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Case Report

Systemic Lupus Erythematosus and Overlap

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Abstract

Connective tissue diseases are autoimmune in nature and have a predominance in younger to middle aged women. Symptoms sometimes can be so vague and ill-defined that it may take a while before they are correctly diagnosed and treatment offered Systemic Lupus Erythematosus (SLE) can have a very diverse clinical manifestation and may present without the typical history of a photosensitive rash, alopecia or oral ulcers. A 40-year-old lady presented to the outpatient department with complaints of joint pains, stiffness and unintentional weight loss of 6kgs. Complete blood picture showed pancytopenia but examination was unremarkable for lymphadenopathy and visceromegaly. A detailed assessment revealed hypothyroidism (TSH >100) along with a positive ENA profile with presence of Anti Ro/La, anti U1-RNP and Anti-Smith antibodies but no specific features of Mixed Connective Tissue Disorder. With low complement levels and positive Anti-DS-DNA antibodies she was labelled as SLE with Overlap and started on Replacement Thyroxine, Steroids and Disease Modifying Anti-Rheumatic Drugs (DMARDS). She showed significant improvement after 3 days of Pulse Therapy with Methylprednisolone and was discharged after 5 days of treatment with a follow up planned both with the Internist as well as the Rheumatologist.

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Introduction

Autoimmune conditions involving the connective tissues mostly have an unknown etiology, however with some genetic and environmental contribution to the disease development.

Also known as collagen vascular diseases, they usually result due to an intolerance to self-antigens that puts the immune system into a dysregulated overdrive1. With clinical, serological data and pre-defined diagnostic criteria, we are able to classify these syndromes into a definitive connective tissue disease (DCTD) with predominantly six phenotypes; Rheumatoid Arthritis (RA), Dermatomyositis (DM), Systemic Lupus Erythematosus (SLE), Polymyositis (PM), Systemic Sclerosis (SSc) and Sjogren Syndrome1. However, in about 25% of the cases, clinical features do not fit perfectly into one of the above-mentioned labels as distinct entities and have overlapping features of two or more CTDs.[2] The term "Overlap" is then used to describe these cases.[3]

While the Mixed Connective Tissue Disorder (MCTD) also implies an overlap syndrome, it is highly evolved and has a fixed diagnostic criteria including features like Raynauds Phenomenon, myositis and presence of Anti U1-RNP antibodies.[4] Therefore, Overlap Syndrome by definition is used when a case satisfies the classification criteria for two different CTDs and not fully conforms to the diagnostic criteria for MCTD.[5]

In our clinical practice, we often come across patients who develop coexisting autoimmune conditions, especially an association of thyroid disease, typically autoimmune hypothyroidism is seen with CTDs, like SLE.[6] In fact, patients with SLE Overlap Syndrome have shown to have a higher cumulative incidence of Hypothyroidism.[6]

We report an interesting case of a young female who had been unwell for over a year with arthralgias, myalgias, pancytopenia and weight loss. She had significant physical limitations and low mood upon presentation. The patient was later discovered to have been suffering from MCTD-SLE Overlap Syndrome and Hypothyroidism.

Case Report

A 40-year-old lady presented to the out-patient department with multiple complaints. She reported myalgias and arthralgias for almost a year with a few months of spontaneous improvement in symptoms in between. This was on a background of secondary infertility for almost 12 years. Her past medical and surgical history

was significant for Pelvic Inflammatory Disease / Endometriosis and Adenomyosis for which she had been under care of her gynecologist. Patient had undergone TAH (Total abdominal hysterectomy) almost 6 months prior to this presentation. She reported on and off lower abdominal pain for which she had taken multiple courses of antibiotics as her pelvic ultrasound was consistent with an ovarian cyst and a possible salpingitis.

Regarding her current illness, her arthralgias worsened significantly in the past 4-6 weeks. She also developed fever that was recorded at 102F and lost about 6kgs of weight unintentionally. Joint pains and stiffness extended to involve both small and large joints of the body, predominantly bilateral wrist, right shoulder joint and left knee joints. The pain had a gradual onset and she experienced morning stiffness that lasted about 1-2 hours. Pain was relieved partially by taking Naproxen and the patient had been overusing NSAIDs in the past few weeks. Recent blood profile then revealed pancytopenia and upon further work up, her iron, vitamin B12 and red cell folate levels were all found to be normal. She was advised blood and ferritin transfusions with which she complied.

