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AN INTERESTING CASE OF OVERLAP SYNDROME

DR.PADMA.V [1], DR.SYED MOHAMMED JAVID M.S.A[2*], DR.NARENDRAN.A[3] AND DR.KARTHIKEYAN.R[2]

[1]Professor of medicine Sree Balaji medical college and hospital.
[2] Post graduate of medicine Sree balaji medical college and hospital.
[3]Assistant professor of general medicine sree balaji medical college and hospital.

ABSTRACT

Overlap syndrome is a condition in which patient will have more than one connective tissue disorder. Definite diagnosis and initiation of treatment have a prognostic significance. We are presenting a case of young female with complaints of dysphagia who presented with features of systemic sclerosis(SSc) and rheumatoid arthritis ,investigated with special investigations and found to be a case of overlap syndrome .patient been treated ,improved with treatment and she is on regular follow up. Awide range of clinical suspicion is needed for diagnosis and early initiation of ideal treatment will help in alleviating the present ailments and preventing further complications of the disease. Young female presenting with esophageal dysmotility, Raynaudsphenomenon should prompt the diagnosis of systemic sclerosis and further work up should be done. we enlighten this case because this case of overlap syndrome with LSc and RA with features of pulmonary hypertension which is a rare presentation.

KEYWORDS: **overlap syndrome, systemicsclerosis, and rheumatoid arthritis.**

DR.SYED MOHAMMED JAVID M.S.A
Post graduate of medicine sree balaji medical college and hospital.

INTRODUCTION

A 25 year old female known case of rheumatoid arthritis under irregular treatment came to outpatient department with complaints of breathlessness on and off for 1 month, dysphagia, vomiting for both solid and liquid for 10 days.Patient had history of raynauds phenomenonon for 2 months.On examination patient had features such as fish mouth, pinched nostrils, sclerodactyly ,swan neck and boutonniere deformity features suggestive of systemic sclerosis and rheumatoid arthritis. Her vitals were stable Systemic examination were uneventful. Investigations revealed Hb13.5gm/dl,, minimal proteinuria(urine protein creatinine ratio 0.383).Special investigations like ANA RAfactor and CCP were positive. Hypocomplementemia C3-26.10mg/dl,C4-2.30mg/dl, AntiCentromere antibody was positive,.2D-Echo revealed moderate pulmonary hypertension .Other investigations such as ANTIdsDNA,Anti-ss-DNA,AntiSmith antibody,AntiSCL-70,U1RNPAntibody were negative.Investigations like liver function test,renal function test,chest x ray PAview,urine routine except for minimal proteinuria were normal.Upper gastrointestinal endoscopy was normal.Diagnosis was confirmed by both clinical examination as well as standard criterias for both disease .Patient was treated with azathioprine and oral corticosteroids,and sildenafil(pulmonary hypertension,raynauds phenomenon).Patient responded well become symptomatically better,Her complement levels came to normal level after few weeks and is on regular follow up.

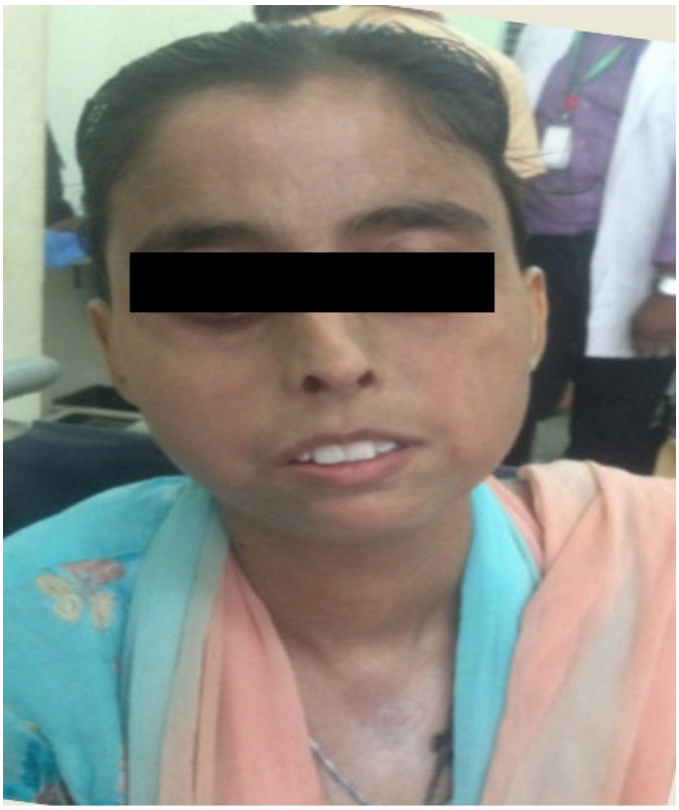

Figure 1
The pictures above shows following features such as pinched nostrils ,microstomia , fishmouth ,absence of normal wrinkling,taut and shiny skin over the face,

