Spondyloarthritis with Connective Tissue Disease Overlap in a Female - First Report

Dr. N Subramanian[1], Dr. Ramesh[2], Dr. Selva Ganesh[3], Dr. Prem Anand[4], Dr. Akshlitha J[5], Dr. Kiranlal Yadav[6], Dr. Shruti[7], Dr. Sivaranjani[7]

[1]Asst Prof and Consultant Rheumatologist, [2]Associate Prof in Medicine, [3]Consultant Cardiologist, [4]Consultant Chest Physician, [5]Senior Resident in Radiology, [6]Postgraduate in MD Medicine, [7]Resident in Medicine
Velammal Speciality Hospital and Research Institute, Anuppanadi, Madurai

Abstract

Ankylosing spondylitis is a chronic spinal inflammatory disease affecting young men and, less commonly, women with a spectrum of manifestations including uveitis, arthritis, sacroiliitis, colitis, and psoriasis. Mixed connective tissue disorder [MCTD] is a complex and heterogeneous autoimmune disease that affects women in their childbearing age. It is characterized by circulating autoimmune antibodies that deposit in tissues, resulting in an inflammatory response, causing irreparable tissue damage. **Overlap and coexistence of these diseases are uncommon, as per literature evidence.**

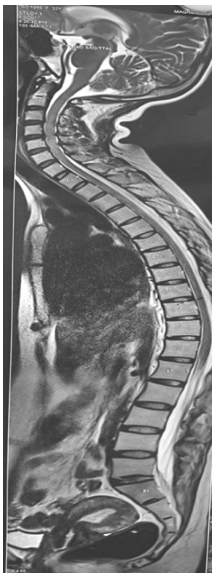

Figure 1-Image showing established ankylosed spine.

We report a 35-year-old female who had HLA B27 – positive spondyloarthropathy for ten years and had been taking sulfasalazine; now presented with neck swelling for four months. She was found to have Raynaud's, arthritis, bilateral cervical lymphadenopathy, and elevated autoantibody titers including ANA, U1SM/RNP, and coombs positive hemolysis. She was evaluated for Infection and returned negative, then concluded as having mixed connective tissue disorder.

Case Report

A 35 years old female came with complaints of multiple swelling in the neck for four months, with ten years history of ankylosing spondylitis on treatment with sulfasalazine. She was recently treated for lymphatic TB for three months without much benefit.

Her clinical examination showed pallor, lymphadenopathy, and stomatitis with restricted spinal movements. There was no history of fever, rashes but she had myalgia and fatigue. She didn't have a contact history with a patient who was on TB therapy.

Initial investigations showed microcytic hypochromic anaemia [Hb: 6.2] with platelet [426], elevated ESR [61] and LDH [1082U/L], CK normal. The direct Coombs test was positive. Peripheral smear showed microcytic hypochromic RBCs with moderate anisopoikilocytosis, target cells, and elliptocytes—WBC-normal counts and distribution with few reactive lymphocytes. Platelets were adequate. Mantoux was negative.

FNAC of submandibular lymph node showed features of reactive lymphoid hyperplasia. HLA B27 was tested positive earlier. (Fig 2, 3)

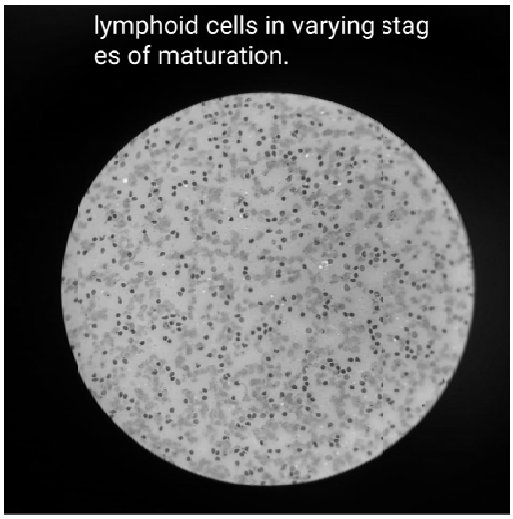

Figure 2:

