Case Report

A Case of Myositis Overlap Syndrome

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ABSTRACT

The term "Myositis Overlap Syndrome" is applied when Dermatomyositis (DM) or Polymyositis (PM) is associated with other well defined connective tissue diseases. Specific pathological autoantibodies and clinical overlap features are important clues to the diagnosis of an overlap syndrome. Antibodies to U1RNP, PM-Scl, or Ku associated with good corticosteroid responsiveness. Intravenous immunoglobulin can be given to the patients with myositis overlap syndrome, who do not respond to corticosteroids, have progressive severe muscular weakness or patients having multi-system involvement for better clinical outcome. Here we report a case of 34 year male diagnosed with Scleroderma-Polymyositis overlap syndrome, exact incidence and prevalence of Scleroderma-Polymyositis overlap syndrome is not known.

Introduction :

All of the major autoimmune connective tissue diseases have varying degrees of overlap with each other. The propensity for this overlap is often correlated with a distinctive autoantibody profile, presentation and response to treatment. Polymyositis (PM) is an inflammatory myopathy that may have a heterogeneous clinical presentation but usually courses with subacute proximal muscle weakness and creatine kinase (CK) elevation. It is rare as a single entity. Myositis overlap syndromes are more common than the classic presentations of polymyositis or Dermatomyositis[1]. It is associated with systemic autoimmune disorders or connective tissue diseases. Pathological autoantibodies (e.g., Scl70, anticentromere, PM/Scl and U1-RNP) are important clues as to the development of an overlap syndrome[1].

Case Report :

A 34 year old male farmer, from Yavatmal presented with complaints of joint pain since 2-3 months, easy fatiguability since 1 month, inability to get up from sitting position & inability to lift both upper limb above head since 8-10 days. Initially patient was able to carry out his daily activities with easy fatiguability, but the weakness progressed gradually and on presentation the patient was unable to get up from bed or turn to side while in supine position. Patient also had history of skin rashes since 2-3 months and dysphagia for the past 15-20 days. The weakness did not have a diurnal variation or episodic nature. Patient gave no history of fever, loose motion, or trauma. There was no history of fasciculations, nasal regurgitation of food, tingling and numbness, bowel and bladder involvement,. Patient was not on any medications for any chronic disease like diabetes, hypertension, thyroid disorder. No past history of Tuberculosis, HIV infection. On examination patient was conscious, oriented and vitally stable. Mouth opening was restricted. On neurological examination patient had bilateral symmetrical wasting in shoulder & hip girdle. Patient had weakness of neck flexors & truncal muscles. Power was 4/5 in bilateral proximal group of muscle of upper limb and 3/5 in bilateral proximal group of muscle of lower limb while normal distally. Deep tendon reflexes were normal in all four limbs & both plantars were flexor. Patient was having a waddling gait. Rest of the neurological examination was normal. On cardiovascular system examination, patient had double apical impulse in left lateral position & grade 3 high-pitched, crescendo-decrescendo, midsystolic murmur heard best at the left lower sternal border. Rest of the systemic examination was normal. Patient's dermatological examination revealed generalised xerosis cutis, tightening of the skin over face, bilateral palmer thickening and fissuring. There were many ill-

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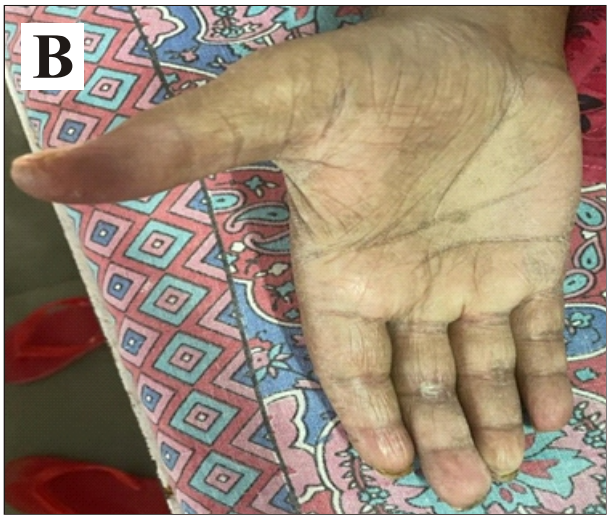


A : Shows symmetrical wasting of the shoulder girdle muscles.