She also reported to have developed extremely dry skin with flaky patches on left leg and scalp. There was some hair loss along with a longstanding history of skin allergies. Her medical history also included loss of appetite and a dull epigastric pain worsened by meals, accompanied by nausea and occasional vomiting.

Family history was significant for thyroid disease with both parents diagnosed with Hypothyroidism and on hormonal supplements. Her mother was also previously diagnosed with Idiopathic Pulmonary Hypertension and later on went to develop Raynauds phenomenon, Interstitial Lung Disease and tested positive for Anti Scl 70 antibodies.

Physical examination revealed multiple warm, tender, and swollen joints with restricted movements, including the second and third proximal interphalangeal joints, third and fourth metacarpophalangeal joints of right hand, second and third distal interphalangeal and third metacarpophalangeal joint of left hand, bilateral shoulders, elbows, and knees. She was pale and appeared distressed due to pain. Abdominal examination showed mild epigastric tenderness. An erythematous rash was also noted on both her legs.

A detailed work up was planned including an autoimmune profile.

Results are as below:

- Renal and liver function tests, Serum Electrolytes were reported as normal. Similarly routine urine analysis and 24-hour urinary protein also came out to be normal.
- Chest X-ray reported normal. ECG showed normal sinus rhythm with no acute changes.
- Echocardiography was done to rule out presence of pulmonary hypertension and turned out to be normal.
- Blood C/S and viral markers were both negative for any ongoing infections.
- Imaging studies, including ultrasound of the abdomen and pelvis, showed left hydrosalpinx, a right simple adnexal cyst, and mild splenomegaly.
- Serum Lipase and Amylase were normal.

Table 1: *Summary of Lab Investigations*

Investigation	Patient value	Normal range
CBC:		
• Hemoglobin	9.3 g/dl	11.5 – 15.4
• Platelet count	132 x 10^9/L	150 – 450
• WBC count	4.7 x 10^9/L	4.0 – 10.0
CRP	**36.2 mg/L**	0.0 – 5.0
Autoimmune Profile	Negative	
• RA Factor		
• Anti-CCP Ab	<8.0 U/ml	Normal: < 17U/ml
• Anti U1-RNP Ab	>60.0 U/ml	Positive: Greater than 5.0U/ml
• Anti – SSA/ Ro Ab	68.94 U/ml	Positive: Greater than 5.0U/ml
• Anti – SSB/ La Ab	>60.0 U/ml	Positive: Greater than 12.5 U/ml
• Anti – Sm Ab	38.0 U/ml	Positive: Greater than 12.5 U/ml
• Anti – DS DNA Ab	Positive	Positive: Greater than 12.5 U/ml
• Anti – Scl 70 Ab	Equivocal – 4.31 U/ml	Negative: Less than 3.2 U/ml Equivocal: 3.2 – 5.0 U/ml Positive: Greater than 12.5 U/ml
• C3 level	41 mg/dl	83 – 193 mg/dl (age and gender matched)
• C4 level	3 mg/dl	15 – 57mg/dl (age and gender matched)
Thyroid Stimulating Hormone (TSH)	>100	0.4 – 4.2

Course during hospital stay

Treatment was initiated with IV Pulse dose Methylprednisolone for 3 days (0.5g IV OD), followed by maintenance therapy with prednisolone, methotrexate and hydroxychloroquine. The patient also received

symptomatic and supportive treatment with IV analgesia, fluids, PPIs and ondansetron. She was started on supplemental thyroxine at 100mcg daily dose with follow up advised at 6 weeks. Additionally, lifestyle modifications were advised, including sun protection to reduce the risk of disease flares and complications. The patient showed significant improvement in symptoms and joint function. Regular follow-up appointments were scheduled to monitor disease activity and adjust the treatment plan as needed.

