Alcohol-Associated Immunoglobulin A Vasculitis: A Case Report and Review of the Literature

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Keywords
Alcohol · Idiopathic · Leukocytoclastic vasculitis

Abstract
Immunoglobulin A (IgA)-mediated leukocytoclastic vasculitis is a cutaneous small-vessel vasculitis characterized by skin findings of palpable purpura. It may occur secondary to infections, neoplasms, drugs, and systemic conditions, although it is most commonly idiopathic. A known, but rare, trigger for IgA vasculitis is alcohol consumption. We present a case of a man with IgA vasculitis associated with alcohol use and review the literature on alcohol-associated vasculitis. Although rarely reported, alcohol-associated IgA vasculitis is an important entity to consider for appropriate diagnosis and management of such patients.

Introduction
Immunoglobulin A (IgA)-mediated leukocytoclastic vasculitis is a small-vessel leukocytoclastic vasculitis that can affect multiple organ systems, including the skin, gastrointestinal tract, and kidneys [1]. Formerly known as Henoch-Schoenlein purpura (HSP), IgA vasculitis occurs most commonly in the pediatric population with rare incidence in adults. The proposed etiology of IgA vasculitis is broad, and the mechanism of pathogenesis is not fully understood. It is often idiopathic but can be triggered by infection, drugs, and systemic disease [2].

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known, but rare, trigger for IgA vasculitis is alcohol consumption [3–5]. We describe the case of a 43-year-old man with recurrent IgA vasculitis following alcohol consumption and review the literature of alcohol-associated IgA vasculitis.

**Case Report**

A 43-year-old man presented to the clinic with episodic lower extremity rash of several years’ duration. Past medical history included diverticulitis and stasis dermatitis, and he was not taking any medications. He reported that the asymptomatic rash appeared on his thighs and legs every few months, hours to days following consumption of alcoholic beverages containing hops. He did not develop this rash when he drank non-hops alcoholic beverages. The rash spontaneously resolved within days, leaving residual dark spots. Associated symptoms included swelling of his ankles, knees, and scrotum. He denied any other systemic symptoms or hematuria. There were no other known triggering factors, including no recent viral-type illness or new medications or supplements.

On cutaneous examination, he had scattered 2–3-mm pink non-blanching macules and papules extending from his bilateral lower legs to the groin (Fig. 1). He had background hyperpigmented patches on the shins, characteristic of stasis dermatitis. On further questioning, the patient described more widespread involvement on the lower extremities and previously raised quality to flat lesions.

Given clinical suspicion for leukocytoclastic vasculitis, we performed a skin biopsy. Hematoxylin and eosin staining of the specimen revealed a superficial and deep perivascular neutrophilic infiltrate with leukocytoclasia, erythrocyte extravasation, and conspicuous eosinophils (Fig. 2). Although no significant fibrinoid necrosis of the vessel walls was identified, in conjunction with the direct immunofluorescence results that revealed vessel wall immunoreactivity for IgA, the findings were consistent with an IgA vasculitis.

Laboratory studies, including a urinalysis, anti-streptolysin O, viral hepatitis titers, complement levels, autoantibody screen, and rheumatoid factor levels, were all negative.

![Fig. 1](image1.jpg) **Palpable purpura in a patient with leukocytoclastic vasculitis.** Distant (a) and closer (b) views of a 43-year-old man with palpable purpura (red arrows) of the lower extremities associated with alcohol consumption. Hypopigmented patches characteristic of stasis dermatitis are also visible on the anterior shin. A 4-mm punch biopsy was performed at site of the blue arrow.
Triamcinolone cream provided little benefit, and the eruption was self-limited. At the 3-month follow-up, the patient reported several recurrences with alcohol use as well as a new-onset itch associated with the lesions. Because he presented to the clinic earlier on in the subsequent flare (with scrotal swelling and arthralgias), a 40-mg prednisone taper over 3 weeks was initiated with the plan to follow-up to the clinic as needed. No recurrences or complications were reported 6 months after his initial visit.

**Discussion/Conclusion**

IgA vasculitis, formerly known as HSP, refers to leukocytoclastic vasculitis mediated by the deposition of IgA immune complexes in vessels. Over 90% of cases occur in the pediatric population, and adult IgA vasculitis is rare. The annual incidence of IgA vasculitis is estimated at 0.8–1.8/100,000 in adults and 3–26.7/100,000 in children [6]. Among adults, idiopathic cutaneous small-vessel vasculitis and IgA vasculitis are the most common subtypes of leukocytoclastic vasculitis [7]. IgA vasculitis has been diagnosed in adults up to the age of 86 years [2]. Most studies have found a slight preponderance of males to females, both in children and adults [2, 6].
While multiple pathogenic mechanisms have been implicated in cutaneous vasculitis, the cause of IgA vasculitis remains unclear, though environmental and genetic risk determinants have been suggested [8, 9]. IgA vasculitis is most often idiopathic, though many triggers have been reported, including infections, neoplasms, inflammatory disorders, and certain drugs. In children, seasonal peaks, frequent occurrence following upper respiratory tract infection, and onset in index cases and in other family members all suggest a transmissible infectious process [6, 7]. Possible infectious triggers in adults include, but are not limited to, Streptococcus, Mycobacterium, hepatitis B and C, Staphylococcus aureus, Chlamydia, Neisseria, and HIV [10]. In adults, alcohol-associated IgA vasculitis is a known but rare trigger; the mechanism by which alcohol may induce purpura is unclear [3, 5]. Three other biopsy-confirmed cases of alcohol-associated vasculitis have been reported in the literature and are summarized in Table 1 [3–5]. A unique aspect of our case is that our patient’s alcohol-associated vasculitis seems to flare with a specific type of alcohol; namely, beers brewed with hops, flowers of the hop plant *Humulus lupulus* that add bitterness and floral or fruity flavors to beer.