B : Shows palmer thickening and fissuring with ill defined hyperkeratotic papules and plaques suggestive of 'Mechanics hand'.

C : Showing head drop due to neck flexor muscle weakness.

defined hyperkeratotic papules and plaque seen over both palms suggestive of 'mechanics hand'. Nails showed hyperkeratotic changes and ragged cuticles.

On the basis of history, age of onset of symptoms, duration of symptoms & neurological examination, we suspected this patient to be a case of acquired myopathy. We further evaluated this patient to find out the cause of myopathy so that specific therapy can be given.

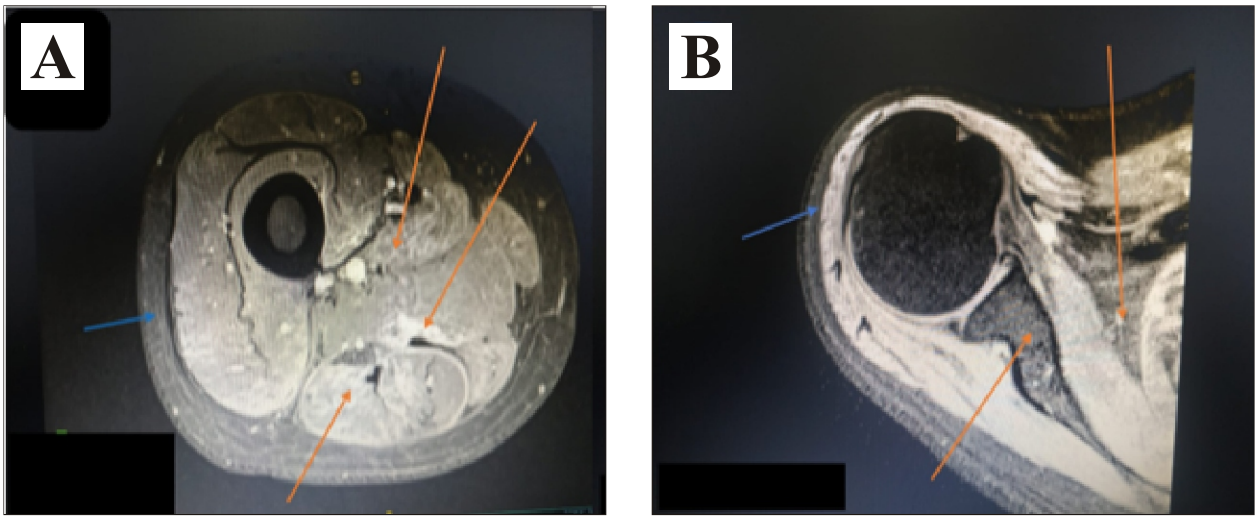
Complete blood count, serum electrolyte and renal function test were normal. Liver function test was deranged with SGOT of 126 IU and SGPT of 228 IU, his Serum Bilirubin and Alkaline phosphatase levels were within normal limits. Total Creatinine-Phospho-Kinase was 1250 IU/L (Normal range 25-200 IU/L). Erythrocyte sedimentation rate was 24 mm/hr. C Reactive Protein was 7 mg/L. Urine myoglobin was present. Thyroid function test was normal. Electromyography showed increased insertional activity with fibrillation potential in distal and proximal muscle. Low amplitude short duration polyphasic motor unit potentials seen, suggestive of myopathy affecting proximal more than distal. Nerve conduction study & repetitive nerve stimulation tests were normal. HIV, HBsAg & HCV were negative. Patient was COVID-19 negative by RT-PCR. Echocardiography was suggestive of Hypertrophic Obstructive Cardiomyopathy.

