



Juvenile Dermatomyositis with a Rare and Severe Complication: Macrophage Activation Syndrome

Juvenil Dermatomiyozit ve Nadir ve Ciddi Komplikasyon Makrofaj Aktivasyon Sendromu

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ABSTRACT

Juvenile dermatomyositis is the most common idiopathic inflammatory myositis in children. It is a rare, chronic, vasculopathic, autoimmune disorder characterized by symmetrical proximal muscle weakness and pathognomonic skin rash. Macrophage activation syndrome (MAS) is a severe and life threatening complication encountered in the patients of chronic rheumatic diseases of childhood. We reported a 12 year old girl presented with MAS due to juvenile dermatomyositis. She had proximal muscle weakness, heliotrope rash, high level of aldolase as specific muscle enzyme, typical myositis findings on magnetic resonance imaging (MRI). According to the diagnostic criteria of HLH-2004 MAS was considered secondary to juvenile dermatomyositis. Fever, splenomegaly, cytopenia, hypertriglyceridemia, hemophagocytosis was present. The patient was treated with intravenous immunoglobulin and metotrexate. After this treatment muscle weakness was improved day by day. On the fifteenth day of this treatment, proximal upper and lower, neck and shoulder motor extremity strength was improved dramatically. We aimed to represent treatment approach for MAS that is secondary to juvenile dermatomyositis and is a rare condition. For a patient with the diagnosis autoimmune disease, MAS should be considered when unexpected situation is encountered during course of the disease and should be treated immediately. *The Journal of Pediatric Research 2014;1(4):218-21*

Key Words: Macrophage activation syndrome, juvenile dermatomyositis

ÖZET

Juvenil dermatomyozit, çocukluk döneminde idiopatik inflamatuvar miyozitler içinde en sık görülenidir. Proksimal kaslarda simetrik güçsüzlük ve kendine özgü döküntü ile karakterize nadir görülen, kronik, vaskülitöpatik otoimmün hastalıktır. Makrofaj aktivasyon sendromu (MAS) çocukluk dönemi kronik romatizmal hastalarda ağır ve hayatı tehdit eden bir komplikasyondur. On iki yaşında Juvenil dermatomyozite bağlı makrofaj aktivasyon sendromu olan bir hasta sunulmuştur. Hastada proksimal kas güçsüzlüğü, heliotrop döküntü, aldolaz yüksekliği ve manyetik rezonans görüntüleme (MRG) miyozit bulguları vardır. Ateş, splenomegali, sitopeni, trigliserit yüksekliği, hemafagositoz saptanan hastaya HLH-2004 MAS tanı kriterlerine göre juvenil dermatomyozit tanısı konuldu. İntravenöz immünglobulin ve metotreksat tedavisi ile kas güçsüzlüğünde giderek düzelmeye gözlemlendi. Tedavinin 15. gününde proksimal üst ve alt ekstremiteler, boyun ve omuz kaslarında belirgin düzelmeye gözlemlendi. Juvenil dermatomyozit hastalığına sekonder nadir olarak görülen MAS tedavi yaklaşımımızı sunmayı amaçladık. MAS otoimmün hastalığı olan hastalarda hastalığın seyri sırasında karşılaşılan beklenmedik bir durum gelişinde her zaman akıldan tutulmalı ve hemen tedavi edilmelidir. *The Journal of Pediatric Research 2014;1(4):218-21*

Anahtar Kelimeler: Makrofaj aktivasyon sendromu, juvenil dermatomyozit

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Introduction

Juvenile dermatomyositis is the most common idiopathic inflammatory myositis in children. It is a rare, chronic, vasculopathic, autoimmune disorder characterized by symmetrical proximal muscle weakness and pathognomonic skin rash (1). Genetic and environmental risk factors have a role in etiology of juvenile dermatomyositis (2). Incidence is 3.2 cases per million children per year in juvenile dermatomyositis and is more common in girls by the ratio of 2:1 (3). Prior to new treatment strategy mortality is reduced. The reported mortality rate was greater than 30 percent in the 1960s, especially when glucocorticoid has become a routine treatment agent, the rate decreased less than 2 or 3 percent in the 2000s with the advent of early combination immunosuppressive therapy (4).

Macrophage activation syndrome (MAS) is a severe and life threatening complication seen in the patients of chronic rheumatic diseases of childhood, particularly juvenile idiopathic arthritis, systemic lupus erythematosus, juvenile dermatomyositis (5). It has been considered that macrophage activation syndrome is the same disorder as the secondary hemophagocytic lymphohistiocytosis (6). Although MAS is seen in chronic rheumatic disorders, few case reports have been published describing MAS in patients with juvenile dermatomyositis (7).

