Case Report
Olgu Sunumu

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Macrophage activation syndrome due to juvenile amyopathic dermatomyositis with atypical onset

Atipik başlangıçlı juvenil amiyopatik dermatolmiyozite bağlı makrofaj aktivasyon sendromu

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Abstract

Macrophage activation syndrome (MAS) is a life-threatening condition associated with rheumatic diseases. It is rarely reported in juvenile dermatomyositis. An 8-year-old girl was admitted with complaints of joint swelling and psoriasiform plaques on the elbows. She was diagnosed with psoriatic arthritis, and methotrexate therapy was started. Three months later, she was readmitted with fever, fatigue, and weight loss. Hepatosplenomegaly was found on physical examination. The muscle strengths were 5/5. Dermatological examination revealed facial edema, widespread maculoerythematous rash, and xerosis. Erythematous-violaceous papulosquamous plaques were seen on the dorsal surfaces of the elbows and metacarpophalangeal and proximal interphalangeal joints. Based on the clinical and laboratory findings, the patient was considered to have MAS secondary to juvenile amyopathic dermatomyositis (JADM). The cutaneous manifestations seen in MAS are not specific but depend on the underlying rheumatic disease. Given the atypical onset, this was considered a case of JADM misdiagnosed as psoriasis, which rapidly progressed to MAS.
Keywords: Connective tissue disorders, pediatric dermatology, psoriasis

Öz

Makrofaj aktivasyon sendromu (MAS), romatizmal hastalıklarla ilişkili, hayatı tehdit eden bir hastalıktır. Juvenil dermatomiyozitte nadiren bildirilmiştir. Sekiz yaşında kız çocuğu eklemlerde şişlik ve dirseklerde psoriaziform plaklar şikayeti ile başvurdu. Hastaya psoriatik artrit tanısı konuldu ve metotreksat tedavisi başlandı. Hasta üç ay sonra ateş, halsizlik ve kilo kaybı şikayeti ile başvurdu. Fiziksel muayenede hepatosplenomegali izlendi. Kas gücü 5/5 idi. Dermatolojik muayenede yüz ödemi, yaygın maküloeritematöz döküntü ve kseroz izlendi. Dirsekler, metakarpofalengeal ve proksimal interfalengeal eklem sırtlarında eritemli-viyolase papüloskuamöz plaklar görüldü. Klinik ve laboratuvar bulguları baz alınarak hastaya juvenil amiyopatik dermatomiyozit (JAMD) sekonder MAS tanısı konuldu. MAS'de görülen deri bulguları spesifik olmayıp, altta yatan romatizmal hastalığa bağlıdır. Burada, atipik başlangıç göstermesi nedeniyle, psoriazis olarak yanlış tanı alan ve hızla MAS'ye ilerleyen JADM'li bir çocuk olgu sunulmuştur.
Anahtar Kelimeler: Bağ dokusu hastalıkları, pediatrik dermatoloji, psoriazis

Introduction

Macrophage activation syndrome (MAS), or secondary hemophagocytic lymphohistiocytosis (HLH), is a serious, potentially fatal complication of rheumatic diseases[1]. It occurs most frequently in systemic juvenile idiopathic arthritis and juvenile systemic lupus erythematosus (SLE), but it has been rarely reported in juvenile dermatomyositis (JDM)[2].

Juvenile amyopathic dermatomyositis (JADM) is characterized by classic cutaneous manifestations of dermatomyositis (DM) occurring for at least 6 months with no muscle involvement, with an onset before the age of 18 years and over[3].

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Pathognomonic cutaneous manifestations of DM include Gottron's papules, Gottron's sign, heliotrope rash, "shawl sign" overlying the photoexposed skin, and periungual changes. On the contrary, classic DM usually presents as classical skin findings accompanying myopathy, and misdiagnosis is common in JADM because the skin lesions are generally more atypical than in adults, and myopathy is not observed[4]. Here, we present the case of an 8-year-old girl with JADM who was misdiagnosed with psoriasis, which rapidly progressed to MAS, because of the atypical onset.

Case Report

An 8-year-old girl was admitted with complaints of joint swelling and psoriasiform plaques on the elbows. She was diagnosed with psoriatic arthritis, and methotrexate therapy was started. Three months later, she was readmitted with fever, fatigue, and weight loss. Hepatosplenomegaly was observed on physical examination. The muscle strengths were 5/5. On dermatological examination, facial edema, widespread maculoerythematous rash, and xerosis were present. Erythematous-violaceous papulosquamous plaques were seen on the dorsal surfaces of the elbows and metacarpophalangeal and proximal interphalangeal joints. The nail-fold capillary pattern was observed as capillary dilatation and tortuosity, and the cuticle was hypertrophic (Figure 1).

