Juvenile dermatomyositis, clinical manifestations and outcome in an Iranian cohort

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Abstract  Objective: Juvenile dermatomyositis (JDM) is the most common inflammatory myopathy of childhood and is characterized by proximal muscle weakness and pathognomonic skin rashes. In this study, we performed a descriptive cross sectional study to assess the clinical manifestations and outcomes of 39 patients with JDM from the northeast of Iran during 12 years and compared our findings with other studies.

Design: 39 patients (16 boys and 23 girls) with juvenile dermatomyositis were studied retrospectively between 2001 and 2013. Gender, age at disease onset and diagnosis, clinical manifestations, laboratory data at onset, treatment and outcome of these patients were reviewed.

Measurements and results: The mean age of onset was 9.42 ± 3.85 years. At the time of presentation, muscle weakness occurred in 100%; heliotrope rash in 51.2%; gottron's papules in 46.1%, calcinosis in 12.8%, and 87.1% had at least one abnormal muscle enzyme result. Muscle biopsy was performed in 15.3% and was abnormal in all. All patients received corticosteroids; but methotrexate, hydroxychloroquine, intravenous immunoglobulin, or azathioprine was added to corticosteroid in some patients. The mean follow-up period was 22.66 ± 23.53 months.

Conclusions: This study was in parallel with other reviews except for calcinosis which was observed with lower frequency. It is suggested that delay in diagnosis and treatment may be associated with calcinosis.

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Introduction

Juvenile dermatomyositis (JDM) is a rare, potentially life-threatening systemic autoimmune disease primarily affecting muscle and skin. It has some extramuscular manifestations such as joint contractures, dysphagia, cardiac disturbances, pulmonary symptoms, and subcutaneous calcifications. Cutaneous findings are often the first manifestation, allowing early diagnosis of the disease.

The incidence of JDM is estimated in 2 to 3 cases per million populations. The diagnosis of this entity is difficult and often delayed due to its rarity and this is a major factor for poor prognosis. The diagnosis is confirmed when patients prove to meet Bohan and Peter’s diagnostic criteria, namely symmetric muscle weakness, increased muscle enzymes,
myopathic changes on electromyography, typical histological findings on muscle biopsy, and dermatologic signs. These five criteria are applicable to its diagnosis, although their sensitivity and specificity have not been validated in children but are probably 45–90% and 90%, respectively. The definite diagnosis of JDM requires the presence of the pathognomonic rash and three of the four mentioned criteria.6

As JDM is a very rare disease in the world and it was not evaluated in Iran so far, we decided to perform this study in this geographic area and review the characteristic of JDM in cohort of thirty nine patients from multicentral referral hospitals of the northeast of Iran over a period of 12 years and compare our patients’ characteristics with other studies.

Patients and methods

In this descriptive cross sectional study, we reviewed the records of 39 patients diagnosed as having JDM according to Bohan and Peter’s diagnostic criteria in the rheumatology units of referral teaching hospitals of the Mashhad University of Medical Sciences located in the northeast of Iran between July 2001 and January 2013. Inclusion criteria were age at disease onset equal to or less than 16 years and patients with characteristic rash and weakness within 6 months. Exclusion criteria were age more than 16 years, diagnosis of other myopathy (inflammatory or non-inflammatory) such as muscle dystrophies, endocrine problems that can affect the muscles, history of using corticosteroids or medications that can cause myopathy or myositis, muscle weakness without characteristic skin rash of JDM.

We filled data sheets with the following data of JDM patients’ files that had been referred to rheumatology clinics of our university referral hospitals or admitted there. These included age, sex, duration of disease, evaluation of muscle weakness, whether rash or muscle weakness (or both) was the first symptom, the interval between disease onset and initial treatment, electromyographical study findings, presence of extramuscular manifestations such as arthritis, dysphagia, cardiac disturbance, pulmonary symptoms, subcutaneous calcifications, and associated disorders such as overlap, mixed connective tissue disease, juvenile idiopathic arthritis, systemic lupus erythematosus, malignancy and also follow-up duration was recorded.

