Acute Myositis with Myoglobinuria

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ABSTRACT

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Myositis is inflammation of a voluntary muscle, with muscle pain, tenderness, swelling, and or weakness. The causes of Myositis include infection and autoimmune conditions. We report here two male children from neighbouring districts of South India, who presented three weeks apart, with persistent Myositis and myoglobinuria of subacute onset. The near simultaneous presentation and the non specific vacuolar changes on muscle histopathology made an infective etiology likely. Both the cases recovered completely with Intravenous Immunoglobulin (IVIg), leaving no residual disease and no renal involvement in spite of gross myoglobinuria. The cases are noteworthy as no published literature on non immune Myositis that recovered completely with IVIg could be located. This report is evidence to show that Myositis can be non self limiting and disabling, unless given specific treatment.

Keywords: Immunoglobulin, Myoglobinuria

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INTRODUCTION

Acute myositis in children is usually self limiting and benign and rarely can be due to Dermatomyositis/ Polymyositis spectrum (DM/PM spectrum) disorders. At one end of the spectrum of infective myositis is the myalgia that accompanies and followsviral infections; with rhabdomyolysis and myoglobinuria at the other end. Myositis faces controversy regarding its etiology; both viral invasionand immune mechanisms are postulated.Adiagnosis of an infective myositis and not myositis due to the DM/PM spectrum disorders, based on musclehistopathology will prevent prolonged drug treatment that is mandatory in the latter.

Case 1

An 11 year old boy was admitted with generalized myalgia, high CK and myoglobinuria. A month prior to admission he had fever for five days, coryza, back and thigh pain followed by mouth ulcers and papulopustular skin lesions. Following admission, the limb power worsened to MRC (Medical Research Council Grade for muscle power) grade 3 for the proximal muscles. Table 1 shows the investigation profile and the subsequent course of events for the two cases. A Complete vasculitic work up, PCR test for H1N1 antigen, Pathergy test, Elisa for HIV, Weil Felix test and Dengue IgG and IgM antibodies were negative. Hemogram, thyroid, liver and repeated renal function tests were normal. Muscle histopathology was normal. Intra Venous administration of Methyl Prednisolone resulted in resolution of oral ulcers and the skin lesions. The pain and weakness persisted. While on maintenance oral steroid, by day 14, he developed deterioration of power at the shoulder and elbow to MRC grade 2, contractures at elbow joints and generalized subcutaneous edema and tenderness. By day 21, he worsened to MRC grade2 power at more muscle groups, had rhinolalia and nasal regurgitation of fluids. At this point, musclebiopsy from the right biceps was normal.

From day 21 he was given a course of Intravenous immunoglobulin (IVIg) 400mg/kg/day for five days. One week after IVIg, he showed complete resolution of the contractures and subcutaneous painful edema. On follow up 11 months later, he was asymptomatic.

Case 2

A ten year old boy presented, three weeks following admission of case 1, with proximal weakness. Three weeks prior to admission, he had fever and coryza for 3-4 days, thigh pain, subsequently difficulty to get up from a squat and to climb stairs. Ten days from onset, he developed rhinolalia and dysphagia.

At admission he had MRC grade 2 and grade3 power

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in the proximal lower and upper limbrespectively, dysphagia and axial muscle weakness. Haemogram, vasculitic work up, Elisa test for HIV,

Dengue IgG and IgM antibodies ANA profile, Weil Felix test, thyroid, liver and repeated renal function tests were normal. He had no arthritis and had minimal subcutaneous edema. His CK and urine myoglobin profile are given in table 1.

A muscle biopsy from the left quadriceps revealed well preserved fascicular architecture with no inflammatory infiltrate, myophagocytosis and regeneration. There was mild variation of muscle fiber size, mild increase in endomysial collagen with numerous vacuoles in the muscle sarcoplasm. (Fig1) The vacuoles were not rimmed, showed granular material, did not reveal glycogen (PAS stain) or lipid accumulation and no characteristic inclusion bodies were seen. On Gomori Trichrome stain, there were no ragged red fibres. Since the histopathological appearance did not conform to any inherited or inflammatory myopathy, the postulation of viralmyositis was strengthened.

He was given a course of IVIg (400 mg/kg/ day for five days. Five days following cessation of IVIg, he showed total resolution of weakness, dysphagia, and nasal twang. At two month follow up he was asymptomatic with CPK 88 IU/L and no myoglobinuria. He continues to be asymptomatic at12 month follow up.

