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When JRA is not JRA.

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## **INTRODUCTION**

Children with juvenile arthritis may have courses in which other rheumatic diseases become superimposed upon their original presentation. We present a case of a 15 year old patient who developed new symptoms, leading to further evaluation and different treatment. We will present this patient in a question-answer format, similar to the approach we have previously described, for use in teaching residents and medical students.

## **CASE PRESENTATION.**

A 15 year old girl is diagnosed with polyarticular juvenile arthritis (JIA), after presenting with synovitis affecting the proximal interphalangeal joints, knees, and ankles. She responds to nonsteroidal anti-inflammatory medications and oral methotrexate. After 6 months, the methotrexate is discontinued, and she remains stable for 1 year. She then develops a chronic cough over 2 months, and gradually finds she is unable to climb stairs because of severe exertional dyspnea. She has no fever, any type of rash, or arthralgia. Physical examination reveals bibasilar rales, respiratory rate 30, no retractions, mild tachycardia, pulse 100. There is no synovitis, and the rest of the examination is unremarkable. What are your next steps? Why?

## PATIENT EVALUATION

The resident or medical student should admit this child, and evaluation should include laboratory testing and imaging. Initial studies include an ESR, CBC, and chest x-ray. The ESR is 55, hgb. 10.5, and the wbc and differential are unremarkable. A chest x-ray shows mild streaking, particularly at the bases. The next step includes studies to evaluate the extent of pulmonary disease and possible etiology. Differential diagnosis in this setting could include rheumatoid arthritis associated interstitial lung disease, methotrexate pneumonitis (although she was no longer on this medication at presentation), SLE, scleroderma, mixed connective tissue disease (MCTD), overlap syndrome and infection. Additional laboratory evaluation for SLE, MCTD, and overlap syndromes should be obtained. The patient had negative screens for anti-Sm, anti-RNP and anti-DNA by crithidia. Her ANA was positive at a high titer. She had normal C3, C4 and CH50 levels.

In this patient, pulmonary function tests with diffusing capacity (DLCO), high resolution CT of the chest and lung biopsy should be performed to exclude infection and evaluate lung pathology. The pulmonary function tests show severe restrictive disease, and DLCO value 70% predicted. The CT below shows severe honeycombing of the bases (Figure 1). Although the pulmonary parenchyma appears relatively spared, a lung biopsy shows interstitial lymphocytic infiltrate, with negative cultures. When asked for a plan of action, the answer being looked for treatment with immunosuppressive medication. This patient received a 6- month course of intravenous cyclophosphamide, given monthly, with a taper to every other month for another 6 months. The patient clinically responded to this treatment with resolution of respiratory symptoms, improvement of PFTs, but no change in the chest CT, repeated 1 year later. This patient started with a clinical course suggestive of juvenile arthritis, only to evolve into an overlap syndrome.



#### **COMMENT**

Overlap syndromes are a group of disorders which comprise systemic manifestations of two or more connective tissue diseases (CTD), including juvenile rheumatoid arthritis, systemic lupus erythematosus (SLE), systemic scleroderma (SS), juvenile dermatomyositis, or vasculopathy. Children with overlap syndromes often meet existing classification criteria for a single particular CTD, but may only partially meet diagnostic criteria for other related diseases. Mixed connective tissue disease (MCTD) is distinct from overlap syndromes. Literature on MCTD is controversial, but in general includes features suggestive of SLE, SS, and polymyositis with high serum titers of antinuclear antibody and antibody to ribonuclearprotein antigen in the absence of antibody to Smith protein and anti-ds DNA. Evolution to scleroderma like pulmonary disease was suspected in our patient; however, although she clearly had evidence of arthritis and interstitial lung disease; she lacked sclerodactyly and Raynaud's phenomenon which accompany SS. She also failed to meet criteria for SLE with negative antibodies to double-stranded DNA and normal complements on multiple occasions. In conclusion, children presenting with features of JRA/JIA can evolve into an overlap syndrome and should undergo complete re-evaluation if systemic symptoms develop.