

A case of atypical urticarial vasculitis associated with thrombosis

Trombozla ilişkili atipik ürtikeryal vaskülitli bir olgu

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ABSTRACT

Urticarial vasculitis is characterized by pruritic, burning or painful, erythematous or edematous, circumscribed wheals with induration. It is most commonly idiopathic and it can occur in association with autoimmune disease, drug reactions, infections, or malignancy. Three forms of urticarial vasculitis has been described. These are normocomplementemic urticarial vasculitis, hypocomplementemic urticarial vasculitis, and hypocomplementemic urticarial vasculitis syndrome. We present a 17-year-old boy with urticarial vasculitis who has atypical lesions and venous thrombosis that related with Factor V Leiden mutation.

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Key words: Atypical, factor V Leiden, normocomplementemic, thrombosis, urticarial vasculitis

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ÖZ

Ürtikeryal vaskülit kaşıntılı, yangılı ya da ağrılı, eritematöz ya da ödematöz, sınırları belirgin endürasyonlu plak ile karakterizedir. Sıklıkla idiyopatik olmakla beraber otoimmün hastalıklar, ilaç reaksiyonları, infeksiyonlar ya da malignitelerle ilişkili olabilir. Üç formu tanımlanmıştır. Bunlar normokomplementemik ürtikeryal vaskülit, hipokomplementemik ürtikeryal vaskülit ve hipokomplementemik ürtikeryal vaskülit sendromudur. Burada atipik lezyonları ve faktör V leiden mutasyonu ile ilişkili venöz trombozu olan 17 yaşında bir erkek hastayı sunacağız.

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Anahtar kelimeler: Atipik, faktör V Leiden, normokomplementemik, tromboz, ürtikeryal vaskülit

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INTRODUCTION

Urticarial vasculitis (UV) is characterized by pruritic, burning or painful, erythematous or edematous, circumscribed wheals with induration. The individual urticarial lesion last frequently more than 24 hours and leave a residual transient hyperpigmentation. Associated features include fever, malaise, myalgia, arthralgia and specific organ involvement^[1].

Urticarial vasculitis is a rare disorder, although the incidence and prevalence are uncertain^[2]. Females comprise 60-80% of the reported cases^[2,3]. The peak reported incidence is in the fourth decade of life^[3,4]. It has also been described in children; the youngest reported case is one year of age^[5].

Urticarial vasculitis is most commonly idiopathic, it can occur in association with autoimmune disease, drug reactions, infections, or malignancy^[6].

Upper extremity deep vein thrombosis represents 1% to 4% of all cases of deep vein thrombosis^[7]. The causes of venous thrombosis can be divided into two groups: hereditary and acquired, and are often multiple in a given patient. Factor V Leiden mutation is the most common cause of inherited thrombophilia in Caucasian populations^[8].

This report describes a 17-year-old boy with UV who has atypical lesions of UV and venous thrombosis related with Factor V Leiden mutation.

CASE REPORT

Seventeen year-old boy admitted to our hospital with a 1-week history of rash on his various regions of the body, angioedema of the lip and edema on his left arm. His rashes were accompanied by burning sensation, itching and resolved in 1-2 days without residual hyperpigmentation. He had no fever, weakness and other symptoms of systemic involvement except for arthralgia. On his physical examination he had angioedema of the lip and some erythematous, painful rashes without wheal formation on his left elbow (Figure 1). Left arm had minimal edema



Figure 1. Angioedema of the lip of the patient.

but there was no hyperemia and pulselessness. Other physical examination was normal. He also developed similar rashes without wheal formation on his palm and right foot on the follow up (Figure 2,3). He had not any history of chronic disease and there was no medical history of thrombosis in his family. The initial laboratory studies were within the normal range, including a complete blood count, thyroid function tests, thyroid autoantibodies, hepatitis markers, liver and renal function tests, urinalysis, stool analysis for parasite ova, total IgE, IgG, IgM, C3, C4, C1 inhibitor levels and function, antinuclear antibodies (ANA), rheumatoid factor, cryoglobulins. Erythrocyte sedimentation rate (ESR) and C-reactive protein levels were 55 mm/h, 15 mg/L, respectively. His blood, urine and throat cultures were negative, also. He underwent doppler ultrasonography because of his left arm edema and it revealed partial thrombosis of left axillary vein.



Figure 2. Rash on the patient's left palm.

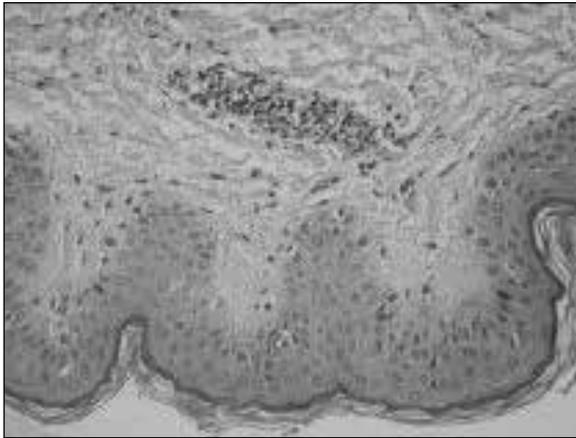


Figure 3. Rash on the patient's right foot.

There were no thrombosis of the other venous systems. Etiological causes of thrombosis were investigated in detail (such as antithrombin III, protein C and protein S activity, factor VIII and factor IX levels, homosistein level, lupus anticoagulant, prothrombin mutation) but only heterozygous factor V Leiden mutation was detected. A biopsy from an affected area of skin showed perivascular and vascular lymphocyte and neutrophil infiltration and extravasation of erythrocytes in the superficial dermis typical of UV. Direct immunofluorescences (DIF) for IgM, IgG, IgA, C3 were negative. He was diagnosed as idiopathic normocomplementemic UV and venous thrombosis. He was treated with low molecule weight heparine and an oral antihistamine. His thrombosis was recanalized after two weeks of anti-coagulant therapy. His arthralgia and rash were reported to be resolved in the follow up visits and no other systemic symptoms developed.

