A case report of Wells' syndrome in a celiac patient

Çölyak hastalığı olan bir hastada Wells sendromu

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Celiac disease is an immune-mediated enteropathy induced by gluten ingestion in a genetically susceptible patient. It has been associated with various skin lesions but predominantly with dermatitis herpetiformis. Herein, we report another skin lesion, eosinophilic cellulitis, which is an inflammatory dermatitis, in a celiac patient who also had Giardia infestation.

Key words: Gluten enteropathy, giardiasis, eosinophilic cellulitis

Çölyak hastalığı, genetik olarak duyarlı bireyde, gluten alımı ile ortaya çıkan immün-aracılı enteropatidir. Başta dermatitis herpetiformis olmak üzere çeşitli cilt lezyonları ile birlikte olabilir. Burada çölyak hastalığı ve giardia enfestasyonu olan bir hastada bir diğer cilt lezyonu olan eozinofilik sellülit raporlandı.

Anahtar kelimeler: Gluten enteropatisi, giardiasis, eozinofilik sellülit

INTRODUCTION

Wells' syndrome (eosinophilic cellulitis) is a recurrent and generally self-remitting inflammatory dermatitis of unknown etiology. Its classical described lesion is a dermatitis resembling cellulitis, which evolves into plaques and ultimately resolves without scarring. To date, it has been associated with drugs, various viral infectious diseases, malignancies, arthropod bites, cutaneous parasitosis, and ulcerative colitis. Among parasitosis, ascariasis, toxocariasis, onchocerciasis and giardiasis have been reported to be associated with Wells' syndrome (1-4). Herein, we report Wells' syndrome in a celiac disease patient with concomitant Giardia infestation. To our best knowledge, this is the first case to be described in celiac disease.

CASE REPORT

A 14-year-old girl with previously diagnosed celiac disease presented with complaints of recurrent pruritic swelling, erythema and crusting papular eruptions with a remitting and relapsing pattern predominant on her extremities (Figure 1a, 1b). Her compliance with a gluten-free diet was poor. Laboratory investigations revealed increased erythrocyte sedimentation rate (29 mm/hour), decreased albumin (3.2 g/dl) and total protein (5.4 g/dl), with normal hemoglobin level (14 g/dl), white blood cell count (8300/mm^3) and platelet count (282000/mm^3). Antiendomysium IgA antibody was still positive despite the advised gluten- free diet. Biopsy specimens were taken from the dorsum of the foot and one of the described papulovesicular lesions on the leg. Histopathologic examination revealed superficial and interstitial dermatitis composed of lymphocytes, eosinophils and macrophages and "flame figures", which were formed by necrotic collagen bundles, multinucleated giant cells and surrounding eosinophils and macrophages (Figure 2). These flame figures extended throughout the dermis and subcutaneous tissue. Immunofluorescent examination of the tissue was negative for IgA deposition. This histopathologic description was consistent with Wells' syndrome. She was treated with sulbactam-ampicillin and a strict gluten-free diet. Cellulitic reaction resolved completely in five days as antibiotic treatment was tapered. The other lesions mentioned on the extremities regressed thereafter in 10 days. Two

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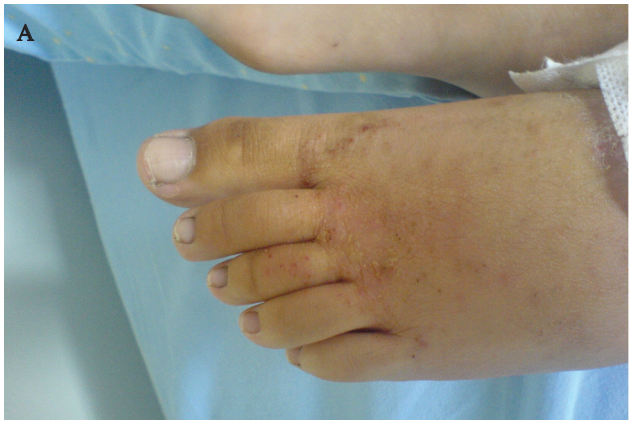

Figure 1a. Cellulitis on the dorsum of the left foot with crusting papules.

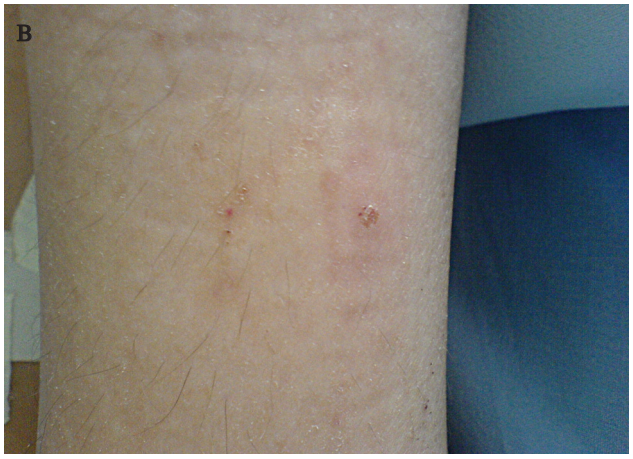

Figure 1b. Papulovesicular lesions on the extremities.

months later the patient was reevaluated due to persistent hypoalbuminemia and increased intestinal wall thickness. The previous intestinal biopsy specimen was reexamined and Giardia trophozoites were observed. She was treated with metronidazole 30 mg/kg/day. Since the mentioned last eruptions, no recurrence was observed.

