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Case Report

Rapidly progressing treatment resistant anti-TIF1 gamma antibody positive dermatomyositis

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ABSTRACT

Dermatomyositis is an idiopathic inflammatory myositis involving progressive muscle weakness with skin manifestations. Incidence of dermatomyositis is 1 per 100,000 in general population. Diagnosis is based on characteristic skin rashes, progressive muscle weakness and elevated muscle enzymes levels (creatine phosphokinase). The diagnosis is confirmed by clinical examination, abnormal electromyogram and autoimmune workup. In this case report, we report a case of difficult to treat dermatomyositis with proximal muscle weakness in an elderly male patient with classical skin lesions. The patient was resistant to steroid and immunoglobulin therapy.

Keywords: Dermatomyositis, Creatine phosphokinase, Electromyogram

INTRODUCTION

Dermatomyositis (DM) is a chronic inflammatory disorder of the skin and muscles. Skin involvement in DM usually manifests with characteristic papules over digits, erythema over the elbows and knees, a heliotrope rash around the eyes, periungual telangiectasias, and dystrophic cuticles.[1] Muscle involvement usually manifests as proximal muscle weakness initially, with or without myalgias or tenderness. There is a well-established association of DM with an increased risk of malignancy.[2]

Other important clinical features of DM include the presence of interstitial lung disease (ILD). Myositis-specific antibodies (MSA) are found circulating in approximately 50–70% of DM patients.[3] One of the DM-specific MSA is the anti TIF1 gamma antibodies (anti p155/140 antibodies) and are relatively common, seen in 13–21% of DM patients.[4,5] These antibodies are associated with severe cutaneous manifestations and higher rate of malignancy.

CASE REPORT

A 70-year-old-gentleman, who is a known hypertensive, visited our hospital with complaints of hyper pigmented rash over his chest, back, elbows and knees since 20 days. He had swelling of bilateral lower limbs up to the knee for 10 days. He then developed difficulty in getting up from sitting position, difficulty in lifting his hands above shoulders and nasal regurgitation since 7 days.

On examination, his vital signs were normal. Pallor was present. He had bilateral pitting pedal edema. Motor examination revealed proximal muscle weakness in all four limbs with flexor plantar reflex. A heliotrope rash was present over the eyelids with periorbital edema. A V-shaped rash was present over the anterior neck and upper chest (Figure 1). Rash over the upper back and posterior neck extending up to bilateral shoulders (Shawl sign +ve) (Figure 2). Rashes were also present over bilateral elbows, wrist, bilateral knees (Gottron's sign +ve), and medial part of the thigh (Figure 4) and Flat-topped papules were

present over bilateral hand digits (Gottron's papules) (Figure 3).

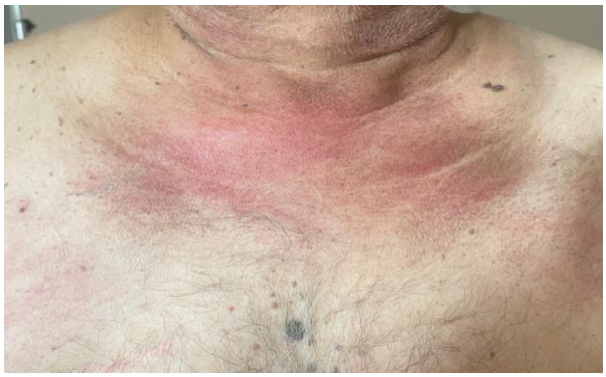

Figure 1: Erythema over anterior neck and chest (v–sign).

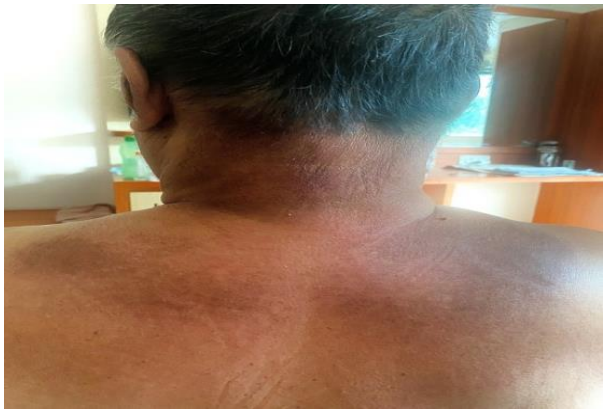

Figure 2: Shawl sign.