The two patients were given optimal hydration and alkylating agents to prevent renal failure due to the myoglobinuria and they had normal renal parameters. Both had no cardiac involvement.

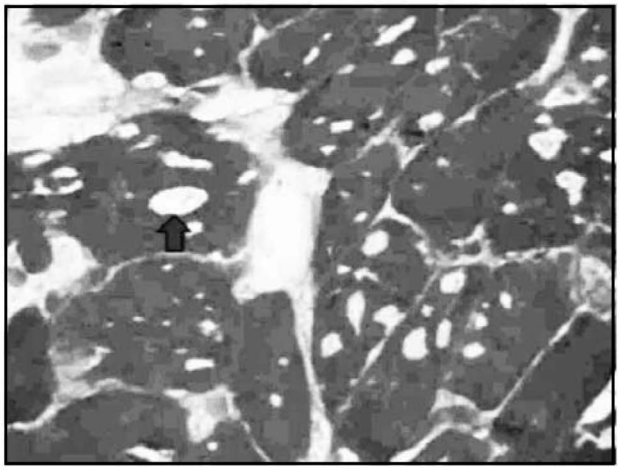

Figure 1. **Photomicrograph showing muscle fibres with multiple cytoplasmic vacuolation (blue arrow) [Haematoxylin & Eosin x 400]**

DISCUSSION

The clustering of these cases of myositis suggested that these children had an infective myositis. Neither of these patients was exposed to myotoxins, had evidence of connective tissue disease or had a family/ previous history of muscle disease. Although the serologic studies for viral and rickettsial infection were negative, the typical prodromal illness in both the children and the histopathological appearance on muscle biopsy of case 2 are in support of viral myositis.

In the series of viral myositis described by Mackay et al and Sarala Rajajee, 84% and 55% respectively were boys.[1,2] In both these reports, unlike in our cases the recovery was spontaneous.

The autoimmune group of myopathies include Dermatomyositis, Polymyositis and inclusion body myosit is (IBM), each with characteristic histopathology which was absent in these patients' muscle biopsy.

Rhabdomyolysis is rare in viral myositis and38% of rhabdomyolysis is due to viral myositis.[3,4,5] The cases reported here are evidence for the fact that renal failure, unlike in adults, is uncommon in children with rhabdomyolysis.[4] The viruses implicated as the etiological agent in viral myositis are influenza A, Influenza B, H1N1, Coxsackie, Echo, Dengue and Aids virus.[3,5]

Vacuolar myopathy is described in metabolic diseases

Table 1. Showing the clinical profile of the two cases

Clinical features and investigation findings	Case 1	Case 2
Skin lesions	Papulopustular	None
Proximal muscle weakness	++++	++++
Thigh pain	+++	+++
Neck and bulbar muscle weakness	+++	++
Muscle contracture	++	-
Initial CK IU/L	13,300	9838
Initial Urine myoglobin	135 ng/ml	10 ng/ml
ESR mm/hr	15	30
ANA Profile	Normal	Normal
Dengue antibody /Throat Swab for H1N1 antigen	Negative	Negative
Weil Felix test	No agglutination	No agglutination
Clinical features and investigations	Case 1	Case 2
Electromyogram	Normal	Myopathic potentials
Muscle biopsy	Normal	Vacuolated muscle cells
Repeat CK IU/l*	5359	6436
Best response to	IVIG	IVIG
Discharged asymptomatic	6 weeks after admission	4 weeks after admission
CK at 2 m* follow up	44 IU/L	72 IU/L
Follow up Urine myoglobin 2m*	1.1 ng/ml	Absent

like the glycogen storage diseases, carnitine deficiency myopathies, the periodic paralyses and X linked vacuolar myopathy. The clinical profile of these diseases is different from the two cases reported here. Vacuolar myopathy is also characteristic of IBM and drug induced myopathies (Colchicine, Vincristine and Chloroquine). However it is described in various infectious myositis including retroviral and Hepatitis C myositis.[6,7] Sporadic IBM is increasingly being attributed to persistent viral myositis.[8] Absence of toxin exposure, clinical setting and histopathological features of a glycogen or lipid storage disease or IBM, despite the presence of vacuolation of muscle fibres, made us suspect an infectious etiology.

Since there were reports of IBM and inflammatory myopathies responding to IVIg, the same was tried successfully in case two and subsequently in case one.[9,10] It is noteworthy that recovery of a persistent acute myositis that did not belong to the DM/PM spectrum with IVIg is not available in the published literature.

END NOTE

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