

# Clinical characteristics and treatment outcomes in patients with urticarial vasculitis

 Gamze Serarslan,  Ebru Okyay

Department of Dermatology, Mustafa Kemal University Faculty of Medicine, Hatay, Turkey

## ABSTRACT

**OBJECTIVE:** Urticarial vasculitis (UV) is an uncommon disease clinically presenting with pruritic urticarial plaques of the skin. The disease is classified as normocomplementemic and hypocomplementemic types according to their complement levels. We aimed to evaluate demographic characteristics, laboratory findings, and response to treatment of patients diagnosed as UV in our clinic.

**METHODS:** Between January 2015 and January 2019, the files of the patients were retrospectively reviewed. Demographic data, clinical features, laboratory findings, suspected triggering factors, disease course, treatment modalities, and treatment results of the patients were recorded.

**RESULTS:** A total of 16 patients (nine males [56.25%], seven females [43.75%]) were included in the study. The mean age at diagnosis was  $45.2 \pm 10.4$  years and the duration of the disease was  $72.1 \pm 62$  months. Twelve (75%) patients had angioedema and two (12.5%) patients had residual hyperpigmentation. The most common extracutaneous finding was arthralgia (43.7%). No hypocomplementemia was detected in the patients. The most common abnormal laboratory findings were CRP elevation (37.5%) and ANA positivity ( $n=4/15$ , 26.7%). Analgesic and antibiotic drugs use were the most common possible triggering factors for the disease ( $n=9$ , 56%). Oral antihistamines, oral corticosteroids, azathioprine, colchicine, dapsone, hydroxychloroquine, doxepin, and omalizumab were among the treatments given to the patients. Complete remission was achieved in three patients.

**CONCLUSION:** Compared with other studies, we found that angioedema was more frequent, postinflammatory hyperpigmentation was lower and long-term treatment was needed to control UV attacks. There are a few studies on UV and we think that more and larger patient groups are needed for standardization of treatment.

*Keywords:* Normocomplementemic; urticarial vasculitis; treatment.

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Urticarial vasculitis (UV) is a form of cutaneous leukocytoclastic vasculitis with urticarial plaques that last longer than 24 h and with inflammatory damage to dermal capillaries and postcapillary venules in the histopathology [1, 2]. UV is reported to be rare and there are no population-based epidemiological studies describing its incidence and prevalence. The disease may be mild or manifest with severe systemic and specific organ findings. UV is often idiopathic however infection, drug reaction,

autoimmune reactions, and malignancy may be among the underlying etiologies [2]. UV is classified as normocomplementemic UV (NUV) and hypocomplementemic UV (HUV). HUV is thought to be driven by the deposition of immune complexes in the skin. This activates the complement (C) cascade, followed by a reduction in complement levels. Low C levels indicate the more severe form of the disease. Therefore, when hypocomplementemia is detected, more organ involvement is likely to occur [2].



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Correspondence: Gamze Serarslan, MD. Mustafa Kemal Universitesi Tip Fakultesi, Dermatoloji Anabilim Dalı, Hatay, Turkey.  
Tel: +90 326 229 10 00 e-mail: gserarslan@hotmail.com

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In this study, we aimed to investigate the demographic data, clinical characteristics, laboratory findings, treatment modalities, and treatment responses of patients diagnosed with UV in our clinic and to compare our findings with previous studies.

## MATERIALS AND METHODS

This retrospective study was performed at a tertiary care hospital in the region of Hatay. Between January 2015 and January 2019, the files of patients who applied to Mustafa Kemal University Faculty of Medicine Department of Dermatology outpatient clinic and diagnosed as UV were retrospectively reviewed. Hatay Mustafa Kemal University Non-Interventional Research Ethics Committee approval was obtained (23.05.2019, 12) before the files were reviewed.

Biopsies are taken from patients with urticaria plaques that last longer than 24 h and/or do not fade with diascopy and/or regress with residual purpura/hyperpigmentation in our clinic. Patients diagnosed with vasculitis on biopsy are diagnosed with UV. Laboratory and imaging tests performed on patients diagnosed with UV include complete blood counts (CBC), erythrocyte sedimentation rate (ESR), urine analysis, BUN, creatinine, ALT, AST, TSH, CRP, HBsAg, anti HCV, ANA, C levels (C3, C4) and chest X-ray. Additional laboratory and imaging tests are performed according to the patient if necessary.

The files of the patients diagnosed with UV were reviewed and their demographic data, clinical features, laboratory findings, suspected triggering factors such as infection and drug before the onset of the lesions, disease course, treatment modalities, and treatment results were recorded. Values were presented as mean  $\pm$  standard deviation (SPSS for Windows, version 21; IBM Corp, Armonk, New York, USA).

