CASE REPORT

A RARE SKELETAL DYSPLASIA-CLOSE MIMICKER OF JUVENILE IDIOPATHIC ARTHRITIS-PROGRESSIVE PSEUDORHEUMATOID DYSPLASIA

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Progressive pseudorheumatoid dysplasia or spondyloepiphyseal dysplasia tarda is caused by a mutation in Wnt1 inducible signalling pathway protein 3 (WISP3) and passes in an autosomal recessive manner. Prevalence underestimated as one per million and most of the cases remain undiagnosed or treated as Juvenile Idiopathic Arthritis (JIA). Differentiation between JIA and PPRD is really challenging however, this case is genetically confirmed from our country. 7-year-old, short stature boy, with multiple joint swellings of hands and feet, initially suspected to have JIA and had been worked up and took treatment for that for the past 2 years. He had progressive stiffness of small joints. Baseline biochemistry, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor and ANA, were within normal limits. He was moderately growth hormone deficient. Thyroid function tests and insulin-like growth factor 1 (IGF-1) were within reference ranges. Skeletal survey showed typical findings of pseudorheumatoid skeletal dysplasia. Physical therapy and genetic counselling were done.

Keywords: Progressive pseudorheumatoid dysplasia; Spondyloepiphyseal dysplasia tarda; Juvenile Idiopathic Arthritis

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INTRODUCTION

Progressive pseudorheumatoid dysplasia (PPD) or spondyloepiphyseal dysplasia tarda with progressive arthropathy (SEDT-PA) is a rare autosomal recessive arthropathy of childhood involving the entire skeleton.[1] Here we report a genetically proven case of PPRD from our country Pakistan. It is often mistaken as juvenile rheumatoid arthritis: however, the joint problems in juvenile rheumatoid arthritis are associated with inflammation, while those in PPRD are not. The radiographs of hands and feet reveal epiphyseal and metaphyseal enlargement. with osteophytic formations. There is platyspondyly on spine x-ray and there is evidence of generalized osteopenia.[2] The definitive diagnosis is established in a proband with characteristic radiologic findings and biallelic pathogenic variants in *CCN6* (formerly WISP3) on genetic testing.

CASE REPORT

Seven and a half years old, vaccinated boy, born to consanguineous parents having weight of 12.5 kg (SDS- 3.0) and height of 104 cm (SDS -4.5) with normal vitals and no significant birth and developmental history, referred to our endocrine OPD for workup of short stature and joint swellings. He had restricted movements in small joints of hands bilaterally and painful right knee joint for last two years. Child had been extensively worked up for juvenile idiopathic arthritis and received multiple oral NSAIDs. No familial disorder of joints or skeleton in the family reported. On examination a young cooperative boy of extreme short stature and lean built. His gait was normal with restricted movements in all Proximal and distal interphalangeal joints (PIP and DIP) of bilateral hands and spindle shaped deformities of all fingers (Figure-1). Spine and Temporomandibular were normal. His Hb was 11.9, TLC 9.1 and platelets were 361 with negative inflammatory markers including ESR and CRP. Serum biochemistry, renal functions and thyroid profile were within normal range. Screening for celiac disease TTg IgA and IgG were negative and he was found to be moderately growth hormone deficient on Insulin tolerance test (ITT). Skeletal survey showed large epiphysis and widened metaphysis of the metacarpals/metatarsal and phalanges of hands showing periarticular osteopenia without erosion. Spine radiographs show inferior beaking, and platyspondyly typical for PPRD (Figure-2).

All of these radiological findings were pointing towards PPRD and later confirmed by gene sequencing. Molecular genetic analysis revealed homozygous pathogenic mutation in *WISP3* at Exon 3, c.156C>A (p.Cys52*) which is associated with PPRD. Moreover another heterozygous state of pathogenic mutation in *B3GAT3*, Exon 4, c.830G>A (p.Arg277Gln) was also found which is associated with multiple joint dislocation and short stature.

Figure-1: Spindle shaped deformities of fingers

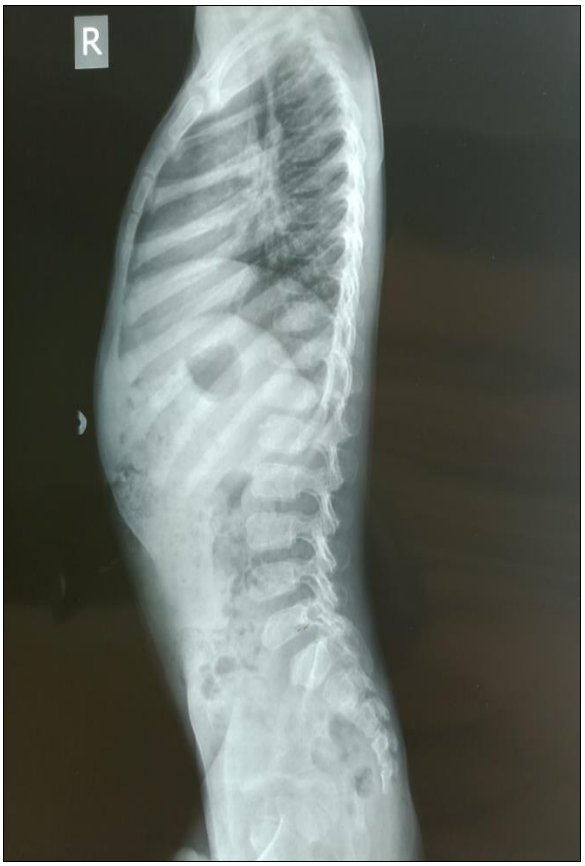

Figure-2: Spine radiograph showing platyspondyly

DISCUSSION

PPRD generally gets into notice between the ages of 2 and 8 years due to characteristic symptoms including, progressive joint stiffness, pain and swelling of joints of extremities. The age of presentation was similar to other case reports from different regions that is 5–8 years.[3] This patient was born to consanguineous parents, and complaints started since the age of five years similar to other reports available.[4] Physical examination revealed symmetric thickening of the DIPs and PIPs of both hands in our patient with no evidence of painful joint effusion as in other case reports available. Five patients from one retrospective case series misdiagnosed as juvenile idiopathic arthritis JIA in early phase, like our patient. A retrospective study of nine patients with progressive pseudorheumatoid dysplasia: to explore early diagnosis and further treatment. PPRD is differentiated from JIA in the absence of pannus formation, synovitis and the persistence of dysplastic bony changes on radiographs.[5] *WISP3* encodes a member of connective tissue growth factor family which is essential for normal growth and function of cartilage.[6–7] This mutated gene found in our case has been previously witnessed in other clinical reports of PPRD as well.[8–10]

Treatment to manage overall condition is NSAIDs which reduce the severity of pain and preserve joint mobility, as no definite cure is available. Genetic counselling was done of the family and they were informed about the risk of recurrence which is 25% in each pregnancy event. One of the child's uncles wanted to get him tested after taking the genetic counselling session from expert geneticist through family variant testing program and later he was found to have heterozygous mutation in the same gene. Further he was counselled about carrier testing of his partner to avoid the risk of having baby with PPRD.

CONCLUSION

As PPRD is so mimic with the JIA, early recognition and accurate diagnosis is crucial, as it may help in avoiding unnecessary investigations and potential toxic effects of drugs used for JIA, which eventually lower the overall morbidity and ensures enhanced patient compliance. Prompt and timely diagnosis can help individuals to get early management including orthopaedic interventions.

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