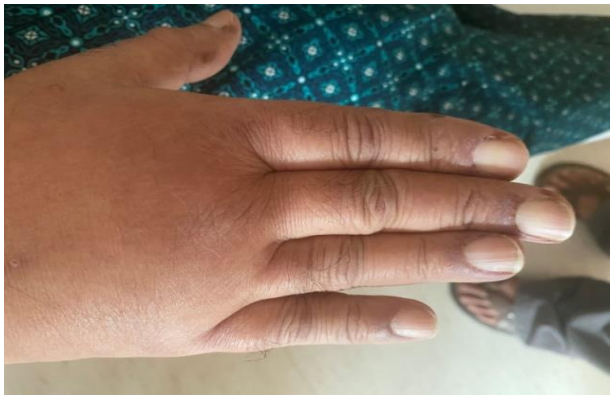

Figure 3: Gottron's papule.

Blood investigations revealed anemia, mild leukocytosis, and transaminitis. Serum CPK levels were elevated (4319 U/l). Autoimmune workup was done ANA positive in indirect fluorescent antibody assay with fine speckled (AC-4) pattern and ANA profile was negative. Myositis workup showed strongly positive for TIF1 gamma. Electromyogram showed insertional irritability and low polyphasic waves. Positron emission tomography-computed tomography (PET-CT) was done which showed diffusely increased metabolic activity in temporalis, pterygoid, sternomastoid, shoulder, chest wall, abdominal wall, gluteal muscles, paraspinal muscles, arm, proximal forearm, bilateral thigh, popliteal, peroneal and some intrinsic muscles of the foot with no scan evidence of malignancy.

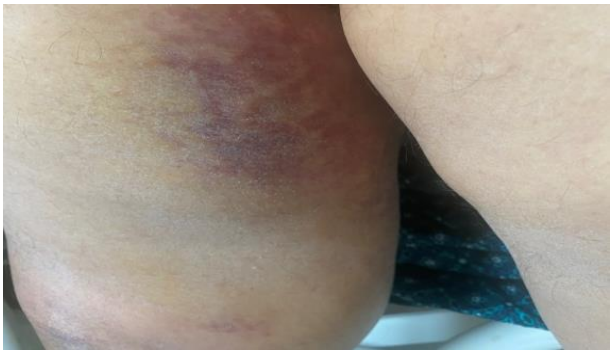

Figure 4: Erythematous skin lesion over right inner thigh.

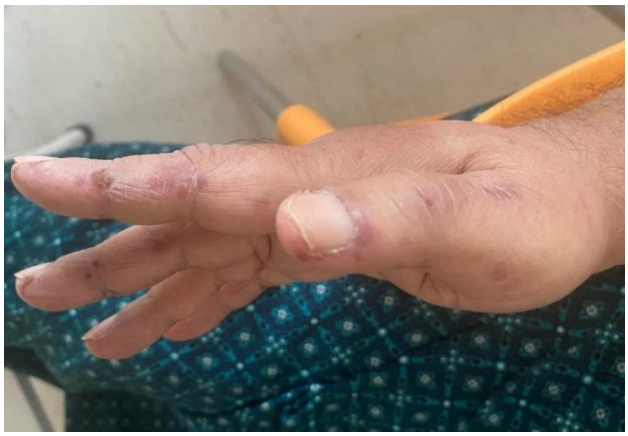

Figure 5: Mechanic's hand.

He was diagnosed with dermatomyositis and was initiated on pulse therapy with methylprednisolone. Ryles tube feeding was initiated in view of dysphagia. As his limb weakness persisted, he developed respiratory distress and he was started on intravenous Immunoglobulin (400 mg/kg), dose adjusted according to his weight (94 kg) given over 5 days.

