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OLGU SUNUMU / CASE REPORT

Does selective IgA deficiency have a good prognostic role on juvenile dermatomyositis? a case report

IgA eksikliğinin juvenil dermatomiyozit prognozuna olumlu etkisi var mıdır? olgu sunumu

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Abstract
Juvenile dermatomyositis is a multisystemic autoimmune disease with uncertain etiology. Both innate immunity and adaptive immunity play a role on the pathogenesis of the disease. Selective immunoglobulin A deficiency is the most common primary immunodeficiency. Association between immunoglobulin A deficiency and autoimmune diseases including few juvenile dermatomyositis patients have been reported. A previously healthy 15-year old girl was diagnosed with juvenile dermatomyositis according to Bohan and Peter criteria and selective immunoglobulin A deficiency due to the low level of immunoglobulin A (<6 mg/dl). After 3 months of immunosuppressive treatment, her physical examination revealed no muscle weakness, no rashes, and normal muscle enzyme levels. While she has been treated with low dose methylprednisolone and subcutaneous methotrexate, muscle strength and muscle enzymes remained in normal levels at 12 months follow-up. Our knowledge about the co-occurrence of immunodeficiency and autoimmunity emerge that patients diagnosed with autoimmunity should have investigations for immunodeficiency or vice versa.
Keywords: Autoimmunity, IgA deficiency, Juvenile dermatomyositis.

Öz
Juvenil dermatomiyozit nedeni tam olarak bilinmeyen, birçok sistemi etkileyebilen otoimmün bir hastalıktır. Doğuştan ve kazanılmış immünitenin hastalık patogenezinde rolü bulunmaktadır. Selektif immünglobulin A eksikliği en sık görülen primer immün yetmezliktir. İmmünglobulin A eksikliği ile otoimmün hastalıkların birlikteliği daha önce birkaç juvenil dermatomiyozit tanılı olguda bildirilmiştir. Öncesinde sağlıklı olan 15 yaşında kız hasta Bohan ve Peter kriterlerine göre juvenil dermatomiyozit ve serum immunglobulin A değeri <6 mg/dl saptandığı için selektif immünglobulin A tanısı aldı. Üç ay immünsupresif tedavi aldıktan sonra fizik muayenede raş saptanmadı, kas gücü normaldi, ayrıca kas enzimleri normal düzeylerdeydi. Düşük doz metilprednizolon ve subkutan metotreksat tedavileri alan hastanın kas gücü muayenesi ve kas enzimleri 12 aylık izlem sonrasında halen normal sınırlarda seyretmiştir. İmmün yetmezlik ve otoimmün hastalık birlikteliği hakkındaki bilgilerimiz, otoimmün hastalık veya immün yetmezlik tanılı hastaların yine bu hastalıklar açısından incelenmesini gerekli kılmaktadır.
Anahtar kelimeler: Otoimmünite, IgA eksikliği, Juvenil dermatomiyozit.

INTRODUCTION

Juvenile dermatomyositis (JDM) is a multisystemic autoimmune disease with uncertain etiology and characterized by proximal muscle weakness and pathognomonic skin rashes. Perivascular inflammation of several organ systems and calcinosis can also be present in different stages of the disease[1,2]. The estimated incidence of JDM is 0.19-4.1 cases per million[3]. At 2006 McCann et al reported a median age at onset of 7 years and female to male ratio of 2.2:1[4]. Etiology of JDM is uncertain; however, environmental triggers such as infections,

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vaccination and drugs may lead to immune dysfunction, organ pathology and chronic inflammation in a susceptible individual. Both innate and adaptive immunity play a role in JDM pathogenesis[1].

Selective immunoglobulin A deficiency (sIgAD) is the most prevalent primer immunodeficiency and defined as the level of serum IgA <7 mg/dl in the presence of normal levels of immunoglobulin G and M in patients older than four years of age. Patients with IgA deficiency are mostly asymptomatic and diagnosed incidentally. However, some patients occasionally have a history of recurrent respiratory tract and gastrointestinal infections[5]. Furthermore, the association of IgA deficiency with allergy (allergic rhinitis/conjunctivitis, asthma) and autoimmune diseases (Celiac disease, Juvenile Idiopathic Arthritis-JIA, Systemic Lupus Erythematosus-SLE) were also occasionally reported in the literature. In this report, we presented a pediatric case representing sIgAD with JDM which have been rarely reported so far[6,7].

CASE

A previously healthy 15-year old girl was referred to our Pediatric Rheumatology Department due to high levels of creatine kinase (CK) and transaminases. Her medical history revealed malaise, difficulty in climbing stairs, rash on the elbows and face for the last 6 months. Her physical examination revealed asthenic constitution, heliotrope rash, and Gottron's papules over the extensor surfaces of the finger joints, elbows and knees. Additionally, proximal muscle weakness was found on the neurological examination.Laboratory tests revealed elevation of white blood cell (WBC), alanine transaminase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH), and CK levels. Acute phase reactants (C-reactive protein-CRP, erythrocyte sedimentation rate) were in normal ranges. Immunological investigations showed a low level of IgA (<6 mg/dl) with normal levels of IgG and IgM. Autoantibodies were all negative including anti-nuclear antibody (ANA), anti-dsDNA and Anti-Jo-1 (Table 1).

