Rhupus arthropathy in childhood-onset systemic lupus erythematosus

This case report describes ruphus arthropathy in a 13-year-old girl with systemic lupus erythematosus. A detailed case description is given, together with laboratory results. Subcutaneous nodules were present on distal interphalangeal joints of the hands and fixed flexion deformity was present at metacarpophalangeal, proximal interphalangeal and distal interphalangeal joints of the fifth digit. Anticyclic citrullinated peptide antibody (antibodies against cyclic citrullinated peptides) titers were 79 U/ml (normal: 5 U/ml), a specific marker for rheumatoid arthritis. Renal biopsy was confirmatory of lupus nephritis. A diagnosis of childhood-onset systemic lupus erythematosus was made according to the modified ACR criteria. Clinicians need to be careful in monitoring the serious manifestations of the disease in childhood-onset lupus patients with rhupus arthropathy, and consider the poor response to standard disease-modifying agents.

KEYWORDS: childhood-onset systemic lupus erythematosus ■ children ■ juvenile idiopathic arthritis ■ rhupus arthropathy

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Case report

A 13-year-old female presented to our hospital for the first time with complaints of pain in joints, which had been present for 3 years. Initially, the patient had pain in the knee joints. Later, the wrist and small joints of the hands were also involved. The patient complained of stiffness and limitation of mobility around all affected joints and she suffered worsening symptoms for 1 month. On examination, weight and height were between the 25th and 50th centile (WHO standards), and blood pressure was 110/68 mmHg (50–90th centile). She had pallor, and subcutaneous nodules were present on the distal interphalangeal joints of the hands and fixed flexion deformity was present at the metacarpophalangeal, proximal interphalangeal and distal interphalangeal joints of the fifth digit (Figure 1). There was nontender swelling of the knee and ankle joints. Movements were restricted at affected joints. There was no rash or lymphadenopathy. The remainder of the systemic examination was unremarkable. Investigations revealed low C3 and C4, as well as positive antinuclear antibodies and dsDNA. Anticyclic citrullinated peptide (CCP) antibody (antibodies against CCPs) titers were 79 U/ml (normal: 5 U/ml), a specific marker for rheumatoid arthritis (Table 1). Ultrasonography of joints showed effusion in both knees. MRI of the knee joints confirmed effusion and mild erosion. The patient had nephrotic range proteinuria and, consequently, a percutaneous renal biopsy was performed. Histopathology showed class V lupus nephritis with an activity index of one out of 24 and a chronicity index of 2.5 out of 12. A diagnosis of systemic lupus erythematosus (SLE) was made as the patient fulfilled the modified ACR criteria for diagnosis of this disease. The patient received six pulses of intravenous cyclophosphamide with prednisolone followed by azathioprine and hydroxychloroquine.

Discussion

Arthritis is the most common manifestation of SLE. Typically, arthritis in SLE is of short duration, nonerosive and nondeforming, involving small and large joints. Chronic polyarthritis is a rare manifestation of childhood-onset SLE. Erosive arthritis has been found in less than 5% of lupus patients during the course of the disease [1]. The presence of erosive and symmetric polyarthritis, concomitantly to lupus diagnosis, associated with the detection of antibodies, such as antinuclear antibodies, anti-dsDNA, rheumatoid factor and anti-CCP antibodies, is defined as 'rhupus syndrome' as described by Panush in 1988 [2]. Studies have found that high levels of anti-CCP antibodies are more frequent in lupus patients with deforming/erosive arthritis [3].