On the basis of history, clinical examination, routine blood investigation and electromyography report, patient was diagnosed as a case of Inflammatory Myopathy (Polymyositis). His Anti-nuclear antibody with Extractable nuclear antigen panel was sent to rule out connective tissue disorder. Anti-nuclear antibody test was moderately positive (Titre 1:320) with nucleolar and speckled pattern.

Extractable nuclear antigen panel was positive for PM-Scl antibodies. These antibodies are specific for Scleromyositis or Scleroderma-Myositis overlap syndrome. Contrast enhanced CT abdomen, pelvis and thorax was done to look for any underlying malignancy, which was normal.

Muscle biopsy was planned but couldn't be done. So MRI of right upper & lower limb muscle was done. MRI showed proximal group of muscle atrophy with patchy hyperintensity signal and moderate patchy post contrast enhancement. These features are suggestive of Inflammatory Myopathy with features of both chronicity and active ongoing muscle inflammation.

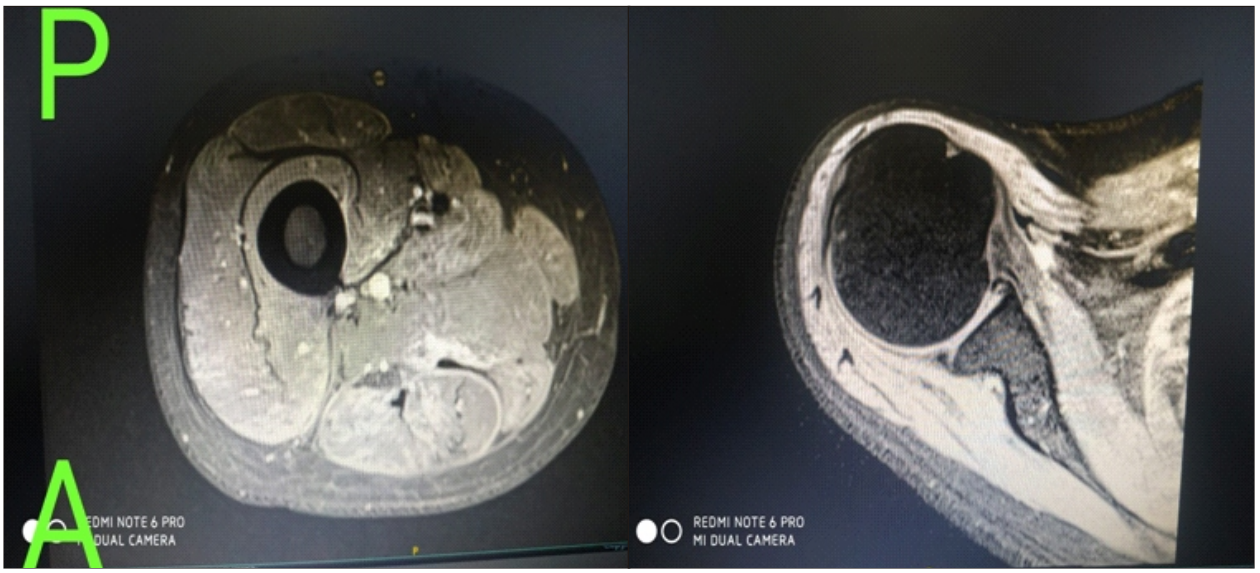
Patient was finally diagnosed as a case of Scleroderma / Polymyositis overlap syndrome. In view of severe muscular weakness and dysphagia patient was given intravenous methylprednisolone infusion 1 gm/day for 5 days then shifted to oral methylprednisolone 1mg/kg/day. After 2 weeks of



A and B are T1, T2 weighted MRI images showing patchy areas of hyperintensity with post contrast enhancement and muscle atrophy in right hip girdle and right shoulder girdle muscles respectively.

