

CASE REPORT

Progressive pseudorheumatoid dysplasia: A rare entity mimicking juvenile idiopathic arthritis

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Abstract

Progressive pseudorheumatoid dysplasia can be confused with juvenile idiopathic arthritis. Treatment is mainly symptomatic and the prescription of immunosuppressive agents is unnecessary. Surgery may be indicated at advanced stages of the disease.

KEYWORDS

juvenile idiopathic arthritis, pediatric radiology, progressive pseudorheumatoid arthropathy of childhood, progressive pseudorheumatoid dysplasia, skeletal dysplasias

1 | INTRODUCTION

Progressive pseudorheumatoid dysplasia (PPRD) is a rare genetic skeletal disease characterized by a progressive degeneration of articular cartilage that leads to a significant disability with pain, stiffness, and joint deformities. PPRD needs to be recognized by rheumatologists in order to prevent delayed diagnosis and unnecessary prescription of immunosuppressive drugs.

Progressive pseudorheumatoid dysplasia (PPRD) is a rare genetic skeletal disease caused by mutations in the Wnt1-inducible signaling protein 3 (WISP3) gene, which is inherited in an autosomal recessive mode. It is characterized by a progressive degeneration of articular cartilage that leads to a significant disability with pain, stiffness, and joint deformities.¹

Progressive pseudorheumatoid dysplasia usually affects children between the ages of 3 and 8 years and may, therefore, be confused with juvenile idiopathic arthritis (JIA). The main clinical presentation includes polyarticular involvement, gait abnormalities, and fatigability. Imaging plays a crucial role in the differential diagnosis between the two diseases, but the definite diagnosis is based on genetic testing.¹

Herein, we report the case of a 25-year-old Tunisian man with suspected PPRD misdiagnosed as seronegative polyarticular JIA.

2 | CASE PRESENTATION

A 25-year-old man, born of a consanguineous marriage, presented to our department in October 2019 complaining of swelling and morning stiffness in proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints that had gradually progressed since the age of five. He had no history of fever, skin eruption, or any other extra-articular manifestation. No similar family cases were reported. Various non-steroidal anti-inflammatory drugs (naproxen, ibuprofen, and diclofenac) have been prescribed but with no improvement. Written informed consent was obtained from the subject described in this report.

Physical examination showed a short stature (158 cm), symmetrical swelling from 2nd to 4th PIP and DIP joints, brachymetacarpia, and brachydactyly. No pain or limited range of motion was noted in the peripheral joints. The

lumbar spine flexion was restricted with a Schober's test at +2 cm. No scoliosis was observed, and the patient's gait was normal.

Laboratory findings revealed normal inflammatory markers with an erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels at 4 mm and 3 mg/L, respectively. White blood cells were at 4900 mm^{-3} , and platelets were at 222.000 mm^{-3} . Rheumatoid factor (RF), anti-citrullinated peptides antibodies (ACPA), and antinuclear antibody (ANA) were negative.

Radiological findings included enlarged epiphyses and metaphyses of the metacarpals and phalanges of hands and feet, with joint space narrowing and osteophytic formations (Figure 1). X-rays showed platyspondyly and flattened epiphyses of femoral heads with short and wide femoral necks (Figures 2–3). A coxa valga was also noted. Bone densitometry revealed osteopenia.

Based on clinical and imaging findings, the diagnosis of PPRD was suspected. The patient was referred to the genetic department for further investigations and to an orthopedic surgeon for assessment and follow-up, as he would probably need corrective surgery with disease progression.

3 | DISCUSSION

Progressive pseudorheumatoid dysplasia is a rare genetic disorder with autosomal recessive inheritance characterized by the predominant involvement of articular cartilage. It is caused by mutations in the WISP3 gene, which encodes for a protein expressed in synoviocytes and chondrocytes that plays a major role in bone and cartilage development.²

Progressive pseudorheumatoid dysplasia is often underdiagnosed because of its rarity, with an estimated prevalence of one per million in the United Kingdom, and its clinical and radiological overlap with JIA and other pediatric musculoskeletal disorders such as spondyloepiphyseal dysplasia tarda.³

The current patient was born from a consanguineous marriage. He presented with swelling and morning stiffness in PIP and DIP joints that had gradually progressed since the age of five. The disease is typically silent at birth and early childhood. It usually manifests between the ages of 3 and 8 years, but the diagnosis is most often made in the second decade. The delay between symptoms onset and diagnosis is shorter among populations with a high rate of consanguinity, which increases the suspicion of genetic disorders.⁴

Initial clinical findings include progressive joint stiffness and enlarged interphalangeal joints of the hands. Unlike in JIA, the swelling has a bony consistency, and the tenderness is mild compared with the severity of the arthropathy. As observed in our patient, there is no elevation of inflammatory markers, and RF and ANA are negative. This may help distinguish between PPRD and JIA. Moreover, no articular improvement was observed with NSAIDs.