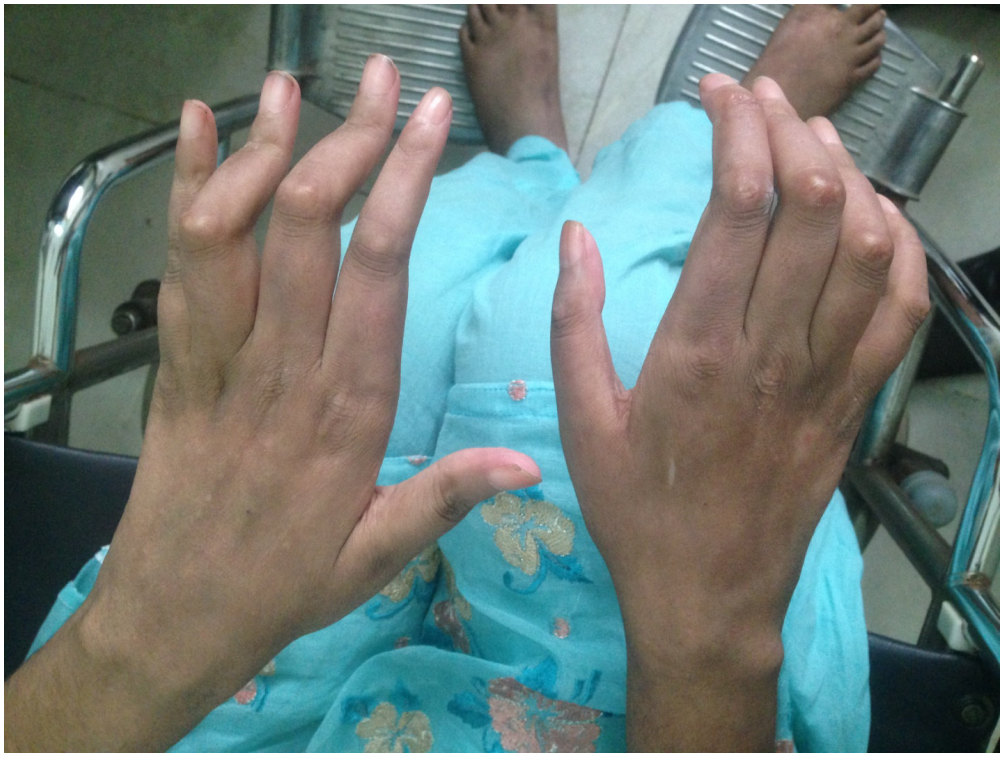

Figure 2
Swan neck deformity and boutennaire deformity in the hands.

In a study conducted at an institution in Debrecen ,eastern hungary with 477 patients with connective tissue disorders, 22 patients were found to have overlap syndrome with combination of systemic sclerosis and rheumatoid arthritis.

DISCUSSION

An overlap syndrome is an autoimmune disease of connective tissue in which a patient presents with symptoms of two or more diseases.
Examples of overlap syndromes include mixed connective tissue disease and scleromyositis. Diagnosis depends from which diseases the patient shows symptoms and has positive antibodies for in their lab serology.
In overlap syndrome,the commonly associated diseases are:
Systemic lupus erythematosus (SLE) [1,2],
Systemic sclerosis,
Polymyositis,
Dermatomyositis,
Rheumatoid arthritis (RA)
Sjögren's syndrome
Churg–Strauss syndrome
Autoimmune thyroiditis
Antiphospholipid antibody syndrome [3]
A variety of mechanisms have been proposed for the development of autoantibodies in SSc [4]. They are
1) Proteolytic cleavage, increased expression, or altered subcellular localization of certain cellular proteins in SSc lead to their recognition as neoepitopes by the immune system, resulting in breakdown of immune tolerance.
2) B cells are implicated in both the autoimmune and fibrotic process in SSc.
3) In addition to antibody production[4], B cells also present antigen, secrete IL-6 and TGF-β, and modulate T cell and dendritic cell function. The antibodies involved in the respective connective tissue disorder and overlap syndromes are listed below.