## RESULTS

A total of 22 patients diagnosed with UV over the years were reviewed. However, six patients (1 M, 5 F) were excluded because of insufficient clinical and laboratory data. A total of 16 patients (nine males [56.25%], seven females [43.75%]) were included in the study. The mean age at diagnosis was  $45.2 \pm 10.4$  years (range 31–65 years) and the duration of the disease was  $72.1 \pm 62$  months (range 2–240 months). The mean follow-up period of the patients was  $38.35 \pm 22.91$  months (range

### Highlight key points

- The most common extracutaneous finding was arthralgia in UV.
- A higher incidence of angioedema and a lower incidence of residual pigmentation was detected when compared to other studies.
- Long-term treatment may be required to control UV attacks in most of patients.

**TABLE 1.** Demographic data and clinical features of the patients and possible causes of triggering the disease

	n
Sex	
Women	43.75
Men	56.25
Age (year; mean $\pm$ SD)	45.2 $\pm$ 10.4
Disease duration (month; mean $\pm$ SD)	72.1 $\pm$ 62
Cutaneous symptoms	
Pruritus-burning sensation	100
Pain-tenderness	87.5
Angioedema	75
Residual hyperpigmentation	12.5
Extracutaneous findings	
Arthralgia	43.75
Dyspnea	31.25
Conjunctivitis	25
Fever	18.75
Cough	12.5
Abdominal pain	6.25
Nausea	6.25
Possible causes of urticarial vasculitis	
Drugs	56.25
Infections	31.25

SD: Standard deviation.

5–77 months), with the exception of 2 patients who were lost to followed-up.

Urticarial plaques were persist for more than 24 h in all patients. 100% of the patients had pruritus and burning, 87.5% had pain and tenderness in the lesions. Twelve (75%) patients had angioedema and two (12.5%) patients had residual hyperpigmentation.

The most common extracutaneous finding was arthralgia (43.7%). Others were dyspnea, conjunctivitis, fever, cough, abdominal pain, and nausea, respectively.

**TABLE 2.** Treatment of patients and treatment duration

Patient number	Sex	Age	Previous treatments	Currently used treatment	Total treatment duration (month)
1	F	49	Doxepin, OCS, OAH, omalizumab+OAH	OAH	46
2	F	52	OAH	OAH	8
3	F	46	OAH, OCS+OAH	OAH	10
4	M	36	OAH, OCS	OAH	30
5	M	60	OAH, OAH+OCS	Remission; follow-up 12 months	39
6	M	37	OAH	Omalizumab	27
7	M	50	OAH, OCS, dapson, hydroxychloroquine	Lost to follow-up	6
8	M	36	OAH, colchicine, OCS+ azathiopurine	Omalizumab	40
9	F	65	OAH	Omalizumab	32
10	F	60	OAH, omalizumab, hydroxychloroquine +OCS	Lost to follow-up	29
11	M	31	OAH, dapson, hydroxychloroquine, omalizumab+OAH, OCS	Remission; follow-up 24 months	53
12	M	53	OAH, colchicine	Remission; follow-up 24 months	31
13	M	43	OAH	OAH	28
14	F	34	OAH, OCS	Omalizumab	51
15	F	33	OAH, OCS	OAH	77
16	M	39	OAH	OAH	5

OCS: Oral corticosteroid; OAH: Oral antihistamine.

No hypocomplementemia was detected in the patients. Elevated serum C4 level was present in one patient. The most common abnormal laboratory findings were CRP elevation (37.5%), ANA positivity (n=4/15, 26.7%), and ESR elevation (12.5%). One of the patients with ANA positivity also had anti dsDNA positivity. During the follow-up period, no systemic condition such as autoimmune connective tissue disease was developed. One patient had hypothyroidism.

Analgesic and antibiotic drugs use were the most common possible triggering factors for the disease (n=9, 56%). Upper respiratory tract infection was detected in three patients at the time of UV attack. Urinary tract infection was also found in two patients and lower respiratory tract infection was also found in one of these patients. Table 1 shows the demographic and clinical findings of the patients and the possible triggering factors that can be detected.

Treatments included oral antihistamines (OAH), oral corticosteroids (OCS), azathiopurine, colchicine, dapson, hydroxychloroquine, doxepin, and omalizumab. Complete resolution was achieved in three patients. Two patients were out of follow-up. A total of 11 pa-

tients, seven of them were using OAH and four of them were using omalizumab were still on medication. The treatments and follow-up information of the patients are shown in Table 2.