Red arrow : showing patchy areas of hyperintensity with post contrast enhancement.

Blue arrow : showing muscle atrophy.



corticosteroid therapy there was no improvement so that Tab Methotrexate 15 mg/week added. Even after 2 weeks of combination therapy, patient had progressive severe muscular weakness and dysphagia, hence the patient was started on Intravenous immunoglobulin in dosage of 2 gm/kg over a period of 5 days in addition to oral corticosteroid and methotrexate. After 1 week of starting intravenous immunoglobulin there was improvement in muscle power, dysphagia improved and the patient was able to carry out his daily activities with minimal support. Patient was discharged on tapering dose of corticosteroid, tablet methotrexate 15 gm/week with physiotherapy. Patient was advised monthly follow up initially for assessing prognosis and monitoring development of complications like interstitial lung disease, renal involvement.

Discussion :

The term overlap syndrome is applied when Dermatomyositis or Polymyositis is associated with other well defined connective tissue disorders like Scleroderma, Systemic lupus erythematous, Sjogren's syndrome and rheumatoid arthritis.

Diagnostic criteria for Myositis overlap syndrome.

- Inflammatory myopathy and
- At least one clinical overlap feature and/or
- Presence of an overlap autoantibody

Definition of inflammatory myopathy

1) Symmetric proximal muscle weakness
2) Elevation of serum skeletal muscle enzymes
3) Electromyographic triad of short, small, polyphasic motor unit potentials; fibrillations, positive sharp waves and insertional irritability; and bizarre, high-frequency repetitive discharges
4) Muscle biopsy abnormalities of degeneration, regeneration, necrosis, phagocytosis, and an interstitial mononuclear infiltrate
5) Typical skin rash of DM, including the heliotrope rash, Gottron sign, and Gottron papules

- Definite myositis : 4 criteria (without the rash) for PM, 3 or 4 criteria (plus the rash) for DM
- Probable myositis : 3 criteria (without the rash) for PM, 2 criteria (plus the rash) for DM
- Possible myositis : 2 criteria (without the rash) for PM, 1 criterion (plus the rash) for DM(1)

Clinical overlap feature

Polyarthritis, Raynaud's phenomenon, sclerodactyly, scleroderma proximal to the metacarpophalangeal joints, typical systemic sclerosis-type calcinosis in the fingers, lower oesophageal or small-bowel hypomotility, diffusing capacity for carbon monoxide lower than 70% of the normal predicted value, interstitial lung disease on chest radiogram or computed tomography scan, discoid lupus, anti-native DNA antibodies plus hypocomplementemia, four or more of 11 American College of Rheumatology systemic lupus erythematosus criteria, anti-phospholipid syndrome.[1]

Definition of Overlap Autoantibodies

- Anti-synthetases (Jo-1, PL-7, PL-12, OJ, EJ, KS),
- Scleroderma specific antibodies : Centromeres, Topo I, ribonucleic acid-polymerases I or III, Th
- Antibodies associated with Scleroderma in overlap : U1RNP, U2RNP, U3RNP, U5RNP, Pm-Scl, Ku),
- Other autoantibodies (SRP, nucleoporins)[1]

Radiological imaging for inflammatory myopathy

MRI of muscle also has a pivotal role in diagnosis of inflammatory myopathy. MRI is highly sensitive but less specific for muscle inflammation. Though muscle involvement in myositis is proximal & symmetrical, sometimes patchy and focal involvement is seen. MRI screens whole limb muscle so that patchy and focal involvement of muscle can be detected on MRI. In contrast patchy and focal involvement can be missed on muscle biopsy due to sampling error. MRI shows hyperintensity, post-contrast enhancement, muscle oedema or muscle atrophy. MRI can also help in

selecting muscle for biopsy. MRI can also used for assessing prognosis of patient[2].