Needle electromyography was not performed. Muscle biopsy revealed characteristic features of myopathy including perivascular fibrosis, perivascular muscular atrophy, capillary damage, and perivascular chronic inflammatory cell infiltration which was consistent with JDM.The diagnosis was confirmed according to Bohan and Peter criteria which include typical cutaneous rashes and three or more of the following signs: 1-symmetric weakness of the proximal musculature, 2-elevation of the serum level of one or more of the following skeletal muscle enzymes: creatine kinase, aspartate aminotransferase, lactate dehydrogenase, and aldolase, 3-electromyographic demonstration of the characteristics of myopathy and denervation, 4-biopsy proven myositis[8]. A diagnosis of dermatomyositis also requires exclusion of all other conditions in the differential diagnosis. On the other hand, she also was diagnosed with selective IgA deficiency due to the low level of IgA

Initially, she was treated with high dose methylprednisolone (2 mg/kg/day). One month after high dose corticosteroid treatment, her physical examination revealed improved skin lesions and increased muscle strength along with the decline in the skeletal muscle enzyme levels on the laboratory tests. While corticosteroid dose reduced, subcutaneous methotrexate (15 mg/m2/w) treatment was initiated as a steroid-sparing agent. Her physical examination at third month revealed no rash, normal muscle strength and normal muscle enzymes on the laboratory tests. While she has been treated with low dose methylprednisolone and subcutaneous methotrexate, muscle strength and muscle enzymes remained in normal levels at 12 months follow-up (Table I).

DISCUSSION

Autoimmunity and immune deficiencies may be considered as two different entities. However, there are various reports and evidence on the co-occurrence of primary immune deficiencies and autoimmune diseases suggesting that they might share similar pathogenetic and pathophysiologic mechanisms[5].

sIgAD is the most prevalent immune deficiency worldwide. Incidence of sIgAD varies among different ethnicities (1/300-1/200). The incidence of IgA deficiency is 0.52% (1/188) among healthy school children in Turkey, according to the report of Bastürk et al[9]. sIgAD patients mostly stay asymptomatic; nevertheless, some patients have an increased risk of developing allergies and autoimmune conditions. Inability to eradicate foreign antigens may lead to an exaggerated chronic

inflammatory response and autoimmunity via several mechanisms such as molecular mimicry. Many of the sIgAD patients presenting auto-antibodies even without clinical autoimmune diseases. The relationship between primary immunodeficiencies and autoimmune diseases has been already shown[10]. Several autoimmune diseases such as JIA, SLE, Sjögren's disease, polyarteritis nodosa, celiac disease, insulin-dependent diabetes mellitus, and Behcet disease have been reported in patients with sIgAD[11]. It is hypothesized that IgA has a protective role against autoimmunity[12]. Aforementioned knowledges about the co-occurrence of immunodeficiency and autoimmunity suggest that patients diagnosed with autoimmunity should be investigated for immunodeficiencies as well. Likewise, a patient diagnosed as having immunodeficiency should be carefully monitored for possible autoimmune diseases..

Table I. Laboratory findings at the disease course.

Parameter	Initial	1st month	3rd month	Normal Values
WBC	16.270	26.560	11.850	4.500-13.500/mm^3
Hct	45.9	48.5	43.9	36-46%
Platelet	347.000	454.000	260.000	156.000-373.000/mm^3
serum AST	212	117	38	14-37 U/L
serum ALT	190	158	58	8-32 U/L
serum CK	7.419	2.718	143	28-204 U/L
serum LDH	1068	688	381	115-304 U/L
ESR	2	2	7	0-20 mm/h
CRP	0.3	0.1	0.2	0-0.8 mg/dl
IgG	964	Nd	nd	639-1349 mg/dl
IgA	<6	<6	nd	70-312 mg/dl
IgM	67	Nd	nd	56-352 mg/dl
ANA	(-)	Nd	nd	
anti-dsDNA	(-)	Nd	nd	
Anti Jo-1	(-)	Nd	nd	
CMAS	14	25	46	

ALT: alanine aminotransferase, ANA: anti-nuclear antibody, anti-dsDNA: anti double stranded DNA, AST: aspartate aminotransferase, CK: creatine kinase, CMAS: Childhood Myositis Assessment Scale, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, Hct: hematocrit, LDH: lactate dehydrogenase, nd: not defined, WBC: white blood cell.

Until now, several studies have been showed the co-occurrence of JDM and IgA deficiency[7,13,14,15]. In this report we, presented the co-occurrence of sIgAD in a patient with JDM. Before the diagnosis of JDM, the patient had no history of recurrent pulmonary or gastrointestinal system infections. Immunologic investigations revealed sIgAD. Although she was diagnosed with sIgAD, the response to immunosuppressive treatment for JDM was very satisfying. Therefore, we *hypothesized that* IgA deficiency may also positively affect the disease activity and leads to milder disease in JDM patients.

In conclusion, the association between JDM and sIgAD is not widely reported and investigated so far. This may be due to the lack of awareness on the importance of immunological screening in patients with autoimmune diseases, particularly JDM. However, because our patient showed a good response to the conventional immunosuppressive treatment, we hypothesized that sIgAD might be a good prognostic factor in the course of the disease and for the response to the treatment in patients with JDM. Further studies investigating the role of IgA levels in JDM patients are needed to support our hypothesis.

Yazar Katkıları: Çalışma konsepti/Tasarımı: SB, MY; Veri toplama: MS, DD; Veri analizi ve yorumlama: DD, RMKE, DUA; Yazı taslağı: SB; İçeriğin eleştirel incelenmesi: RMKE, MY; Son onay ve sorumluluk: SB, RMKE, DD, MS, DUA, MY; Teknik ve malzeme desteği: -; Süpervizyon: RMKE, DUA; Fon sağlama (mevcut ise): yok.
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