DISCUSSION

Celiac disease is an immune-mediated enteropathy induced by gluten ingestion and is associated with several intestinal and extraintestinal manifestations. Some of its manifestations, including abdominal distention, diarrhea, osteoporosis, and anemia, are attributed to enteropathy resulting in various degrees of mucosal atrophy and intestinal malabsorption, while its extraintestinal manifestations like ataxia, seizures, polyneuropathy, alopecia, hypertransaminasemia, and dermatitis herpetiformis may be due to the deranged autoimmune response (5). To date, among the skin manifestations, a special interest has been given to dermatitis herpetiformis, which is a gluten-dependent condition, characterized by symmetric pruritic blisters with granular subepidermal IgA deposition (6). Herein, we have reported another skin disease, Wells' syndrome, associated with celiac disease. Wells' syndrome (eosinophilic cellulitis) is a rare inflammatory skin disease with unknown etiology. Histologically, it is characterized by distinct but non-pathognomonic features, the so-called "flame figures". Its pathological course is described in three stages: In the acute phase, the dermis is infiltrated with neutrophils and eosinophils. In the subacute phase, eosinophils and histiocytes adhere to collagen bundles. Basophilic collagen bundles are then coated with eosinophilic major basic protein due to eosinophilic degranulation, so characteristic flame figures appear. As eosinophils disappear, histiocytes and giant cells surround the flame figure, forming small granuloma in the resolution phase (7). Flame figures are highly suggestive but they are not unique to Wells' syndrome. Thus, a clinicopathological correlation is mandatory for diagnosis. Although flame figures with cellulitis and ulcerating plaques are more suggestive of Wells' syndrome, in conjunction with celiac disease it should be differentiated from dermatitis herpetiformis. Rose et al. (8) reported flame figures in dermatitis herpetiformis as well. However, in the present case, absence of granular subepidermal IgA deposition differentiated Wells' syndrome from dermatitis herpetiformis.

We identified five cases in the literature whose gastrointestinal pathologies were associated with Wells' syndrome. Two different groups, Sakaria et

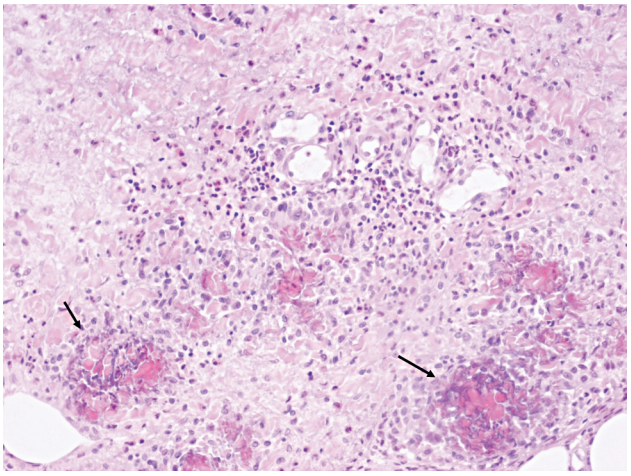

Figure 2. Flame figures: necrotic collagen bundles surrounded by eosinophils and macrophages.

al. (9) and Andutikal et al. (10), reported Wells' syndrome associated with ulcerative colitis. In both cases, remission was related to ulcerative colitis remission and was achieved with sulfasalazine plus steroid and steroid, respectively. Ghislain et al. (11) reported an unusual presentation of Wells' syndrome with hypertransaminasemia in a 54-year-old man. Colon cancer and ascariasis infestation were also reported to be associated with Wells' syndrome (2, 12). Canonne et al. (1) presented a patient with Giardia infestation and a history of recurrent skin lesions consistent with Wells' syndrome; both skin lesions and parasitic infestation resolved with antiparasitic treatment and reappeared with reinfection with Giardia and again resolved with metronidazole treatment. In the present case, we suggest that Wells' syndrome developed in association with celiac disease since it was recurrent for many years and resolution was observed before anti- parasitic treatment.

Although the pathogenesis of Wells' syndrome has not yet been elucidated, its response to steroids and the autoimmune nature of both ulcerative colitis and celiac disease may draw attention to the reactive immune mechanisms.

Even though spontaneous remission is seen, therapeutic modalities consisting of systemic corticosteroids, antihistaminics, cyclosporine and azathioprine as well as treatment of the underlying condition have been applied in Wells' syndrome (7, 13, 14). In our patient, we achieved clinical remission with re-emphasis of the gluten-free diet compliance. However, since spontaneous resolution is highly possible, we can not say with certainty that resolution was strictly associated with gluten withdrawal, as it is in other treatment modalities.

To date, celiac disease has been associated with various skin manifestations. Herein, we have reported the association of Wells' syndrome and celiac disease. Our case together with the ulcerative colitis case may point to an autoimmune reaction in the pathogenesis of Wells' syndrome. Although we observed remission with the gluten-free diet, further reports and evidence are still needed to understand the behavior and treatment response of Wells' syndrome in celiac patients.

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