Skeletal changes become more severe over time and are responsible for kyphoscoliosis, progressive hip disease, and gait abnormalities. A camptodactyly is also described in the late stage of the disease.¹ None of these signs had yet been noted in the current patient.

Characteristic radiological features in PPRD are flattened and enlarged epiphyses and metaphyses, platyspondyly, and diffused osteopenia predisposing patients to fractures.⁵ In later stages, secondary osteoarthritis may be seen including

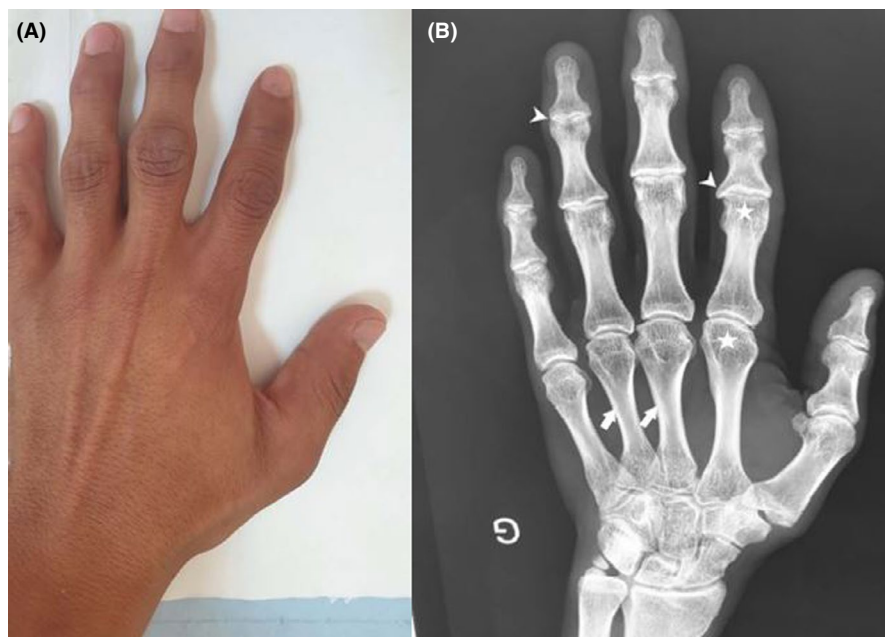


FIGURE 1 (A) Swelling of proximal and distal interphalangeal joints associated with brachymetacarpia and brachydactyly. (B) Left-hand X-ray showing enlarged epiphyses (stars) and metaphyses (arrows) of the metacarpals and phalanges, with joint spaces narrowing and osteophytic formations (arrowheads)



FIGURE 2 Lumbar X-rays showing platyspondyly (arrows) in the third, fourth, and fifth lumbar vertebrae



FIGURE 3 Pelvis X-rays showing enlarged and flattened femoral heads (arrows) and short femoral necks (stars)

joint space narrowing, osteophyte formation, and subchondral cyst formation, particularly in the hip.⁶

Magnetic resonance imaging (MRI) findings are reported to be more specific of PPRD and less likely to show overlap with JIA as demonstrated by the absence of an inflammatory process such as joint effusions and synovitis, articular erosions, and surrounding soft tissue edema. However, X-rays remain the first-line technique of imaging in patients with PPRD.⁷

In the absence of formal diagnostic criteria, PPRD should be suspected in early childhood basing on clinical and imaging findings and confirmed with molecular genetic testing.⁸ In the current case, genetic diagnosis has not been established, but PPRD was strongly suspected based on a typical presentation.

The treatment of PPRD is only supportive and includes pain medication, physiotherapy, and surgical interventions. No etiological treatment is currently available.

In conclusion, PPRD needs to be recognized by rheumatologists in order to prevent delayed diagnosis and unnecessary prescription of immunosuppressive drugs. Early rehabilitation is indicated to avoid potential late disability. Genetic counseling should also be offered to patients and their families.

ACKNOWLEDGMENT

Published with written consent of the patient.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

KM, HF, DK, and WH analyzed and interpreted the patient data and provided advice for treatment. KM ensured the clinical follow-up of the patient. HB and KM were major contributors in writing the manuscript, and all the authors read, revised, and approved the final manuscript.

ETHICAL APPROVAL

Written informed consent was obtained from the subject described in this report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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