CASE STUDIES

Anti-SRP antibody related inflammatory myositis: A heterogeneous group of necrotizing myositis

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Abstract

Anti-SRP antibody related necrotizing myositis is a rapidly progressive, severe, proximal muscle weakness with atrophy. The present study deals with two cases with poor prognostic course, concluding anti-SRP antibody related myositis as a heterogeneous group of inflammatory myositis. One patient had subacute onset proximal muscle weakness of both lower limbs, raised CPK, and biopsy showing typical changes of anti-SRP related necrotizing myositis. He responded well to steroids and methotrexate. The other patient had 3 months history of subacute onset weakness of both lower limb and was admitted with quadriparesis, bulbar palsy, aspiration pneumonia and respiratory distress. Even after treatment with intravenous immunoglobulin, broad spectrum antibiotics, steroids, and ventilatory support, the patient succumbed to the illness.

Keywords: myositis, anti-SRP, CPK, creatine phosphokinase, methotrexate

Introduction

Anti-SRP (signal recognition particle) antibody (Ab) related myositis is a group of necrotizing myositis with rapidly progressive, severe, proximal muscle weakness followed by atrophy of affected muscles and extremely high creatine phosphokinase (CPK) levels at presentation. The histology of muscle biopsy reveals that it has sparse inflammatory infiltrate, but significant muscle necrosis and endomysial capillary involvement.[1,2] Although clinically it may mimic polymyositis (PM), it may differ significantly from PM, as having more frequent relapse and resistance to multiple treatment modalities.[3] The present study deals with two such cases where one case responded well to immunosuppressants and the other with grave course.

Case 1

A 42-year-old male presented with a 6-month history of non-radiating aching pain and weakness of both the thighs. Examination revealed reduced tone in both lower limbs, reduced power at hip flexors /extensors /abductors /adductors with normal sensory system, and decreased reflexes. Examination of upper limbs, neck and spine was normal. Based on the history and examination, a provisional diagnosis of progressive symmetrical bilateral proximal lower limb weakness without sensory/bowel/bladder involvement/dermatological manifestation was made. A clinical diagnosis of idiopathic inflammatory myositis (IIM) was made.

Routine blood investigations were within normal range. Initial CPK level was 9000 IU/L. Muscle biopsy revealed maintained fascicular architecture with mild variation in fiber size and interspersed regenerating fibers. Adipose tissue infiltration was noted in the perimysium. There was granular membrane attack complex deposit on endomysial blood vessels. Inflammatory cell infiltrate was sparse, mainly involving cytotoxic T cells. Elevation of MHC class-1 and 2 were noted only in regenerating fibers. It was suggestive of dermatomyositis, however immune-mediated necrotizing myositis should be ruled out. Myositis antibody profile was strongly positive for anti-SRP and anti-Ro52.

He was treated with intravenous methylprednisolone 1 gram for 5 days and shifted to oral prednisolone 60 mg/day with other supportive treatment. Glucocorticoids were gradually tapered with addition of tablet methotrexate 15 mg once a week. Patient had normal CPK, without any weakness on 15 mg of oral methotrexate and oral glucocorticoids after 6 months of treatment. Glucocorticoids were gradually tapered and stopped over next 12 months. After 3-year follow-up, a significant improvement had been noted with

normal CPK level (49 IU/L).

Case 2

A 56-year-old male presented to the clinic with acute onset weakness of all the four limbs with difficulty in swallowing, acute onset breathlessness and cough with expectoration. One day after admission, the patient was intubated following severe respiratory distress, and was shifted to ICU. Provisional diagnosis of bulbar weakness, aspiration pneumonitis and quadriparesis was made. Patient had history of weakness in both the lower limbs for 3 months before admission and was treated with steroids with provisional diagnosis of inflammatory myositis. He did not improve and admitted with worsened disease and initial CPK of 729 IU/L (normal range: 20-195 IU/L).

CBC showed anemia and leukocytosis. The patient had elevated liver enzymes (SGPT, SGOT, LDH, ALP, and GGT) with severe hypoalbuminemia. Myositis antibody profile was positive for anti-SRP and anti-Ro 52.

Pulse steroids were deferred due to infection (aspiration pneumonia, raised procalcitonin) and hydrocortisone injection was given in septic dose. Broad spectrum antibiotics, ventilator support and other required supportive measures were given to the patient. In view of life-threatening myositis, intravenous immunoglobulin was administered (2 gram/kg over 5 days). Despite all these interventions, the patient did not improve and ultimately succumbed to multiorgan dysfunction syndrome (MODS).