Discussion

In comparison to a definitive diagnosis of pure lupus syndrome, an overlap with another CTD is usually seen in about 17-38% of individuals.[7,8] The clinical manifestation of lupus is widespread almost involving all body systems. Patients usually present with oral ulcers, alopecia, polyarthritis and malar rash and occasionally more serious involvement of the kidneys and central nervous system is seen. Similarly, these patients may test for multiple autoantibodies including anti-DS DNA, anti-ro/la and anti-smith antibodies.[9] However, the severity of organ involvement differs from person to person and may vary at a given point in time for the same individual as well.[7] Management of such patients who present with an SLE-Overlap syndrome will depend largely on suppression of the dysregulated immune system as well symptom improvement. The mainstay of therapy remains to be corticosteroids, antimalarials and immunosuppressants. For more refractory cases, newer biologic agents like anti-TNF alpha or anti-CD20 monoclonal antibodies may need to be administered.[10] Based on the SLE Doris framework, it is attempted to attain full remission with the treatment strategies in place.[11] SLE may also be accompanied by an autoimmune thyroid disease particularly Hashimotos thyroiditis and these patients may test positive for anti-thyroglobulin and anti-thyroid peroxidase antibodies.[12,13] This involvement is favored by the occurrence of Anti-Sm antibodies[12]. Patients with overlapping autoimmune diseases such as this case specially need to be educated and treated holistically. While the treatment of SLE has significantly improved over the last decade or so, each patient requires a tailor-made comprehensive plan to care for both the problems that occur as part of the disease and therapy.[14]

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References

1. Shah S, Chengappa KG, Negi VS. Systemic lupus erythematosus and overlap: A clinician perspective. Clin Dermatol Rev. 2019;3(1):12-7.
2. Brasington R. Mixed connective tissue disease, overlap syndromes, and undifferentiated connective tissue disease. Rheumatology Secrets E-Book. 2019; 33(67): 185.
3. Handa R, Handa R. Undifferentiated Connective Tissue Disease, Mixed Connective Tissue Disease, and the Overlap Syndromes. Clin Rheumatol. First Edition. 2021: p.143-5.
4. Maikap D, Deosale S, Singh P, Panda SS, Padhan P. A comparative study of mixed connective tissue disease and overlap syndromes–A single-center study from India. Indian J Rheumatol. 2023:10(1):4103
5. Alekperov RT. Mixed connective tissue disease, undifferentiated connective tissue disease and overlap syndromes. Almanac Clin Med. 2019;47(5):435-44.
6. Liu YC, Lin WY, Tsai MC, Fu LS. Systemic lupus erythematosus and thyroid disease–Experience in a single medical center in Taiwan. J Microbiol Immunol Infec. 2019;52(3):480-6.
7. Shah S, Chengappa KG, Negi VS. Systemic lupus erythematosus and overlap: A clinician perspective. Clin Dermatol Rev. 2019;3(1):12-7.
8. Lockshin MD, Levine AB, Erkan D. Patients with overlap autoimmune disease differ from those with 'pure' disease. Lupus Sci Med. 2015;2(1):e000084.
9. Raissi TC, Hewson C, Pope JE. Repeat testing of antibodies and complements in systemic lupus erythematosus: when is it enough?. J Rheumatol. 2018; 45(6): 827-34.
10. Mohamed A, Chen Y, Wu H, Liao J, Cheng B, Lu Q. Therapeutic advances in the treatment of SLE. Int Immunopharmacol. 2019;72(7):218-23.
11. Saeed M, Pasha A, Rizvi SH, Munawar M, Elias ZA, Shafi MI, Gazdar T, Lakhdir MP. Remission and clinical patterns of systemic lupus erythematosus (SLE) in Pakistan: a retrospective cohort study. medRxiv. 2022: 2022-11.
12. Athanassiou P, Athanassiou L, Mavroudi M, Tsakiridis P, Koukosias N, Kostoglou-Athanassiou I. PO. 4.89 Hashimoto's thyroiditis in systemic lupus erythematosus patients.
13. Bibi H, Raza AB, Naz F. Occurrence of Autoimmune Thyroid Dysfunction in Juvenile SLE. Pak J Med Health Sci. 2022 Jul 8;16(06):229.
14. Fang K, Orr-Skirvin JA. Systemic lupus erythematosus, its treatment, and future directions. US Pharm. 2019; 44(8):3-7.