Clinically, patients with IgA vasculitis present with palpable purpura located on the bilateral lower extremities. Symptoms may include tenderness, pain, and pruritus [7]. Two patients with alcohol-associated IgA vasculitis, including our patient, experienced symptomatic purpuric eruptions: tenderness and burning pain, respectively. The joints, gastrointestinal tract, kidneys, and occasionally other organs, can also be involved in IgA vasculitis [11]. Unlike the other cases of alcohol-associated IgA vasculitis, our patient was the only one to have extra-cutaneous manifestations; namely, scrotal edema and arthritis.

No definitive clinical criteria have been established to diagnose IgA vasculitis or HSP. The European League Against Rheumatism (EULAR) consensus criteria include palpable purpura with at least one of the following: diffuse abdominal pain, any biopsy showing IgA deposition, arthritis or arthralgias, or renal involvement (proteinuria or hematuria) [12]. However, vascular IgA deposition is non-specific for HSP diagnosis, and the utility of immunofluorescence studies for vasculitis is influenced by the clinical presentation and level of suspicion for HSP [13]. A skin biopsy within 24–48 h of the appearance of a new lesion is preferable [14]. Characteristic findings, as observed in our patient, include neutrophilic infiltration of the dermal small blood vessel walls associated with fibrinoid necrosis and disruption of the vessel wall, nuclear debris (leukocytoclasis), endothelial swelling, and extravasation of erythrocytes [7, 14].

Notably, many of the clinical features of IgA vasculitis and histopathologic findings of leukocytoclasis can be seen in other small-vessel vasculitides in adults. Evaluation for systemic lupus erythematosus or complement-mediated vasculitis, microscopic polyangiitis, urticarial
vasculitis, and ANCA-associated small vessel vasculitis may be warranted [8, 9, 14]. In the presence of arthralgias, type II cryoglobulinemia may also be considered in the clinical differential diagnosis. All previously reported cases of alcohol-related IgA vasculitis, with the exception of the 26-year-old woman, underwent comprehensive laboratory evaluation that was negative for underlying disease [3]. Additionally, other alcohol-associated dermatoses, including Schamberg’s disease (progressive pigmented purpura) and idiopathic thrombocytopenic purpura, may be worth consideration and further evaluation as warranted.

IgA vasculitis is often a self-limited disease, but a subset of patients experience a relapsing-remitting disease course. Renal involvement, which has greater incidence in adults, is the major long-term detrimental prognostic factor [1]. None of the previously reported cases of alcohol-associated vasculitis had evidence of renal involvement. Treatment of skin disease is primarily supportive. Antihistamines are often helpful for pruritus [9, 15]. Mid-potency topical corticosteroids, as prescribed to our patient, may also have some benefit, particularly for cutaneous ulcers or bullae [9]. Finally, when there is a known trigger, it is important to counsel patients on avoidance. All 4 patients with alcohol-associated IgA vasculitis did not experience recurrence after abstaining from alcohol [3–5]. Non-steroidal anti-inflammatory drugs (NSAIDs) can be used in patients with mild to moderate joint or abdominal pain [16].

For severe pain and failed response to NSAIDs, systemic steroids have been used. Oral prednisone 1–2 mg/kg/day or equivalent doses of intravenous methylprednisolone is recommended with slow taper to prevent relapse of symptoms [17]. Systemic steroids have also been used in cases of scrotal swelling and arthritis [18]. For patients who relapse after systemic steroids, case studies on steroid-sparing agents (such as colchicine or dapsone) have demonstrated improvement during treatment and recurrence upon discontinuation [19–21]. Doses of 50–150 mg/day of dapsone are typically utilized with improvement often noted as early as 1 week after initiation of therapy. Potential adverse effects, including hemolytic anemia, must be carefully monitored in patients receiving dapsone [19, 20]. Colchicine for leukocytoclastic vasculitis is usually started as a 0.6-mg dose twice daily, with initial response usually within 1–2 weeks [21]. Our patient was recommended avoidance initially given the resolution of extra-cutaneous symptoms prior to presentation. However, due to the patient’s dislike of the appearance of the rash, he was prescribed topical triamcinolone followed by oral prednisone (particularly given the scrotal swelling and arthralgias present at subsequent flare) without significant improvement of the purpuric eruption. Those patients with significant renal disease, gastrointestinal bleeding, mobility-limiting joint pain, or changes in mental status, should be managed through a multidisciplinary approach.

In conclusion, alcohol-associated IgA vasculitis is a rare but important entity for dermatologists and dermatopathologists to be aware of in order to ensure appropriate management, counseling, and prevention of recurrent episodes of disease. To our knowledge, ours is the only case of alcohol-associated vasculitis triggered specifically by hops and the first case reported with extra-cutaneous symptoms and use of specific therapeutic agents.

**Statement of Ethics**

All subjects have given written informed consent to publish this case (including publication of images).

**Disclosure Statement**

The authors have no conflicts of interest to declare.
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Author Contributions

Study design: P.B. and S.D. Drafting of the manuscript: P.B. and S.D. Critical revision of the manuscript for important intellectual content: R.M.N. and E.R.-G. Administrative or technical support: S.D. Study supervision: S.D.

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