Laboratory findings such as creatine kinase (CK), alanine and aspartate aminotransferase (ALT, AST), antinuclear antibodies (ANA), rheumatoid factor (RF), electromyography and muscle biopsy were analyzed.

Follow-up of the patients had been performed at 1–3 month intervals. We assessed their muscle strength, skin rashes and their laboratory data such as inflammatory parameters and muscle enzymes in accordance with patients’ files. Evaluation of outcomes had been performed on all patients except 8 patients who did not return after discharge from hospital and we only found their admission data and data before hospitalization, when they visit a rheumatologist in clinic. The outcomes of juvenile DM patients during the evaluation period were defined as (1) remission: disappearance of skin manifestations, normalization of muscle strength, normal function of major organs, normalization of both serum muscle enzyme levels and electromyographic abnormalities after therapy discontinuation; (2) improvement: improvement of muscle strength and skin manifestations, functions of involved major organs, and biochemical data with therapy; (3) deterioration: worsening of muscle strength and skin manifestations, functions of involved major organs, and biochemical findings despite therapy, and (4) death: death of patient despite therapy during the follow-up period.

Descriptive analysis of demographic data, clinical features and treatment variables were reported by correspondent absolute and percentual frequencies. Quantitative variables were described by median and range.

Results

Our study included 39 JDM patients, 16 boys and 23 girls, with a mean age of 9.42 ± 3.85 years and sex-ratio of (M/F) 1:1.4. Age of onset was variable from 3–15 years. The mean duration of the disease before diagnosis was 3.33 ± 3.32 months. The mean follow-up duration was 22.66 ± 23.53 months (ranging from 1 to 90 months). Of the 39 children, 33 patients had definite JDM and 6 had probable disease.

Constitutional signs and symptoms

Fever in the range of 38 °C to 40 °C was observed in 16/39 (41.02%) patients but it was not the reason for the first presentation. All patients showed fatigue, malaise and anorexia. Early fatigue as a first presentation was noticed in 32/39 (82.05%) patients.

Muscloskeletal manifestation

Muscle weakness was the first symptom in 29/39 (74.3%) cases. Within 3 months, all patients (100%) showed symmetrical proximal muscle weakness. Seventeen (43.5%) patients had myalgia. Neck flexor muscle weakness was noticed in 3/39 (7.6%) patients, pharyngeal muscle weakness and dysphagia were noticed in 12 (30.7%) of the patients which were confirmed by the Barium swallow study. None of the patients showed facial, extra-ocular or neck extensor muscle weakness.

Within the first 4 months of JDM diagnosis, arthritis and arthralgia were developed in 19 (48.7%) and 13 (33.3%) of the patients respectively. Arthritis in the knee was noticed in 10 (25.6%), ankle in 4 (10.2%), wrist in 5 (12.8%), elbow in 6 (15.8%) and metacarpophalangeal, metatarsophalangeal and proximal interphalangeal joints in 4 (10.2%) patients.

Mucocutaneous manifestations

The first clinical manifestation was cutaneous in 35 (89.7%) patients, and within 1–3 months after the first presentation, rash was seen in all patients. Dermatological signs were dominated by heliotrope rash in 20 (51.2%), gottron’s papules in 18 (46.1%) and nonspecific rashes including photosensitive rash, located over the neck (V sign) and shoulders (shawl sign), skin lesions on the fingers (periungual erythema, nail-fold telangiectasias), livedo reticularis and palpable purpura in 20 (51.3%) of the patients. Two patients had livedo reticularis, palpable purpura and skin ulcer and two had periungual and palmar erythema and Raynaud’s phenomenon. Skin biopsy of these
patients showed vasculitis. In 9 (23.07%) patients, rashes appeared first and both rashes and muscle weakness were noted first in 26 (66.6%) cases. Fig. 1 shows different cutaneous manifestations in these patients.

