RESEARCH BRIEF

Disease Patterns of Juvenile Dermatomyositis From Western India

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A retrospective assessment of clinical characteristics, complications/ associations, laboratory investigations, treatment modalities and outcome in an inceptional cohort of 22 (male-13) children with juvenile dermatomyositis (JDM) receiving treatment at Jaslok Hospital, Mumbai during 1997- 2012 was performed . Mean age at diagnosis was 7.52 ± 3.99 years. Typical skin rash and muscle weakness were present in all children. Common complications included cutaneous ulcers (27.27%), dysphagia (22.72%) and calcinosis (18.18%).All patients presented with at least one of the serum muscle enzymes elevated. Absence of mortality and cardio-pulmonary complications and a monocyclic course in 72.7% of our patients are at variance from Western series.

Keywords: *Calcinosis, Juvenile dermatomyositis, Outcome.*

Juvenile dermatomyositis (JDM) is a rare systemic autoimmune disease with diffuse vasculopathy of the skin and muscles, characterized clinically by proximal muscle weakness and typical rash. Though the inflammatory process primarily affects these tissues, it can also involve various other organ systems, with significant mortality from cardiovascular, respiratory and gastrointestinal sequelae of the disease [1]. There is paucity of data regarding disease patterns and outcome in children with juvenile dermatomyositis from the Indian subcontinent.

METHODS

We conducted a retrospective review of children diagnosed with JDM and receiving treatment at Jaslok Hospital, Mumbai between 1997 and 2012. Patients were diagnosed to have probable or definite JDM using the Bohan and Peter criteria [2], which include a typical rash (mandatory) and two or more of the following: symmetric proximal muscle weakness, raised serum muscle enzymes, electromyographic abnormalities and consistent muscle biopsy findings .

Patients with evidence of mixed connective tissue disease or overlap syndrome, those whose disease was managed elsewhere prior to referral, and those with no evidence of muscle weakness or inflammation (JDM sine myositis) were excluded.

The review included clinic visit notes, physical examination including the Childhood Myositis Assessment Scale (CMAS), laboratory investigations including serum muscle enzymes and radiological investigations, when indicated. Magnetic resonance imaging (MRI) was used to supplement the clinical features, eliminating the need for electromyography or muscle biopsy. Echocardiography and chest radiographs were performed in all cases to look for cardiopulmonary involvement.

The clinical course was categorised into monocyclic (achieving a remission and remaining well thereafter), relapsing or polycyclic (relapse again after an initial remission) and chronic progressive (unable to achieve a remission) [3]. Remission was defined as no residual muscle weakness discernible on clinical examination [3].

RESULT

22 patients of a total of 38 (male-13) were studied. The mean age at diagnosis was 7.5 ± 3.99 years (range 3.0-18.2 years) and the mean time from the onset of symptoms to diagnosis was 7.2 ± 7.15 months (range 3 weeks-2 years).Besides the typical skin rash and proximal muscle weakness seen in all, the other frequent clinical features included fatigue (81.8%), fever (68.2%) and arthralgia (54.5%). The commonly observed complications included cutaneous ulcers in 6 (27.3%), dysphagia in 5 (22.7%), calcinosis in 4(18.2%) and lipodystrophy in 3 (13.6%) patients. One had associated insulin-dependent diabetes mellitus and chronic hepatitis, while another developed vitiligo. Hirsutism was observed in four cases. Complications of therapy observed were intercurrent pyogenic infections in 2 (9%) (inguinal abscess and retropharyngeal abscess in one each).Clinically significant osteoporosis and posterior subcapsular cataract were diagnosed in one patient each.

No patient in the cohort presented with or developed cardiopulmonary complication or malignancy over the entire period of follow-up.

All patients presented with at least one of the four serum muscle enzyme (creatine kinase, aspartate aminotransferase, lactate dehydrogenase and aldolase) levels elevated. A normal range of creatine kinase (CK) at presentation was seen in 59% of the patients. Antinuclear antibody (ANA) by indirect immuno-fluorescence was positive in 8/20 of our patients. Electromyography was done in 5 patients and muscle biopsy in one to confirm the diagnosis. Magnetic resonance imaging (MRI) of the thigh muscles was used as an aid to diagnosis in 12 patients and was abnormal in all, showing hyperintensity of the thigh or calf muscles on T2-weighted images. Echocardiography and chest radiograph were found to be normal in all.

