

# Omalizumab Combined with Cyclosporine for the Treatment and Management of Refractory Urticarial Vasculitis

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**Abstract:** Urticarial vasculitis (UV) is a clinicopathologic entity characterized by urticarial lesions disclosing histopathologically leukocytoclastic vasculitis, mainly of postcapillary venules. A 61-year-old woman with a four-month history of widespread, pruritic urticarial lesions was diagnosed with urticarial vasculitis. The patient received a subcutaneous injection of Omalizumab (300 mg) every 28 days, combined with oral Cyclosporine (3 mg/kg/day). Significant clinical improvement was noted within five days post-treatment. This case highlights the difficulties in treating refractory urticarial vasculitis while demonstrating the successful use of Omalizumab plus Cyclosporine, providing a viable treatment option for similar patients.

**Keywords:** omalizumab, cyclosporine, urticarial vasculitis

## Introduction

Urticarial vasculitis (UV) is a rare condition characterized by the presence of urticarial lesions that persist for more than 24 hours and can last for several days. These wheals are typically non-blanching or partially blanching, with central dark red or brownish macules. It is a type of small vessel leukocytoclastic vasculitis, which can lead to significant discomfort and may mimic other dermatological conditions, complicating the diagnostic process. The pathophysiology involves an immune-mediated response that results in inflammation of the blood vessels, leading to the characteristic skin manifestations. Recognizing UV is crucial due to its potential link with systemic disease. UV is classified into hypocomplementemic (HUV) and normocomplementemic (NUV) types. HUV, a rare systemic vasculitis, is characterized by urticarial skin lesions accompanied by systemic symptoms such as arthritis or arthralgia, glomerulonephritis, uveitis, recurrent abdominal pain, and chronic obstructive pulmonary disease. In contrast, NUV is a form of vasculitis confined to the skin.<sup>1,2</sup> UV may be associated to autoimmune connective tissue diseases, infections, drugs or neoplasia, although most of the cases are idiopathic.<sup>3,4</sup> There is considerable clinical overlap between the rare condition UV and the more prevalent Chronic Spontaneous Urticaria (CSU). The two conditions can be morphologically indistinguishable, frequently presenting a considerable diagnostic dilemma for physicians.<sup>5</sup> Diagnosis typically relies on clinical evaluation and may be confirmed through skin biopsy, which reveals histopathological features consistent with vasculitis, such as perivascular infiltrates and fibrin deposits.<sup>6</sup> The worldwide prevalence of UV is unknown. In the US population the incidence of UV was found to be 0.5 per 100,000 person-years.<sup>7</sup>

The condition can be challenging to treat, with standard antihistamines often proving ineffective. Current treatment options include systemic corticosteroids, immunosuppressants, and biologics such as omalizumab, which has shown promise in managing chronic spontaneous urticaria and may also benefit patients with urticarial vasculitis.<sup>8</sup>



## Case Presentation

A 61-year-old female patient presented to the outpatient clinic with complaints of widespread urticaria associated with pruritus persisting for over four months. Upon examination, the patient exhibited urticarial lesions over the entire body, particularly notable on the lower extremities, with some lesions merging into larger plaques. The patient was diagnosed with urticarial vasculitis. Comprehensive laboratory investigations were conducted, including complete blood count, liver function tests, renal function tests, antinuclear antibody (ANA) test, all of which returned within normal results. Fluid Immunology: Immunoglobulin G: 10.3g/L, Immunoglobulin A: 2.23g/L, Immunoglobulin M: 0.54g/L, Complement C3: 0.98g/L, Complement C4: 0.35g/L, Immunoglobulin E: 40.2IU/mL. Erythrocyte sedimentation rate: 36mm/h. C-reactive protein: 2.3mg/L. Initially, the patient was treated with intravenous dexamethasone phosphate at a dose of 10 mg, along with oral ebastine and desloratadine for one week. However, this treatment was ineffective, and the patient continued to experience recurrent episodes (Figure 1). Subsequently, dexamethasone phosphate was discontinued. The patient was started on an injection of omalizumab at a dose of 300 mg subcutaneously every 28 days, in conjunction with oral cyclosporine at a dosage of 3 mg/kg/day. After five days of the aforementioned treatment (Figure 2), the patient showed significant clinical improvement. The patient continues to receive omalizumab injections every 28 days and has reduced the oral cyclosporine dosage to 25 mg once daily. Notably, the patient has not experienced any recurrence of the rash.