We report a case of a 12 year old girl presented with macrophage activation syndrome due to juvenile dermatomyositis.

Case Report

A 12 year old girl admitted with intermittent fever, muscle weakness, fatigue, myalgia lasting 6 months. She suffered from morning stiffness especially in shoulder muscles. On physical examination her weight was 38.5 kg (10-25 p), height was 157 cm (75-90 p), vital signs showed body temperature 38.5 °C, blood pressure 110/70 mmHg, heart rate 85 per minute and respiratory rate 20 per minute. Eyelids and her face was erythematous called heliotrope rash. There were lots of anterior and posterior cervical milimetric lymph nodules. Her liver was palpable 2 cm and spleen was palpable 3 cm below the costal margin. Traube was dull. On neurologic examination, no cranial nerve deficits were noted. Sensation was intact. Proximal upper and lower motor extremity strength was 3-4/5. Neck and shoulder muscle strength was 2-3/5. Deep tendon reflexes were observed as normoactive. Nail fold capillary pattern observed as capillary dilatation, tortuosity.

Admission blood count showed a haemoglobin level of 8.4 g/dL, the mean corpuscular volume 68.8 fL, white blood cell count 6920/mm³, with 76% neutrophils, 22% lymphocytes, 2% monocytes, platelet count 144000/mm³. The serum level of C-reactive protein was 14.7 mg/dL (reference range: 0-0.8 mg/dL), and the erythrocyte sedimentation rate exceeded 82 mm in 1 h. Serum amylase A was 683 mg/

dL (reference range: <3.3 mg/dL) Alanine aminotransferase (ALT) was 59 IU/L (reference range: 3-10 IU/L), aspartate aminotransferase (AST) 205 IU/L (reference range: 15-40 IU/L), alkaline phosphatase (ALP) 249 U/L (reference range: 100-350 IU/L); gamma glutamyl transferase was 118 IU/L (reference range: 0-38 IU/L), total protein was 7.4 (reference range: 6.4-8.3 gr/dL) albumin was 2.6 mg/dL (reference range: 3.5-5.2 gr/dL) Lactate dehydrogenase (LDH) was 1085 U/L (reference range: 100-250 U/L), creatine kinase (CK) 25 IU/L (reference range: 34-145), aldolase was 23.4 IU/L (reference range: 1.5-6 IU/L), Serum ferritin 14657 ng/mL (reference range: 7-140 ng/mL). Blood lipid revealed that triglycerid was 541 mg/dL (reference range: 100-150 mg/dL), hypergamma globulinemia was present [IgG: 1800 mg/dL (875-1347), IgA: 362 (91-185), IgM: 243 (85-172)], serum complement levels were normal [C3: 170 (90-180) C4: 27.8 (10-40)], Antinuclear antibody titres (ANA) and RF was negative. Von Willbrand Factor antigen was 304%. Bone marrow aspiration smear showed one hemophagocytic cell and there were not atypical cell. Muscle biopsy was performed but myositis didn't show as histopathologically. Magnetic resonance imaging was used to demonstrate muscle inflammation. Magnetic T2 weighted magnetic resonance imaging of the lower extremities demonstrated high intensity areas in the muscles, indicating inflammatory muscular lesions.

Based on proximal muscle weakness, heliotrope rash, high level of aldolase as specific muscle enzyme, typical myositis findings on MRI juvenile dermatomyositis was diagnosed. According to the diagnostic criteria of HLH-2004 MAS was considered secondary to juvenile dermatomyositis. Fever, splenomegaly, cytopenia, hypertriglyceridemia, hemophagocytosis was present.

Intravenous immunoglobulin, pulse methylprednisolon, methotrexate, hydroxychloroquine were given as treatment drug. After this treatment muscle weakness was improved day by day. On the fifteenth day of this treatment, proximal upper and lower, neck and shoulder motor extremity strength was improved dramatically to 5/5 (Table I).