On histopathological examination of the papulosquamous plaque on the elbows, necrotic keratinocytes, lymphocyte exocytosis, basal vacuolar degeneration, mild perivascular lymphocytic, and neutrophilic infiltration were detected (Figure 2). Laboratory findings of the patients are summarized in Table 1. Serological studies and polymerase chain reaction analyses did not detect evidence of recent infection with Epstein-Barr virus (EBV), cytomegalovirus, adenovirus, or herpes simplex viruses.

According to the diagnostic criteria of HLH-2004, the patient was considered to have MAS secondary to JADM[5]. Informed consent was obtained.

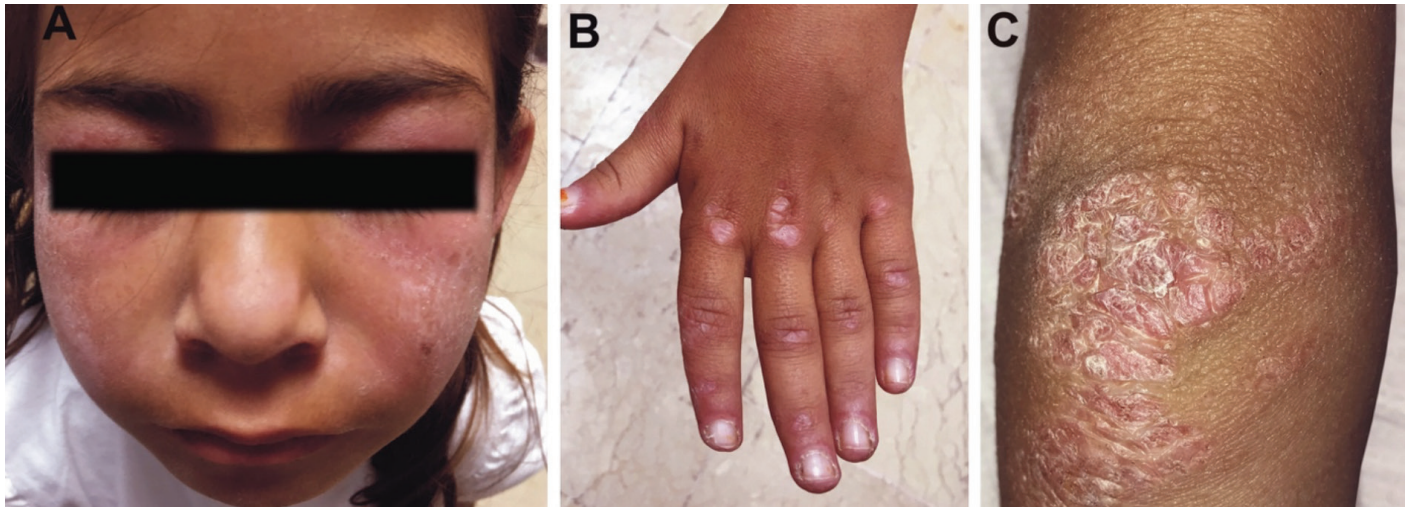

Figure 1. (A) Facial edema, maculoerythematous rash, and xerosis on the face, **(B)** erythematous-violaceous papulosquamous plaques on the dorsal surfaces of the metacarpophalangeal and interphalangeal joints, the cuticle was hypertrophic, **(C)** erythematous-violaceous papulosquamous plaques on dorsal surfaces of the elbows were observed

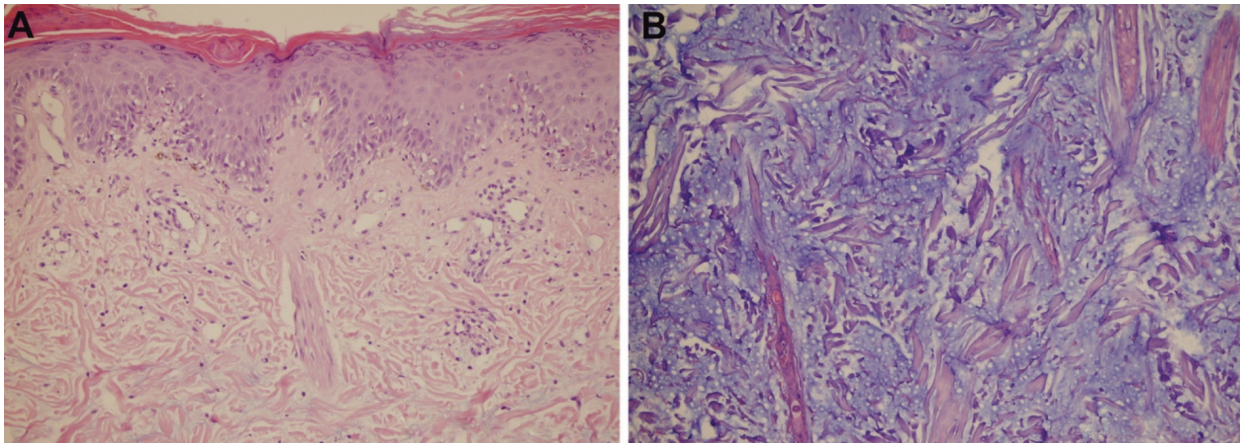

Figure 2. Histological images of the skin biopsy specimen from a papulosquamous plaque on the elbow. Histopathological examination shows **(A)** mild spongiosis, necrotic keratinocytes, vacuolar degeneration of the basal layer, mild perivascular lymphohistiocytic infiltration (hematoxylin-eosin staining, x200) and **(B)** increased dermal mucin highlighted by Alcian blue stain (x200)