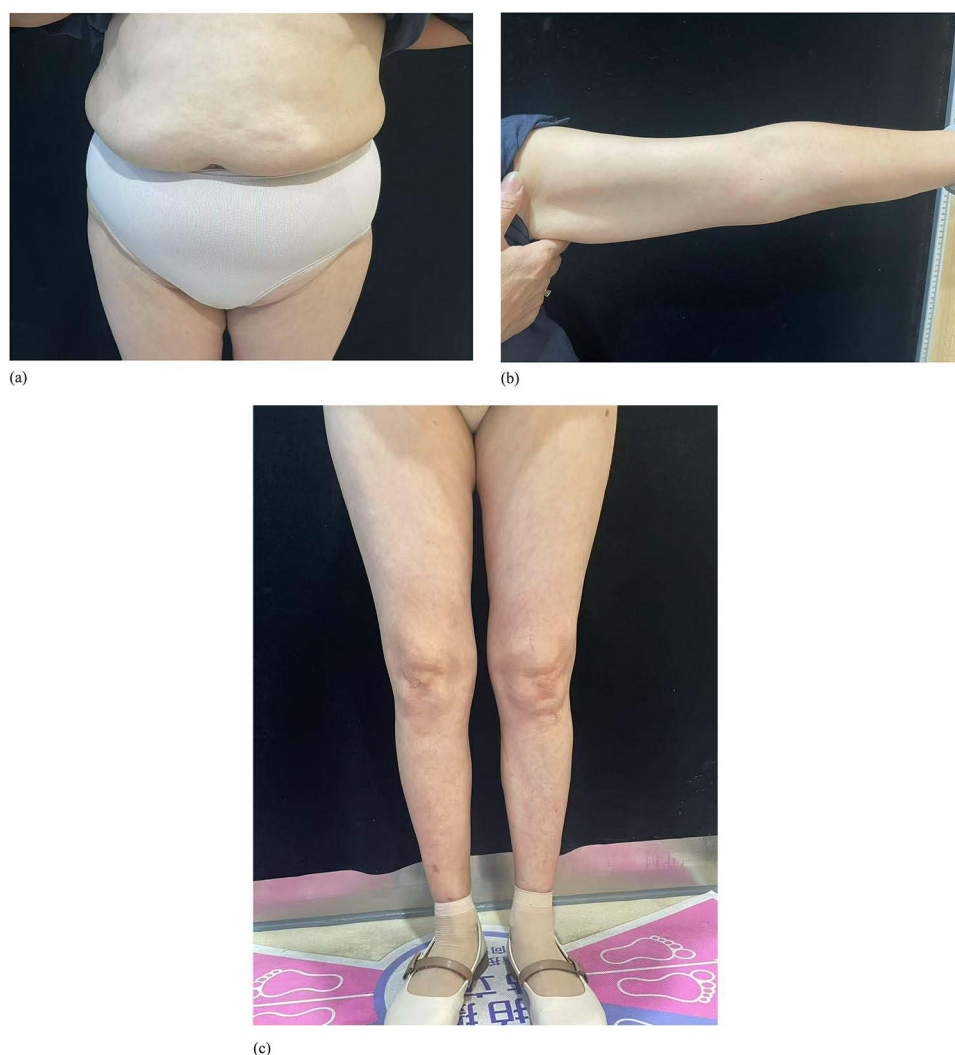
## Discussion

This case is significant as it highlights the complexities involved in treating urticarial vasculitis, particularly for patients who do not respond well to treatment with high doses of glucocorticoids.

Omalizumab can be effective for the treatment of skin symptoms of UV, and addition of immunomodulatory or immunosuppressive agents allows corticosteroid tapering and improves the efficacy of therapy.<sup>9</sup> For cases of UV that are ineffective with glucocorticoid treatment, first-line immunosuppressants such as azathioprine, cyclophosphamide, cyclosporine A, or mycophenolate mofetil can be considered.



**Figure 1** Physical examination of the patient (Before treatment). (a) Buttocks, (b) Lower limbs, (c) Upper limbs.



**Figure 2** Physical examination of the patient (After treatment). (a) Abdomen and Lower limbs, (b) Upper limbs, (c) Lower limbs.

In cases that do not respond to glucocorticoid therapy, first-line immunosuppressive agents including azathioprine, cyclophosphamide, cyclosporine A, or mycophenolate mofetil may be considered.<sup>10–12</sup> Omalizumab is currently a mature treatment option for chronic spontaneous urticaria. Studies have shown that the response rate for patients with urticarial vasculitis treated with omalizumab can reach 73%.<sup>13</sup> Omalizumab seems to be particularly effective in treating normal complement patients, but its effect on treating low-complement urticarial vasculitis is not obvious.<sup>14</sup> There are also documented cases of the successful use of this drug in combination with methotrexate.<sup>15</sup> The initial treatment with dexamethasone and antihistamines, including ebastine and desloratadine, proved ineffective after one week, leading to the decision to switch to a more aggressive therapeutic approach. Based on the efficacy and safety of omalizumab, as well as the absence of relevant contraindications for patients to cyclosporine, we chose to use omalizumab in combination with cyclosporine for treatment. Following the administration of omalizumab and cyclosporine, the patient's condition improved significantly within just five days, underscoring the rapid therapeutic effects of these agents. This result emphasizes the need for timely intervention in cases of urticarial vasculitis where initial treatments fail. The patient's ongoing management with regular subcutaneous injections of omalizumab every 28 days, along with a tapered dose of cyclosporine, suggests a proactive strategy to maintain symptom control and prevent recurrence, which is crucial in chronic conditions such as this.

## Conclusion

This case illustrates the challenges of managing urticarial vasculitis, particularly in older patients with complex presentations. It also reinforces the importance of exploring alternative therapeutic options, such as omalizumab combined with cyclosporine treatment, when initial therapies are ineffective.

## Ethics Approval

The publication of case report does not require ethical approval. We confirm that no institutional approval was required for publishing the case details.

## Consent for Publication

Informed consent was obtained for the publication of the case. This article adheres to the applicable CAse REport (CARE) guidelines.

## Informed Consent for Publication

The patient had signed informed consent and provided consent for the publication of the case details and any accompanying images.

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## Disclosure

The authors report no conflicts of interest in this work.

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