The percentage of the patients in whose case both rashes and weakness appeared first was 26 (66.6%).

Calcinosis was detected in 5/39 (12.8%) patients (3 boys and two girls). In 4 patients calcinosis appeared 3 years after the diagnosis of JDM. Three of them had calcinosis in the subcutaneous tissue of knees; one had calcinosis in the subcutaneous tissue of the knees, elbows and the deep tissue of the hip region, which was detected by radiography. The last patient presented with calcinosis in the subcutaneous tissue of the elbow which was ulcerated and infected, 4 years after the diagnosis. In these five patients, the mean interval between the development of the disease and diagnosis was 10 months, compared to 3 months in children who had no calcinosis.

Extramuscular manifestations

Auxiliary lymphadenopathy was detected in 5 (12.8%) patients. In two patients fine reticulonodular pattern was reported in chest radiography, but they did not display any respiratory symptoms. Pulmonary function test showed a mild restrictive pattern. Cardiac involvement was not observed in our patients.

In one patient, the disease began with fever, gottron’s papules, periungual and palmar erythema, muscle weakness, arthralgia in shoulders, arthritis in both knees and ankles and morning stiffness. With the diagnosis of JDM, treatment with prednisolone was started. Despite this treatment for 5 months and improvement in myositis, the arthritis was continued and the overlap of juvenile idiopathic arthritis and juvenile dermatomyositis was diagnosed. Another patient presented with photosensitivity, oral ulcer, malar rash, heliotrope rash and gottron’s papules, vasculitis, hemolytic anemia with positive coombs test, positive ANA and high titer of anti-dsDNA and myositis, who was diagnosed with the overlap of systemic lupus erythematosus (SLE) and juvenile dermatomyositis. One patient, 2.5 years after the diagnosis of JDM, presented with photosensitivity, proteinuria and a rise in anti-dsDNA titer [391U (<100)], who was also diagnosed with the overlap of SLE and JDM. None of the patients showed mixed connective tissue disease, scleroderma or malignancy.

Fig. 2 demonstrates the percentage of different clinical features of these patients at the time of presentation.

Laboratory findings

Muscle enzymes increased in 34 (87.1%) of the patients (84.6% for creatinine phosphokinase and 82% for other enzymes).
ANA was present in 15.3% of the patients. RF was detected in 12.8% of the patients. Electromyography was performed for all patients, which revealed a myogenic tracing in 87.17% of the cases. Because of incomplete criteria in 6 (15.3%) patients, muscle biopsy was done in these patients and biopsy of all of them showed inflammatory infiltrates including interstitial or perivascular mononuclear cells together with degeneration, necrosis and regeneration of myocytes.

**Treatment and follow-up**

For all the patients treatment was started with a daily prednisolone dose of 1–2 mg/kg. The dose was decreased after 4–6 weeks depending on the degree of clinical improvement and side effects of the drug. The dose of prednisolone was reduced by almost 10–20% of the initial dose every 1–2 weeks, with a subsequent slower rate of reduction to one daily dose. Oral methotrexate (5–15 mg/week) or azathioprine (2–3 mg/kg) was started in combination with prednisolone in 9 patients who had inadequate improvement in muscle strength, persistence of elevated serum levels of muscle enzymes in response to a closely monitored glucocorticoid program or glucocorticoid dependence, overlap of JDM and JIA or SLE and vasculitis. Hydroxychloroquine with a dose of 6 mg/kg/day was added if the patient presented with extensive skin rash and needed to take high dose steroids or had overlap of JDM and SLE. For two patients intravenous gammaglobulin (IVIG) was administered because they were steroid resistant and had refractory arthritis. These patients exhibited a good response at follow-up points. Rehabilitation and muscle strengthening exercises were recommended for most of the patients.

Calcification was treated in two patients by surgical excision because of the severity and its bad location but it relapsed in one and surgical excision was performed again. In three, medical treatment such as bisphosphonate and calcium channel blockers was started. However they did not respond and the result had been disappointing.