His muscle weakness progressed despite steroid and IVIg therapy. He developed aspiration pneumonia and was started on intravenous antibiotics. He developed type 2 respiratory failure and was intubated and mechanically ventilated. A tracheostomy was done due to requirement of prolonged ventilation. He was given two doses of rituximab as his respiratory weakness persisted and was started on tofacitinib (5 mg twice daily) along with oral steroids.

He improved and weaned off the ventilator one week later. His limb weakness improved gradually as well as his skin lesions. He was later discharged and was advised to

continue tofacitinib along with steroids on tapering dose and regular physiotherapy.

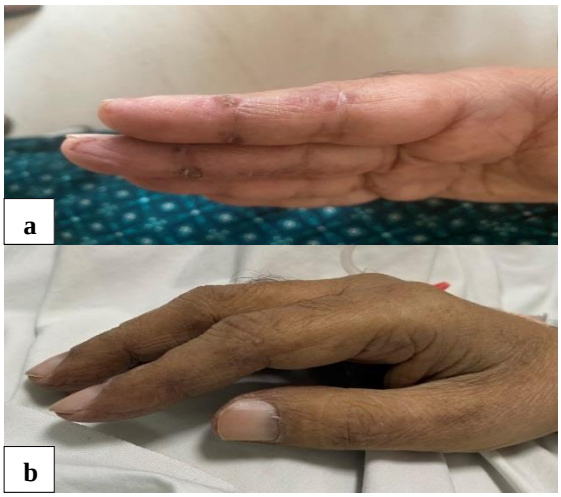

Figure 6: (a) at onset and (b) 2 months since treatment.

DISCUSSION

The diagnosis of DM is traditionally based on the classification criteria published by Bohan and Peter.[6] Four of these criteria were present (proximal muscle weakness, elevated muscle enzymes, EMG showing insertional irritability, typical cutaneous changes) which made the diagnosis of dermatomyositis definite in our patient.

Anti-TIF-1γ antibodies was positive in the patient. Anti-TIF-1γ and anti-nuclear matrix protein NXP-2 (anti-NXP-2) antibodies are two antibodies that are frequently positive in DM patients.[7] These two autoantibodies are present in most patients with cancer-associated DM (found in 83% cases - 31% anti-NXP-2 and 52% anti-TIF 1-γ) and should prompt the clinician to initiate cancer screenings.[7,8] These antibodies are almost exclusively non-overlapping.[7] A significant proportion of anti-TIF1-γ positive adult patients with dermatomyositis have no detectable malignancy at the onset of the disease as in our patient, thus continued cancer surveillance and reassessment is critical in patients who relapse with dermatomyositis symptoms.[8]

As for treatment of dermatomyositis, patients are usually started on systemic steroid therapy. In patients with severe disease, steroid pulse of intravenous methyl prednisolone 1000 mg for three consecutive days is usually given. Oral prednisolone at an initial dose of 0.5–1 mg/kg/day followed by a slow progressive dose reduction is recommended.

In addition, the introduction of IVIG or immunosuppressive medications such as methotrexate, azathioprine, cyclophosphamide or cyclosporine is another option if the patient does not respond to steroid therapy or suffers adverse side effects.[9] Our patient did not respond well to steroid therapy alone and he was given iv immunoglobulin for 5 days. In patients who are resistant to steroid therapy initial IVIg dosage is 2 g/kg over a five-day period (0.4 g/kg/day), followed by monthly three-day courses for three to six months.[10]

Our patient was given 2 doses of Rituximab and after starting on tofacitinib his upper limb and lower limb weakness improved and his skin lesions started resolving well. B-cell depletion therapy with rituximab used alone or in combination with other immunosuppressive therapies like JAK inhibitors is a viable option in steroid resistant DM.[11,12]

CONCLUSION

Dermatomyositis is a treatable disease and may achieve a complete or good functional remission. Treatment of Dermatomyositis mainly depends on drugs that suppress the immune system. Patients who are resistant to steroids or who relapse with reduction of steroid dosage require other immunosuppressive or immune modulatory treatment. Early institution of appropriate therapies could be helpful with higher remission rates and could reduce morbidity and mortality. JAK inhibition is a potential treatment option in steroid resistant dermatomyositis.

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