Systemic sclerosis has a widespread heterogeneity of disease expression, ranging from a diffuse cutaneous disease, with a poor prognosis, to a limited cutaneous involvement, with a mostly good prognosis. Systemic sclerosis often has overlaps with one or more connective tissue disorders. Systemic sclerosis overlap syndromes include Scl variants such as CREST, Inflammatory myopathy, myositis associated with sclerodactyly and mixed connective tissue disease (MCTD). They were predominantly female (82.5%), with a mean age of 48 years, and developed musculoskeletal involvement more frequently (62.5%) than patients with limited Scl (32.2%) or diffuse Scl (43.3%)[1]. Erythrocyte sedimentation rate is usually normal in systemic sclerosis, an elevation may signals myositis overlap or coexisting malignancy.

Polymyositis (PM) may be associated with systemic sclerosis, including its variant without skin involvement. Polymyositis Scleroderma overlap is usually associated with anti PM/Scl antibodies. This autoantibodies are found in a significant proportion of SSc patients, but in the absence of other Scleroderma-specific autoantibodies anti PM/Scl antibodies are found in 3% of patient and associated with a distinct clinical phenotype. Anti-PM/Scl antibodies are reactive with several proteins of the nucleolar PM/Scl macromolecular complex. The two major components of anti PM/Scl antibodies are the PM/Scl-75 and PM/Scl-100 epitopes. Antibodies to PM-1 (the major component of PM/Scl-100) are positively associated with a younger age of onset, inflammatory myopathy, calcinosis, inflammatory arthritis, and overlap features. They are negatively associated with interstitial lung disease, renal involvement and gastrointestinal involvement[3]. They produce a pattern of nucleolar staining on indirect immunofluorescence[4].

Anti-PM-Scl antibody is strongly associated with SSc with limited cutaneous involvement in overlap with inflammatory myopathy. In comparison with SSc patients without this antibody, patients with anti-PM-Scl antibodies has a reduced frequency of peripheral vascular disease, pulmonary arterial hypertension and gastrointestinal involvement. Although anti-PM/Scl antibody positive patients had a somewhat increased frequency of pulmonary fibrosis, the severity of interstitial lung disease was reduced in these patients[5]. In one study by D'AOUST et.al shows that there is decreased frequency of interstitial lung disease in patients with anti-PM/Scl antibodies[4].

Anti-PM/Scl antibody positive patients have the best survival and excellent prognosis of all Systemic Sclerosis related serologic subsets[6,7]. Antibodies to U1RNP, PM-Scl, or Ku tend to be associated with corticosteroid responsiveness[1]. In a patients of Scleroderma-myositis overlap with anti-PM/Scl antibody, we should focus on the activity and severity of both myositis and interstitial lung disease. This can be treated with anti-inflammatory/immunosuppressive therapy to improve functional status or halt disease progression[5].

According toliterature, patients with scleroderma-myositis overlap with anti PM/Scl antibodies have a good response to corticosteroids, but in a patients not responding to steroid as a monotherapy we can consider other immunomodulator drugs like Mycofenolate mofetil. Azathioprine or Methotrexate. Patients who present with severe muscular involvement, rapidly progressive disease, interstitial lung disease, oesophageal involvement and who do not respond to first and second line immunosuppressive therapy, can be treated with intravenous immunoglobulin for better clinical outcome[8]. At present, no definitive guidelines are available regarding initial dose, total days of administration, and timing or dosing of subsequent administration of IVIG for inflammatory myopathy. Several studies suggested IVIG at a dose of 2 g/kg body weight over a 5-day period, followed by monthly doses over 1 to 5 days for a period of 3 to 6 months[8]. The improvement in strength can be seen as soon as 2 weeks after the first infusion. Intravenous immunoglobulins are effective and can be a therapy of great impact on the quality of life of

the patient, even when apparently irreversible injury is established[8]

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