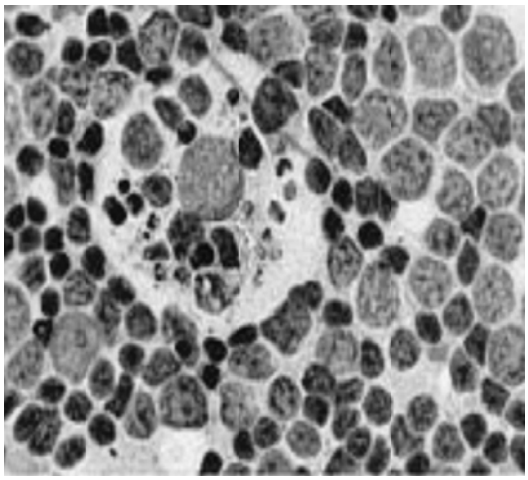

Figure 3

Imaging-Ultrasound abdomen was normal. ECHO showed no evidence of pulmonary hypertension or pericardial effusion. (Fig 4, 5)

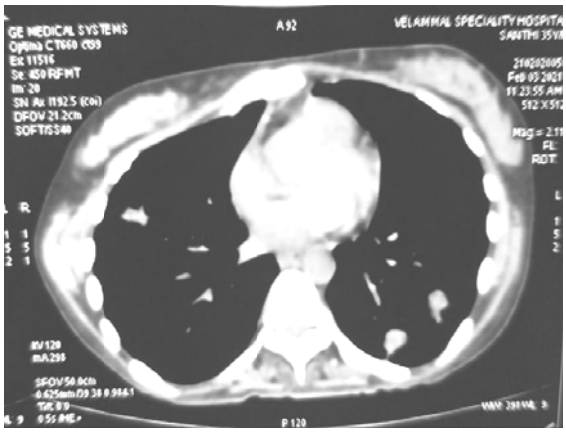

Figure 4

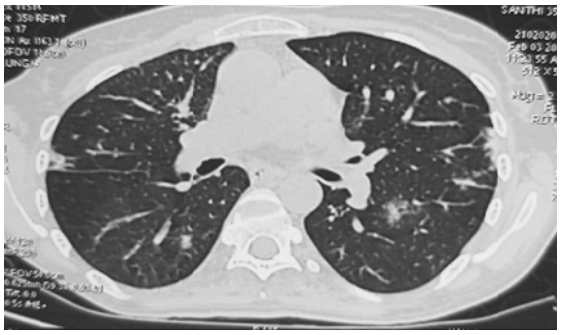

Figure 5

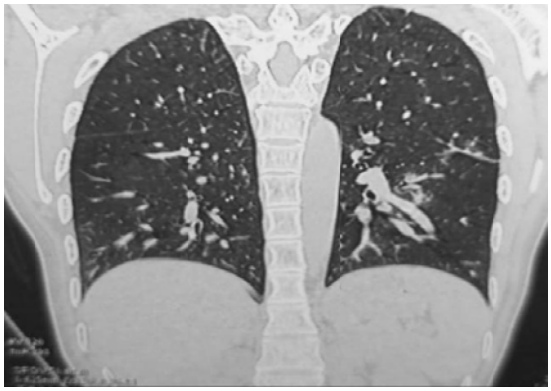

Figure 6

CT chest showed multifocal patchy areas of consolidation in bilateral lung fields. Focal subpleural ground-glass appearances with a surrounding tree in bud pattern in the left upper lobe.(image above) No evidence of pleural effusion. (fig 6)

Immunology: ANA strong Positive, U1RNP antibodies strong positive and borderline positive for Anti MI- 2, smith Negative, dsDNA – Normal, P-ANCA & C- ANCA were Negative. Covid RT-PCR negative and antibodies SARS CoV-2 IgG (0.09), IgM (0.42) were negative.

In conclusion, she had a long-standing ankylosed spine with features of Connective tissue disease with Coombs positive hemolytic anemia and U1 RNP strong positivity. **Hence MCTD was the working diagnosis and treated with appropriate therapy.**

Features here include Polyarthritis, oral ulcers, weight loss, lymphadenopathy, Raynaud's, U1RNP, hemolysis.