DISCUSSION

Urticarial vasculitis is distinct clinicopathologic entity in which the majority of patients presents with generalized wheals which last > 24 hour and leave residuel transient hyperpigmentation^[9]. Our patient's lesions were atypical; due to lack of wheal formation and resolving without residual hyperpigmentation. Dincy CV et al. reported that burning pain and wheals resolving with residual hyperpigmentation were observed

in 22% to 17% of the cases^[10]. In this study, only 1.4% of the patients presented with morphology other than wheals^[10]. Apart from wheals, other skin lesions that have been described with UV include annular lesions, palpable purpura, target lesions, livedo reticularis and bullae^[11]. Urticarial vasculitis can present as angioedema when the vasculitis involves the capillary or post capillary venules of the deeper layers of the dermis and submucosa^[12]. The frequency of angioedema varies between 23.4% to 50% in patients with UV^[9,10].

The most common abnormal laboratory results associated with UV include ESR, hypocomplementemia (usually decreased C3, C4, C1q), circulating immune complexes and positive ANA. Our patient's ESR was elevated. It is not generally related to the severity of the disease or to the extent of systemic involvement^[11]. An elevated ESR can also be found in patients with typical urticaria without evidence of vasculitis.

Three forms of urticarial vasculitis has been described. One of them is normocomplementemic UV. It is typically a self-limited subset of hypersensitivity vasculitis, generally idiopathic, and benign. The other form of UV is hypocomplementemic UV (HUV). Two categories HUV was described. Primary or idiopathic, usually not associated with systemic disease, and secondary is more likely to be a chronic disorder, often associated with a systemic inflammatory disease^[13]. The third form of UV is hypocomplementemic UV syndrome (HUVS). HUVS is a rare, distinct, and potentially severe form of UV with multiorgan involvement. It is associated with an involvement of organ systems and characterized clinically by persistent urticarial skin lesions and a variety of systemic manifestations, including severe angioedema, laryngeal edema, ocular inflammation, arthritis, arthralgia, obstructive lung disease, recurrent abdominal pain, and glomerulonephritis^[14,15]. In accordance with all of this information, patients with hypocomplementemia had more severe clinical course than those with normocomplementemia. And disease

duration of the HUV was found statistically significantly longer than the patient with NUV^[9]. Our patient was normocomplementemic and he had a benign course as described in the literature.

Urticarial vasculitis may be associated with other systemic diseases or it may be idiopathic^[6]. Systemic diseases associated with UV include serum sickness, systemic lupus erythematosus (SLE), Sjogren's syndrome, infection with hepatitis A, B, C and Epstein-Bar virus, malignancies, IgG and IgM gammopathies, cold exposure, Wegener's granulomatosis, polyarthritis nodosa, Henoch-Schonlein purpura, adverse drug reactions and hereditary and acquired angioedema^[12]. In a study by Kultahan et al. reported that cause of UV could be identified only in 30% of the patients and most common identified cause was infection, followed by drugs, malignancy and SLE^[9]. Our patient had also thrombosis but no other symptoms or signs of systemic disease detected.

Immunofluorescence reveals deposits of immunoglobulins, complement, or fibrin around blood vessels in most patients with UV^[2]. Davis et al. reported that 96% of patients with HUV and 1% with NUV had a continuous strong granular deposition of immunoreactants along the basement membrane zone compatible with SLE in addition to vascular fluorescence on DIF^[5]. It was found that the prevalence of immunoreactant deposits in the skin lesions of patients with UV as detected by DIF was 54.7%^[9]. DIF was negative in our patient's skin biopsy.

The treatment of UV is often challenging and therapy is not standardized. Agents are chosen based upon the severity of the disease and presence of systemic involvement. Antihistamines are used as first line therapy in all patients with UV/HUVS and any degree of cutaneous disease^[12]. Our patient has responded antihistaminic therapy.

The majority of cases of upper extremity deep vein thrombosis are due to secondary causes of venous thrombosis related to central venous cannulation (eg, central line, pacemak-

er) or prothrombotic states (eg, thrombophilia, malignancy)^[16]. The most common cause of inherited thrombophilia in Caucasian populations is factor V Leiden mutation^[9]. The prevalence of heterozygosity for the factor V Leiden mutation in Caucasians ranges from 1 to 8.5 percent^[17]. The factor V Leiden mutation leads to a hypercoagulable state for two reasons, due to the critical position of factor V in both the coagulant and anti-coagulant pathways^[18]. Our patient had partial axillary venous thrombosis and heterozygous factor 5 Leiden mutation. He did not have a history of central venous cannulation. In our opinion our patient's thrombosis was related with factor V Leiden mutation but we will follow up him for the development of systemic diseases associated with thrombosis and UV. Our patient had anti-coagulant therapy for only three months because of no family and individual history of thrombosis before. We think that thrombosis and UV are two distinct entities and not related each other. But we will follow the patient to development of systemic disease that related thrombosis.

In conclusion; we present an atypical case of UV without wheals and residual hyperpigmentation. Urticarial vasculitis may present like this and it may be confused with other situations. If there is any clinical suspicion of UV, skin biopsy must performed although C3-C4 complements are normal. Our patient had venous thrombosis, also. Urticarial vasculitis and venous thrombosis are two distinct entities that are not reported together previously.

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