Discussion

Although juvenile dermatomyositis is the more common of idiopathic inflammatory myositis (1), the incidence of JDM is about 2-3 per million children per year (8). Skin rashes and proximal muscle weakness are the most common symptoms, heliotrope rash around the eyelids, erythematous rash on the extensor surfaces and proximal muscle weakness are also pathognomonic. Gastrointestinal, pulmonary, cardiac, and joint involvement can be found but is less common (9). We report a case of macrophage activation syndrome associated with juvenile dermatomyositis. In this case juvenile dermatomyositis was diagnosed from diagnostic criteria schema was first described by Bohan and Peter in 1975 (10). Diagnostic criteria are muscle weakness, elevation of muscle enzyme, abnormal EMG suggestive of inflammatory myopathy, abnormal muscle biopsy suggestive

Table I. Patients laboratory values and therapies

	On admission	1st week	2nd week	3rd week	4rd week	2nd month	3rd month	4rd month	5th month
SAA	40	42,5	29,2	22	13,3	4	3,3	3,3	3,3
Aldolase	23,4	22	10	9	8,6	5,3	3,3	1,3	0,7
ESR	82	100	92	69	20	9	8	8	8
Ferritine	14657	10000	9678	6615	300	18	19	10	10
Therapy									
IVIg 1 gr/kg		+							
PMP		+		+	+				
Oral steroid			+	+	+				
Mtx			+	+	+	+	+	+	+
HQK			+	+	+	+	+	+	+

SAA: serum amyloid A, ESR: erythrocyte sedimentation rate, IVIG: Intravenous immunoglobulin, PMP: pulse metil prednisolone (3*30 mg/kg/after day), Oral steroid (prednisolone 2 mg/kg/day), Mtx: methotrexate 15 mg/m²/week, HQK: hydroxychloroquine

of inflammatory myopathy. At least three following criteria must be found. Symmetrical weaknesses of the proximal muscles, elevation of the serum level of one of the muscle enzymes were present in our case. Muscle biopsy performed but not shown myositis.

Affected children cannot get a diagnosis because of inability and difficulty of invasive techniques such as EMG, muscle biopsy. In recent years magnetic resonance imaging (MRI) has played an increasingly important role in the diagnosis of inflammatory muscle disease. Changes in clinical practice over time have resulted in many clinicians using non-invasive techniques, such as magnetic resonance imaging, instead of EMG and muscle biopsy. Therefore, the diagnostic criteria of Bohan and Peter modified by Children's Arthritis and Rheumatology Research Alliance (CARRA) (11). Although we couldn't demonstrate myositis as histopathologically, MRI showed myositis of the lower extremities. Our goal is to demonstrate the benefit of magnetic resonance imaging as a diagnostic modality of Juvenile Dermatomyositis (12)

Our case fulfilled the criteria of HLH-2004. Similar to classical HLH, MAS is characterized by proliferation of macrophages and T-lymphocytes MAS is a clinical and histological entity characterized by the proliferation and overactivity of macrophages with hemophagocytosis throughout the reticuloendothelial system. It is resulting in continuous fever, purpura, hepatosplenomegaly, mental status changes, prolongations in the prothrombin time and the activated partial thromboplastin time, hypofibrinogenemia, and a reduced erythrocyte sedimentation rate. Among rheumatic disorders, MAS occurs most frequently in systemic juvenile idiopathic arthritis (sJIA). In sJIA, MAS belongs to the clinical picture of disease being present in subclinical form in 30-40% of patients, whereas the overt form occurs in 10-20% (13). In addition, in recent years this syndrome has been increasingly reported in patients with juvenile systemic lupus erythematosus (SLE) (11). Still's disease and other rheumatic disorders such as Kawasaki disease is also established in the literature (12-16).

Treatment of MAS in patients with rheumatic diseases has not been standardized yet, but it commonly includes a variety of agents such as corticosteroids, cyclosporine A, intravenous immunoglobulins, etoposide, cyclophosphamide, anti-TNF- α , methotrexate, hydroxychloroquine, G-CSF (granulocyte colony-stimulating factor), and in some cases plasmapheresis. There are differences between disciplines in the choice of treatment. Corticosteroids and methotrexate are first line medications used by US pediatric rheumatologists while the European/Latin American studies show that corticosteroids are similar as US but usage of methotrexate is less (11). In our case intravenous immunoglobulin, pulse metilprednisolon, metotrexate, hydroxychloroquine were given as treatment drug. After this treatment muscle weakness was improved day by day. On the fifteenth day of this treatment, proximal upper and lower, neck and shoulder motor extremity strength was improved dramatically.

Treatment should be started without delay, yet it should be kept in mind that the use of immunosuppression may further delay the diagnosis and definitive treatment. Intravenous immunoglobulin and metotrexate were given the first week as treatment drug. After this treatment muscle weakness was improved day by day.

In conclusion, we want to represent that JDM is rare condition of MAS and also want to offer treatment approach. MAS should be come in mind each time patient with the diagnosis autoimmune disease. Also it should be considered when unexpected situation is encountered during course of the disease and should and treated immediately.

Conflicts of Interest: The authors reported no conflict of interest related to this article.

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