Table 1
Autoantibodies in scleroderma

Anti-DNA topoisomerase I (Scl-70)	Diffuse scleroderma
Anticentromere (proteins A, B C)	Limited scleroderma
Anti-U3RNP (fibrillarin)	Diffuse scleroderma—severe disease
Anti-7-2/8-2 RNP (Th/To)	Limited scleroderma
Anti-PM-Scl	Diffuse scleroderma, renal crisis
Anti-RNA polymerases I, II, III	Scleroderma overlap
Anti-Ku	Scleroderma overlap
Antipyruvate dehydrogenase complex (M2)	Limited scleroderma and scleroderma overlap

Table 2
Overlap syndromes in autoimmune rheumatic disease and associatedAutoantibodies[4]

Mixed connective tissue disease	UnRNP; hnRNP(A2/RA33 complex); U1RNA
tRNAsynthetase syndrome	Jo-1, PL-7, PL-12, OJ, EJ
Polymyositis/scleroderma	Ku; PM-Scl; U2 RNP; DNA-PK
Secondary Sjögren's syndrome	Ro/SSA; La/SSB; Ki/SL
Scleroderma (CREST)/primary biliary cirrhosis	Centromere; pyruvate dehydrogenase complex
Systemic lupus erythematosus/autoimmune hepatitis	tRNA
Polymyositis/pulmonary fibrosis	KJ

hnRNP- heterogeneous nuclear ribonuclear protein; PM- polymyositis Scl--scleroderma overlap syndrome

Systemic sclerosis (ssc)
Progressive disease that affects the skin and connective tissue (including cartilage, bone, fat, and the tissue that supports the nerves and blood vessels throughout the body). There is an increased deposition collagen in interstitium of small arteries and connective tissue and sclerotic changes in skin and internal organs
CLASSIFICATION OF SYSTEMIC SCLEROSIS
(adapted according to J.R. Seibold, 1994)
I. diffuse – skin thickening - trunk, face and limbs
II. Limited - skin thickening localized distally of elbows and knees, with face involvement, CREST
III. Sine scleroderma – without skin involvement (except of face), fibrotic changes of visceral organs, vascular and serological findings.
IV. Overlap syndrome - fulfilled criteria of SSc and of SLE, RA or polymyositis
V.undifferentiated connective tissue disease - Raynaud's phenomenon with clinical and/or laboratory abnormalities - anticentromere antibodies, skin
Vascular trophic changes.
OVERLAP SYNDROMES:
Classification into overlap syndromes is facilitated by detection of autoantibodies
• Mixed connective tissue disease (MCTD, Sharp's syndrome) (anti-nRNP autoantibodies, or anti-p70),
• Antisynthetase syndrome (ASS) (anti-Jo-1, anti-PL-7, 12 etc.)
• Polymyositis/scleroderma overlap (PM/Scl) (anti-PM/Scl antibodies)
• Scleroderma/polymyositis (anti-Ku antibody).

Scleroderma or systemic sclerosis[5] is a connective tissue disease involving sclerotic changes in the skin and many other organ systems. The condition includes a spectrum of disorders that range from localised forms like morphoea with limited cutaneous involvement to diffuse cutaneous disease accompanied by early internal organ involvement.[6]To establish diagnosis and treatment for patients with scleroderma overlap syndromes, it is important that the associated clinical and serological features are diagnosed.Scleroderma has been associated with SS, SLE, DM, Hashimoto's thyroiditis, and primary biliary cirrhosis.[7] Scleroderma overlap syndromes[8] are referred to as MCTDs; however, overlaps also occur in patients who do not have antibodies to nRNP and are associated with ANA of nucleolar staining pattern. A prospective study with 794 patients of systemic sclerosis conducted in the connective tissue disorder clinic of Royal Free Hospital, London showed that pulmonary hypertension was associated with poor prognosis. .The causes of death in these disorders are due to involvement of heart, lung and kidney. The treatment of overlap syndrome is mainly based on the use of corticosteroids and immunosuppressants. biologic drugs, i.e. anti TNFα or anti-CD20 monoclonal antibodies.[9]
Treatment for Raynaud's phenomenon:
- Often unresponsive to glucocorticoids
- Warmed gloves
- Calcium channel blockers, ACE inhibitors
- Prostaglandin infusions
Treatment of pulmonary hypertension:
-endothelin receptor antagonists bosentan or sitaxentan .
-Phosphodiesterase-5 inhibitor sildenafil.
-Long-term anticoagulation.
-Tyrosine kinase inhibitor imatinib mesylate This has shown to improve pulmonary fibrosis in MCTD.

CONCLUSION

In our case there was an association of pulmonary hypertension with SSc 5 which is seen in only 10-15% of scleroderma patients.Its association is associated with poor prognosis.Many studies have shown that incidence of overlap syndrome involving systemic sclerosis and rheumatoid arthritis is less than 10% among the connective tissue disorders We are presenting this case as it is a rare presentation .Early diagnosis and treatment is associated with good prognosis.

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