The median follow-up duration of our patients was 22.66 ± 23.53 months. Of these 39 patients, 21 (53.8%) had remission, 10 (25.6%) had partial improvement and 8 patients did not show up again to the rheumatology clinic after being discharged from hospital. None of these 31 patients died during the follow-up.

In three patients, there was an interval between the first symptoms and diagnosis. This delay was observed in those where muscle weakness was the first presenting complaint because this symptom was often unnoticed or ignored at first.

**Discussion**

Juvenile dermatomyositis is a multi-system disease characterized by vasculopathy of the skin and/or muscles causing subacute (over several weeks to months), progressive, proximal muscle weakness and typical skin rashes. It is at least 10–20 times more common than polymyositis in children and tends to have a more acute and severe onset. It is known that DM has a bimodal age distribution: one peak occurs between 5–14 years of age and a second larger peak occurs between 45–64 years of age. In our report, the age at the onset of the disease was similar to other series of juvenile DM. It is reported that females outnumber males by 2:1, and our study also showed a female predominance.

Within the first 4 months of diagnosis 33.3% of the children in our study reported arthralgia and 48.7% showed arthritis that is similar to other studies. Arthralgia and arthritis in JDM is transient and nondeforming, sometimes accompanied by tenosynovitis or flexor contractures. Early development of flexion contractures is common and usually represents the effects of muscle inflammation rather than synovitis. In our study one patient had chronic arthritis despite the remission of dermatomyositis which could be due to an overlap with juvenile idiopathic arthritis.

It is important to recognize the skin manifestation of JDM because it facilitates earlier diagnosis. Puchman et al., in a study on 166 patients found that skin rash is the first observed manifestation in 65%. In our study, most patients with juvenile DM showed rashes and proximal muscle weakness within 4 months with the rash preceding muscle weakness in 23.07% of them.

Calcification of the skin or muscle is rarely observed in adults, but may occur in up to 40% of children or adolescents with DM. In our study, subcutaneous calcifications were found in only 5 of our patients (12.8%) which were lower than those found in previous studies, but like other studies, delay in diagnosis was associated with calcinosis in these children. This extramuscular manifestation is particularly difficult to treat and studies are aimed at attempts to elucidate predictors.

Interstitial lung disease (ILD) is often associated with considerable morbidity and mortality in JDM. Asymptomatic pulmonary involvement may occur in up to 50% of children. Interstitial pneumonitis is rare and may be refractory to treatment. In our study, interstitial pneumonitis was found in two patients without any clinical symptoms.

Clinical features of our 39 patients with JDM are compared with those in three other studies in Table 1. Malignancy is more common in dermatomyositis and with older patients (> 50 yr) and rare in childhood. In our study, malignancy was not observed in any of the patients.

In laboratory findings, the rise in the muscle enzymes in our patients was variable. CPK was not elevated in 15.4% of the patients. Although this may be due to taking glucocorticoids before admission, the findings emphasize the importance of complete enzymatic profile in the diagnosis of JDM.

Glucocorticoid therapy was the main treatment that our patients received, which resulted in significant improvement in many patients. There are few prospective studies about immunosuppressants effect in JDM. In our study immunosuppressants were added to corticosteroids in severe and resistant cases and those with overlap and special problems including vasculitis.

Mortality in inflammatory myopathy appears to be influenced by age, race, and sex. Children with inflammatory myositis, for instance, have a low mortality rate. In this study, we also did not encounter any mortality within the follow-up period.

Several studies have evaluated the short and long term outcomes of DM. We observed that 53.8% of juvenile DM patients achieved remission whereas 25.6% partially improved and no patient was bedridden. Our findings are compatible with other studies showing DM remission rates varying from 25% to 70%.
In conclusion, the study of our 39 juvenile patients with dermatomyositis with a mean follow up of 22.6 months revealed that the occurrence rate of calcinosis was less than several previous studies. With early and proper treatment, the outcome of the disease was relatively favorable in most of our patients.

Conflict of interest

None.

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