatment modalities have been tried, but none has proven effective until date.

The prevalence and incidence, in India, are not precisely known. In the UK, the prevalence has been estimated at one per million [8]. However, the disease is underdiagnosed due to the overlap of clinical features with JIA. To date more than 160 families with molecularly confirmed PPRD have been reported. The largest series has been published from India [9,10].

In general, the radiological examination is highly accurate in the diagnosisof PPRD. However, it is confirmed with identification of biallellic pathogenic variants in WISP3 on molecular genetic testing [8]. JIA is the disorder most commonly confused with PPRD but skeletal changes seen in JIA such as erosions, overgrowth of epiphyses, periostitis, and osteopenia; joint inflammation, elevation of ESR and CRP are not seen in PPRD [8].The usual variety of SED-tarda is an X-linked disorder and peripheral skeleton is relatively unaffected and IP joints are normal [11]. The condition may confused with Scheuermann disease which presents at puberty, whereas in PPRD, spinal abnormalities appear before the age of 10 [3].

Other rare conditions that may be considered in differential diagnosis are Stickler's syndrome, a dominantly inherited disease characterized by ocular abnormalities; Kniest syndrome, an autosomal dominant condition with facial dysmorphia. Other disorders with platyspondyly, such as mucopolysaccharidosis, spondylometaphyseal dysplasia and rare forms of spondyloepimetaphyseal dysplasia, have relatively characteristic features and small joints of hand and larger joints like the knee are normal [8,11]. Ankylosing spondylitis is again a seronegative chronic inflammatory spondyloarthropathy, typically begins in adolescents. The hallmark is "sacroilitis." Inflammatory markers are raised and involved joint shows erosions and sclerosis.

Musculoskeletal tuberculosis (TB) accounts for 1-3% of TB. Tuberculous spondylitis, generally, presents as potts abscess, vertebral body collapse with gibbus deformity. Tuberculous arthritis is characteristically monoarticular and peripherally located osseous erosions are characteristic features. In tuberculous dactylitis lesions appear as cyst-like cavities, with the expansion of the diaphysis. In this case, there were no such features and tuberculin skin testing was non-reacting; there was no history of contact, and X-ray chest was normal. Previously published cases of PPRD had a history of consanguinity, kyphosis, scoliosis, and abnormal facies; however, in our case, these features were absent.

CONCLUSION

In spite of the first symptoms appearing in early childhood, the diagnosis of PPRD is most often made only in the second decade and affected children often receives unnecessary anti-inflammatory and immunosuppressant treatments. Thus, increasing awareness of PPRD especially, among pediatricians is essential to allow for timely diagnosis, avoid needless investigations and trials of medication.

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