Initial therapy comprised of oral steroids (2 mg/kg/day) and gradually tapered with improvement in clinical features and muscle enzymes) and methotrexate (10 mg/m^2/week subcutaneously). Hydroxychloroquine (4-6 mg/kg/day) was added in those with significant cutaneous manifestations. Pulse steroids (methyl prednisolone 30 mg/kg/day) were used to induce remission in 11 patients and as a rescue for relapses in 2 patients. Intravenous immunoglobulin (IVIG) was successfully used as rescue therapy in 2 children (both having severe muscle weakness with CMAS <5 and poor response to pulse methyl-prednisolone; one of them also having dysphagia). 5 children had inadequate response, ulcerative disease or hepatotoxicity and received azathioprine (5/5), cyclosporine (1/5), cyclophosphamide (1/5) as additional therapy. One child with extensive calcinosis with inadequate response to monthly pulses of intravenous methylprednisolone and IVIG is being treated with infliximab in addition to diltiazem, alendronate and colchicine. All children received physiotherapy.

22 patients were followed up for a mean (SD) of 3.84 (2.72) years with cumulative follow-up period of 84.71 patient-years (range- 0.58-12.17 years, median-3.71 years). A monocyclic course was seen in 16 (72.7%), polycyclic course in 4 (18.2%) and a chronic progressive course in 2 patients. Five of our patients are in remission off medications for more than 6 months. No mortality has been observed till date.

DISCUSSION

JDM, an uncommon disease, accounts for about 2.5% of the cases seen in our pediatric rheumatology clinic. The mean age at diagnosis of our cohort is 7.52 years, similar to the other published figures [3-5].

Western literature has consistently shown a female preponderance [4-7]. Our patients had a slight male preponderance similar to that reported from other centres in India [3, 8], Saudi Arabia [9] and Japan [10]. In our series, the duration of disease prior to diagnosis was lesser than that of 1.18 years reported from Chandigarh [3]. However, this is in contrast to the data from most western series, where children have reported to hospital within a few weeks of onset of symptoms [11]. This highlights the need for recognition of subtle and early features of JDM such as the cutaneous signs and muscle weakness by the primary paediatrician.

The pathognomonic rash of JDM, which is the mandatory criterion for diagnosis as per the Bohan and Peter criteria, was present in all the patients, as was proximal muscle weakness. Cutaneous ulcers have been reported in 6 to 30% of the cases in various studies [6, 8, 12]. Five children developed dysphagia necessitating tube feeding and more aggressive therapy. Dysphagia due to weakness of the pharyngeal musculature is associated with severe forms of JDM.

Calcinosis cutis has been reported with an incidence of 20-40% and increasing with disease duration [13] similar to that found in our study. These children received diltiazem and colchicine. Riley, *et al*. [14] have reported major clinical benefit following the initiation of the anti-TNF-á monoclonal antibody, infliximab in 5 cases of refractory JDM with calcinosis and the same is being tried in one patient.

The importance of serum levels of muscle enzymes for diagnosis and monitoring the effectiveness of the therapy has been emphasised. CK does not always correlate with disease activity [15]. 59% of our patients had a normal CK at presentation inspite of having muscle weakness. Similarly, in a study from Brazil, CK levels were normal in 31% of the patients [6]. Considerable individual variation in the pattern of enzyme elevation is observed. Therefore, it is recommended that at least in early disease, CK, LDH, SGOT and aldolase be measured to obtain a baseline evaluation. ANA was positive in 40% of our cases, comparable to 40% [6] and 56% [5] in other studies. MRI has proven to be useful in the diagnosis and has largely eliminated the need for a muscle biopsy [13].

The disease course in JDM can be variable.72.7% of our patients had a monocyclic course, similar to the study from Chandigarh [3], but in contrast to two recently published studies, which have reported a monocyclic course in 37% [16] and 41.3% [7]. Delay in diagnosis, absent mortality, absence of cardio-pulmonary complications and a monocyclic course are at variance from several western series.

WHAT THIS STUDY ADDS?

- There is a considerable delay at the primary care level for the diagnosis of JDM.
- Absence of mortality and cardio-pulmonary complications, and a monocyclic course in 72.7% of patients.

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