In a recently published article detailing a series of eight patients with rhupus arthropathy, the diagnosis was rheumatoid arthritis in seven patients at disease onset. They developed SLE after an average of 2.8 years [4]. Similarly, our patient diagnosis of childhood-onset SLE was made 3 years after the onset of clinical symptoms of arthritis. Some authors have observed

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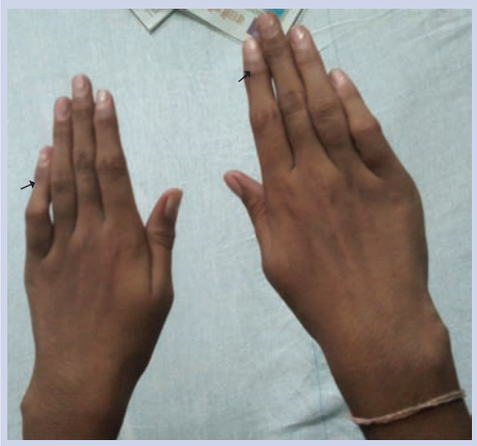

Figure 1. Subcutaneous nodules on the distal interphalangeal joints of the hands and fixed flexion deformity of small joints.

severe disease in adult lupus patients with erosive arthritis, such as glomerulonephritis, as found in our case. There is a paucity of reports on rhupus arthropathy in children, with few case reports. Ours is the only report of renal biopsy in children showing class V lupus nephritis. Some authors believe that rhupus arthropathy is a serious articular involvement of lupus and it is different from a superposition or overlap of rheumatoid arthritis and SLE, while other authors believe that rhupus syndrome is combination of SLE and chronic erosive polyarthritis, and the last group believes that rhupus is an overlap of rheumatoid arthritis or juvenile idiopathic arthritis (JIA) and SLE. In rhupus, simultaneous clinical features of JIA and SLE may not be complete at presentation [5]. In adults, the majority of polyarticular erosive arthritis is the most common manifestation, but in children, features of JIA dominating asymmetrical erosive and/or nonerosive oligoarticular involvement may be a common manifestation [6]. Ziaee *et al.* have suggested the term 'juvenile rhupus' for overlap of JIA and childhood-onset SLE [7]. Treatment options include NSAIDs and disease-modifying antirheumatic drugs, such as azathioprine and methotrexate, depending upon the systemic involvement. There is a poor response to standard disease-modifying agents alone [5].

To conclude, rhupus arthropathy is an overlapping syndrome of rheumatoid arthritis and systemic lupus erythematosus. Our case highlights the importance of anti-CCP antibodies in lupus arthropathy. A high index of suspicion is required while evaluating children with chronic polyarthritis for antinuclear antibody and anti-CCP-antibody positivity and development of rhupus athropathy.

Table 1. Laboratory investigations.

Investigation	Value
Hemoglobin	9.3 g/dl
White blood cell count	12,300
Differential leukocyte count	P75/L22/E2/M1
Erythrocyte sedimentation rate	60 mm at 1 h
Peripheral smear	Normocytic normochromic
Serum urea	43 mg/dl
Serum creatinine	1.0 mg/dl
C-reactive protein	24 mg/dl
Rheumatoid factor	Negative
Antiphospholipid antibody	Negative
Antistreptolysin titer	110 U/ml
Complement 3 level	53.6 mg/dl
Complement 4 level	4.6 mg/dl
Urine routine	Urine protein/urine creatinine 2.1; red blood cells 8/high power field
Anticyclic citrullinated peptide	79.1 U/ml (normal is <5 U/ml)
Antinuclear antibody	1:100 diffuse (3+) positive, mitosis positive
Anti-dsDNA	110 IU/ml
Nucleosomes	Positive (3+)
Histones	Positive (1+)

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Informed consent disclosure

The authors state that they have obtained verbal and written informed consent from the patient for the inclusion of their medical and treatment history within this case report.

Executive summary

- Rhupus arthropathy is an overlapping syndrome of rheumatoid arthritis and systemic lupus erythematosus.
- High levels of anticyclic citrullinated peptide antibodies are more frequent in lupus patients with deforming/erosive arthritis.
- Long-term follow-up is required in children with chronic polyarthritis for development of antinuclear antibody, anticyclic citrullinated peptide antibody positivity and rhupus athropathy.
- In future, the term 'juvenile rhupus' may be used for the overlap of juvenile idiopathic arthritis and childhood-onset systemic lupus erythematosus.

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