## DISCUSSION

Although UV can be of any age, it is reported to be more common in the fourth decade of life and the disease is also more common in women [2]. We found that UV was more frequent in male patients. However, when we include patients with UV to the study who have been excluded due to lack of data, we find that the disease is more common (54.4%) in women. Dincy et al. [3] reported that 51.8% of NUV patients were women. In another study, 60% of patients with NUV were reported as women [4]. The mean age of our patients was 45.2 and the mean duration of the disease was 72.1 months. When the literature information was reviewed, it was found that the mean age at diagnosis ranged between 35 and 51 years [5–8] and the mean disease duration was ranged from 24 to 56.3 months [7–9].

UV is usually characterized by urticarial plaques that persist longer than 24 h, but may also last for <24 h [9]. Often itchy and may be painful. Angioedema, purpura and livedo reticularis can also be seen [1, 2]. In our study, urticarial plaques persisted longer than 24 h in the patients, and itching and burning sensation were present in the lesions of all of the patients. Pain and tenderness of the lesions were present in 87.5% of the patients. When the results of other studies were reviewed, it was seen that itching, inflammation, and pain were common symptoms, but in some studies, inflammation and pain were less common [3, 5, 6, 8, 9]. 12.5% of patients had residual hyperpigmentation in our study. The rate of residual hyperpigmentation reported in patients with UV in the literature is quite different from each other. Kulthanan et al. [6] found residual hyperpigmentation in 82.8% of patients. Moreno-Suárez et al. [8] reported that residual hyperpigmentation was present in 60% of patients. In another study, residual hyperpigmentation was reported in less than 1/3 of the patients [3].

In our study, 75% of the patients had angioedema. In a study, angioedema was detected in 23.4% of patients, in another study it was reported that angioedema was detected in 44.4% of patients with NUV and 21.4% of patients with HUVS [3, 6]. Akarsu et al. [7] reported that 30.2% of patients with UV had angioedema. Compared with other studies, angioedema was quite high in our study.

The three most common extracutaneous findings of UV were arthralgia, dyspnea, and conjunctivitis, respectively, in our study. Similar to our study, the most common extracutaneous manifestation of UV has been reported as arthralgia in other studies [3, 5, 7–9]. Other frequently reported findings included fever and abdominal pain [3, 6–9].

Elevated ESR in patients with UV is generally the most common abnormal laboratory finding [6, 7, 9]. Abnormal CBC, CRP elevation, and abnormal urine analysis are also not uncommon abnormal laboratory findings [5–7, 9]. In our study, the most common abnormal laboratory findings were CRP elevation, ANA positivity, and ESR elevation, respectively. Dincy et al. [3] found ANA positivity in 15.2% of patients with NUV. Kulthanan et al. [6] reported ANA positivity in 10.9% of patients and one of these patients was diagnosed with SLE. Akarsu et al. [7] found ANA positivity in 23.3% of patients with UV. It was reported that ANA positivity and low C level

were related in UV [3, 8]. In our study, ANA positivity was found in 26.7% of patients and hypocomplementemia was not present. In addition, these patients did not develop the autoimmune disease during the follow-up period. Similar to our study, Tosoni et al. [9] reported that patients with altered immunological tests do not have fully developed autoimmune disease.

In our study, the possible factors that triggered the disease were drugs (NSAID, antibiotics) and infection, respectively. Previous studies have reported that drugs, infection, and malignancy are the most common triggering factors of the disease [3, 6, 7].

OAH, OCS, azathioprine, colchicine, dapsone, hydroxychloroquine, doxepin, and omalizumab were the treatments given to our patients. We determined that the most commonly used drugs were OAH (n=16, 100%), OCS±OAH (n=8, 50%) and omalizumab±OAH (n=7, 43.7%) respectively. Remission was achieved with systemic corticosteroid in one patient, antihistamine plus systemic corticosteroid in the other patient, and colchicine in the third patient. Two patients were out of follow-up. Treatment of remaining patients has been continued with OAH or omalizumab. Although these patients did not have UV attacks and/or the number of attacks decreased, it was determined that the disease was relapsed when the drugs were interrupted. Therefore, these drugs are still in use. There are case reports in the literature that omalizumab is effective in NUV [10, 11]. In our study, four patients responded to omalizumab treatment, while three did not.

Although the clinical findings and extracutaneous symptoms of our patients generally overlap with the literature, we detected a higher incidence of angioedema and a lower incidence of residual pigmentation compared to other studies. We also found a low rate of complete resolution of patients with treatment. Long-term treatment may be required to control UV attacks in most of patients.

### Conclusion

Although the clinical findings and extracutaneous symptoms of our patients generally overlap with the literature, we detected a higher incidence of angioedema and a lower incidence of residual pigmentation compared to other studies. We also found a low rate of complete resolution of patients with treatment. Long-term treatment may be required to control UV attacks in most of patients.

**Ethics Committee Approval:** The Hatay Mustafa Kemal University Non-Interventional Research Ethics Committee granted approval for this study (date: 23.05.2019, number: 12).

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