Table 1. Laboratory investigations

Investigations	Patient	Normal range
WBC (10^3/dL)	3.7	3.8-8.6
Hemoglobin (g/dL)	10	11.1-17.1
Platelets (10^3/dL)	89	140-360
CRP (mg/dL)	3.2	<5
ESR mm/h	39	0-20
ALT (IU/L)	133	<40
AST (IU/L)	618	<40
GGT (IU/L)	200	<55
LDH (IU/L)	337	120-246
Total protein (g/dL)	6.9	6.6-8.7
Albumin (g/dL)	3.2	3.5-5.3
Ferritin (ng/mL)	968	2-276
Fibrinogen (mg/dL)	202	170-420
CK (IU/L)	86	24-195
Triglyceride (mg/dL)	205	40-180
ANA	Positive (1/100, granular pattern)	

ALT: Alanine transaminase, ANA: Antinuclear antibody, AST: Aspartate transaminase, CK: Creatine kinase, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, GGT: Gamma-glutamyl transferase, LDH: Lactate dehydrogenase, WBC: White blood cell count

Discussion

The main clinical features of MAS are prolonged high fever, hepatosplenomegaly, and diffuse lymphadenopathy, which can be accompanied by skin rashes, edema, hemorrhagic manifestations, and neurological symptoms[6]. The progression of MAS to multiorgan failure is related to the uncontrolled production of several proinflammatory cytokines, reflecting cytokine storms[1]. The cutaneous manifestations seen in MAS are not specific but depend on the underlying rheumatic disease. MAS-associated cytokine storm may cause more atypical skin lesions, such as facial or generalized edema, severe xerosis, generalized maculoerythematous rash, and urticaria-like lesions. In the literature, the most common skin findings in patients with MAS secondary to JDM are heliotrope erythema, Gottron's papules, Gottron's sign, and periungual changes. MAS-associated cytokine storm may cause more atypical skin lesions, such as facial or generalized edema, severe xerosis, and generalized maculoerythematous rash. Indeed, facial erythema, generalized erythematous skin rashes, facial or generalized edema, urticarial itchy skin rash, and purpuras were reported[7].

Poddighe and Dauyey[7] reviewed JDM cases developing MAS; only 2 of 12 patients were diagnosed with amyopathic forms. Unlike other pediatric rheumatologic diseases, MAS was usually the onset presentation of JDM, as in our patient. The mortality rate in JDM might be quite similar to MAS in other rheumatic diseases[7].

The pathogenic factors underlying the development of MAS in rheumatic diseases remain unclear; however, most cases of MAS develop in the context of either high disease activity or intercurrent infection[8]. Many viral, bacterial, and fungal factors can trigger MAS. EBV and varicella-zoster virus are the most common pathogens[9]. Recent studies have shown a relationship between hyperinflammation and severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), and studies have suggested that Coronavirus disease-2019 (COVID-19)-associated cytokine storm plays a role in COVID-19 pneumonia and exacerbation by causing MAS[10-12]. A case of MAS caused by SARS-CoV-2 was also reported in a patient with SLE[13].

In the present case, we did not detect any infectious agents, and the clinical findings of MAS appeared after the initiation of methotrexate therapy. Sterba et al.[14] reported a patient with JDM who developed MAS after starting methotrexate treatment, as in our case.

Classic DM usually presents as classical skin findings accompanying myopathy, and misdiagnosis is common in JADM because the skin lesions are generally more atypical than in adults, and myopathy is not observed. JDM cases misdiagnosed as psoriasis and psoriatic arthritis have been reported[15]. Although Gottron's papules may contain scaling because of scratching, erythematous-violaceous color is more pronounced in DM, and psoriasis may have a thicker, silvery, or micaceous scale.

MAS may result in a progressive multiorgan failure, and if not treated timely, it can be fatal; thus, early diagnosis is critical. In MAS with atypical skin findings, even if it is not accompanied by myopathy, JADM should be considered in the differential diagnosis.

Ethics

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.İ.Y., M.K.G., İ.Ç., Concept: E.İ.Y., B.D., Design: E.İ.Y., B.D., Data Collection or Processing: E.İ.Y., M.K.G., İ.Ç., Analysis or Interpretation: E.İ.Y., B.D., M.K.G., İ.Ç., Literature Search: E.İ.Y., M.K.G., Writing: E.İ.Y., B.D.

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