Differential Diagnosis: tuberculosis, Covid Infection, SLE, Lymphoma

The patient was treated with antibiotics in view of consolidation and then given steroids.

Following up AFTER 6 WEEKS, a repeat CT scan showed near-total resolution of changes in the lung. (Fig:7)

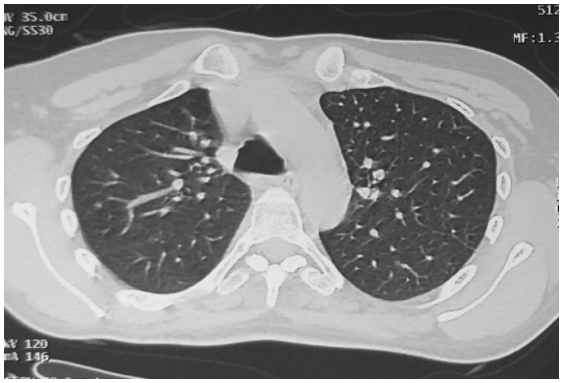

Figure 7

Discussion

Spondyloarthropathies (SpA) and connective tissue diseases (CTD) are clinically distinct entities. However, a link between SpA and CTD has been suggested by few case studies either due to altered immunological behavior or due to drugs like sulfasalazine and biologics like TNF inhibitors. Lee et al. l in 1999 (1) and Pham et al. in 1999(2) described earlier case reports of connective tissue disease in patients with ankylosing spondylitis. Brandt J and colleagues reported in 2002 (3) the development of Sjogren's syndrome in a patient with ankylosing spondylitis while Dharmapaliah in 2018(4) reported pulmonary hypertension in a patient with ankylosing spondylitis developing CTD. All these four reports were described in male patients and had HLA B27, which is understandable and expected.

Our case is female and had HLA b27 positivity with ankylosed spine and had given birth to children. She had been on low-dose sulfasalazine and managing reasonably well. Fever, weight loss, and fatigue naturally prompted evaluation and started on ATT because chest X-ray showed signs of patchy infiltrates and neck nodes were swollen. As she failed to respond to ATT, a rheumatologist was consulted, and then a full evaluation was done.

She didn't manifest with typical features of hand edema or myositis or mechanical hands; however, she had synovitis, fever, oral ulcers, Raynaud's, lymphadenopathy, and lung infiltration with immunology showing u1 RNP antibodies, suggesting the development of MCTD.

She promptly responded to steroids. Sulfasalazine has been implicated in CTD development; however, further studies should throw more light on this.

This is the first case report of a female with ankylosing spondylitis developing MCTD and responding to treatment.

Learning points: Although unusual, ankylosing spondylitis and HLA B27 can happen in females, and the development of fever, lymph nodes, and weight loss should prompt evaluation for Infection and CTD.

References

1. Lee JK, Jung SS, Kim TH, Jun JB, Yoo DH, Kim SY. Coexistence of ankylosing spondylitis and mixed connective tissue disease in a single patient. Clin Exp Rheumatol. 1999; 17(2):263. PMID: 10342061
2. Pham T, Daumen-Legre V, Lafforgue P.Concomitant spondylarthropathy and CREST syndrome..Clin Exp Rheumatol. 1999 Nov-Dec; 17(6):754.PMID: 10609082
3. Brandt J, Maier T, Rudwaleit M et al. Co-occurrence of spondyloarthropathy and connective tissue disease: Development of Sjögren's syndrome and mixed connective tissue disease (MCTD) in a patient with ankylosing spondylitis. Clinical and experimental rheumatology. 2002; 20:80-4.
4. C. Dharmapalaiah1, B. Ms2,P. Sn2: Stiff Spine and Weak Heart: A case of long-standing ankylosing spondylitis developing pulmonary hypertension secondary to mixed Connective tissue disease.. http://dx.doi.org/10.1136/annrheumdis-2020-eular.3454