Discussion

Anti-SRP is a myositis specific antibody (MSA) targeting ribonucleoprotein involved in translocation. It has been noted in pure polymyositis, dermatomyositis and in patients with less severe muscle weakness and extramuscular manifestations like ILD and arthritis.[4,5] There are certain subtle differences between polymyositis, dermatomyositis,

Table 1: Comparative analysis of different types of inflammatory myositis

	Diagnostic features	Dermatomyositis	Polymyositis	SRP-related myositis	Childhood-onset dermatomyositis
1	Age	Children and adults	Adults	32-70 years	5-10 years, girls 2-5 times more prone than boys
2	Skin changes	Yes	No	No	Yes
3	Calcinosis	Yes	Rarely	No	Yes (30-70%)
4	Interstitial lung disease	Yes	Yes	No	Rare
5	Associated malignancy	Yes	Yes	No	No
6	Muscle biopsy	Perifascicular atrophy, capillary depletion, MHC class I expression and microinfarcts	CD8+ T cell invasion of non-necrotic fibres and MHC class I expression on fibres	Active myopathy including muscle fibre necrosis and regeneration, prominent endometrial fibrosis but little or no inflammation	Perifascicular atrophy, perivascular mononuclear infiltrate, overexpression of MHC class I molecule
7	Vascular membrane attack complex	Present	Absent	Present	Present
8	Immunoglobulin deposition on blood vessels	Present	Absent	Absent	Present
9	Anti-SRP antibodies	-/+	+	+	-
10	Perifascicular atrophy	+	-		
11	Perivascular and perimysial inflammation	+	-/+	-/+	+
12	Microinfarcts	+	-	-	-
13	Inflammatory cells in myocytes	Predominant CD4 lymphocytes	Predominant CD8 lymphocytes	Scarce inflammatory infiltrates	-

childhood onset dermatomyositis and anti-SRP related myositis (Table 1)

Anti-SRP related myositis is a rare disease. A Japanese study involving 100 patients has evaluated the clinical characteristics and autoantibodies status of an anti-SRP related myositis cohort. The study noted increased female preponderance with a mean age of 51 years. All the patients had lower limb weakness and a significant number of subjects had neck weakness, muscular atrophy and dysphagia. Extramuscular manifestations were virtually absent. All the patients demonstrated poor response to glucocorticoids and required stronger immunosuppression. Pediatric onset SRP-related myositis was the only poor prognostic factor.[6] The clinical profile of anti-SRP myositis can be summarized as a subacute onset, symmetric progressive lower limb proximal muscle weakness along with probable involvement of neck flexors, trunk muscle and pharyngeal muscles, without extramuscular manifestations and skin lesions and no increased risk for connective tissue disease and malignancy.

A study involving 7 patients with myositis and SRP-related antibodies by Miller et al. has shown that myopathies associated with anti-SRP antibodies might have seasonal onset (August-January).[1] The study findings showed that none of the patient had dermatomyositis-like rashes, but the serum CPK was very high (3000 to 25 000 IU/L). Muscle biopsies showed an active myopathy, including muscle fiber necrosis and regeneration. There was prominent endomysial fibrosis, but little or no inflammation. Endomysial capillaries were enlarged and reduced in number, associated with deposits of the terminal components of complement (C5b-9, membrane attack complex). Improvement in muscle power was noted in several patients after corticosteroid treatment.

Patients with anti-SRP myopathy have been treated with steroids and many other immunosuppressive therapies based on the difference in clinical response. Initial experience with steroids and immunosuppressants is good in terms of treatment response, although it might not be long lasting and the disease may relapse with resistance. Newer therapies including rituximab, plasmapharesis are associated with variable treatment response.[7,8] Poor prognostic factors of inflammatory myopathies are 1) older age at onset, 2) delay in diagnosis and treatment, 3) pulmonary, cardiac and gastrointestinal involvement, 4) cancer-associated myositis, 5) presence of anti-SRP, anti 155/140, anti CADM 140 autoantibodies and 6) poor response to immunosuppressive therapy. Anti SRP-related myopathy itself is a poor prognostic condition due to presence of anti-SRP antibodies and inherent nature of poor response to treatment.[9]

Myositis antibody profile of 124 Indian patients showed the presence of anti-SRP in 20% the subjects and 4 out of 6 patients had poor response to multiple drugs. ANA positivity was noted in 69% of the patients.[10] Another study involving 131 patients from south India has shown that anti-PM75 and anti-SRP were the commonest autoantibodies in the cohort and anti-SRP antibodies were associated with fever. No other disease characteristics were found to be associated with anti-SRP.[11]

The current two cases indicate that anti-SRP antibody-related myositis is a heterogeneous group of disorder where some patients respond well to treatment and in certain cases, the disease progresses rapidly with poor response to immunosuppressants and has a devastating course.

Conclusion

Anti-SRP-related myositis is a heterogeneous group of inflammatory myositis with poor and recalcitrant course. Use of immunosuppressants like methotrexate, azathioprine, and biologics has to be supported with more evidence, as present knowledge on treatment of anti-SRP related myositis is limited. Although initial response with steroid and methotrexate is good in some cases, long-term effect on disease course is still a matter of debate. Further studies are required to identify markers that can predict severity of disease, progression of illness, rapidity of progression, and response to treatment of anti-SRP related myositis.

Competing interests
The authors declare that they have no competing interests.

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