SHORT COMMUNICATION

IgA Vasculitis Induced by Ustekinumab During Treatment for Crohn's Disease: A Case Report

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Submitted Jun 30, 2025. Accepted after revision Jul 25, 2025
Published Aug 13, 2025. DOI: 10.2340/actadv.v105.44276. Acta Derm Venereol 2025; 105: adv44276.

Immunoglobulin A (IgA) vasculitis has been frequently reported as a complication associated with anti-tumour necrosis factor (TNF)-α therapy in patients with Crohn's disease (1, 2). In contrast, to date, only a single case of IgA vasculitis associated with ustekinumab, an interleukin (IL)-12/23 inhibitor used in the treatment of Crohn's disease, has been reported (3). Herein, we describe one case of IgA vasculitis arising during ustekinumab therapy for Crohn's disease and review the previously reported cases.

CASE REPORT

A 53-year-old Japanese man was referred to our department with palpable purpura localised to the buttocks and legs, accompanied by pain in the ankle and elbow joints. These symptoms developed 5 months after the initiation of ustekinumab therapy for small intestinal Crohn's disease, which had been initiated by our department of gastroenterology. The patient had no other medical treatment. Physical examination revealed multiple purpuric lesions on the buttocks and lower extremities (**Fig. 1**A). Laboratory investigations showed elevated levels of C-reactive protein (6.14 mg/dL), erythrocyte sedimentation rate (104 mm/h), and serum IgA (895 mg/dL), while factor XIII activity was reduced to 67%. Urinalysis was unremarkable.

Histopathological examination of the lesion demonstrated a perivascular neutrophilic infiltrate with leukocytoclastic vasculitis in the superficial dermis (Fig. 1B). Direct immunofluorescence (DIF) assay revealed IgA deposition within the walls of affected blood vessels in the dermis (Fig. 1C).

Based on the findings, a diagnosis of IgA vasculitis induced by ustekinumab was established. The patient was treated with a 3-day course of Fibrogammin, followed by oral prednisolone initiated at 30 mg/day. The prednisolone dose was subsequently tapered in 5 mg increments and eventually discontinued.

DISCUSSION

IgA vasculitis is classically defined as a small-vessel vasculitis characterized by the deposition of IgA-containing immune complexes in capillaries, venules, and arterioles,

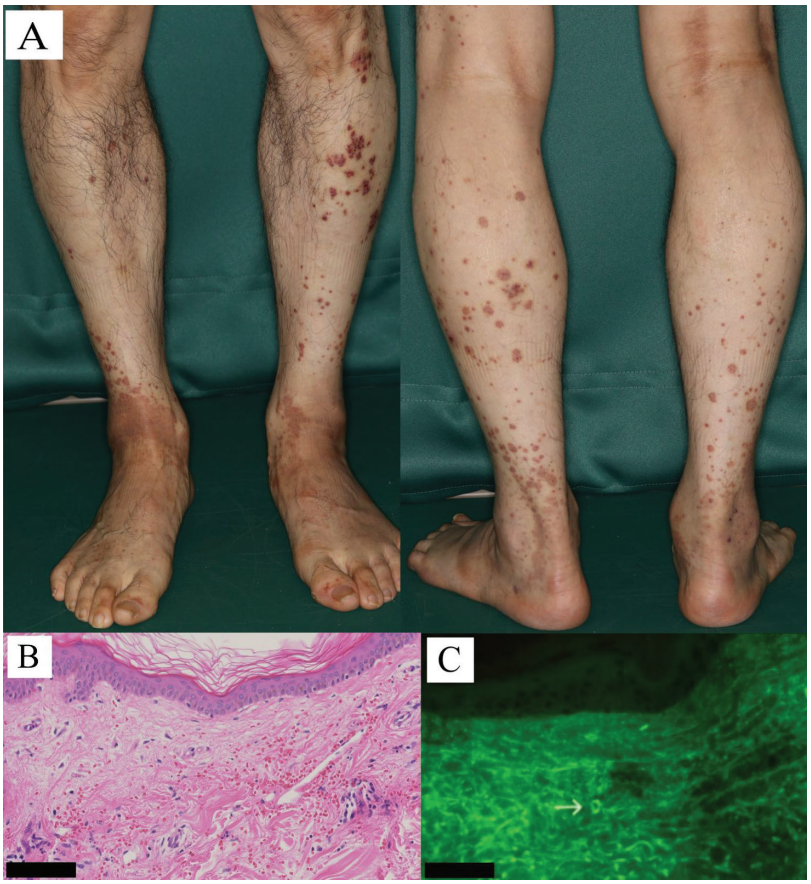

Fig. 1. (A) Numerous purpuric lesions were symmetrically observed on both buttocks, extending to the lower legs. (B) Histopathological examination of a purpuric lesion on the left thigh revealed perivascular infiltration of inflammatory cells, predominantly neutrophils, in the superficial dermis, accompanied by leukocytoclastic vasculitis (Scale bar: 100 μm; haematoxylin and eosin (H&E) stain). (C) Direct immunofluorescence assay demonstrated IgA deposition within the walls of blood vessels in the dermis (Scale bar: 50 μm).

Table I. Reported cases of leukocytoclastic vasculitis (LV) in Crohn's disease (CD) patients during ustekinumab (UST)

Year	Reference	Age/Sex	Diagnosis	Histopathologic examination	Duration from use of UST to the development of vasculitis	Therapy
2019	Costa-Moreira et al. (8)	28/F	LV	HE	3 years	Prednisolone
2020	Chugh et al. (9)	26/F	LV	HE	5 weeks	Colchicine
		29/F	LV	None	3 months	Prednisolone
	Buck et al. (6)	70/F	LV	HE	6 weeks	Increased doses of budesonide
2025	Aykut et al. (10)	20/F	LV	HE	3 weeks	Steroid
	Velasquez Ospina et al. (3)	40/F	IgA V	HE and DIF	3 weeks	Prednisolone
	Present case	53/M	IgA V	HE and DIF	5 months	Prednisolone

IgA V: IgA vasculitis; HE: haematoxylin and eosin staining; DIF: direct immunofluorescence.

leading to inflammation and tissue damage in multiple organs – most notably the skin, gastrointestinal tract, and joints. The onset of IgA vasculitis is frequently associated with triggers such as infections, medications, food allergies, and insect bites (4). A recent study employing Mendelian randomization analysis explored the potential association between inflammatory bowel disease (IBD) and either IgA vasculitis or immune thrombocytopenia (ITP). The findings suggested that Crohn's disease, a major subtype of IBD, may increase the risk of developing IgA vasculitis due to its genetic predisposition (2).

In the present case, no alternative trigger other than ustekinumab therapy was identified through the patient's medical history or clinical findings. Therefore, ustekinumab, an IL-12/23 inhibitor, was considered the most probable causative agent of IgA vasculitis.

To our knowledge, more than 100 cases of vasculitis associated with anti-tumour necrosis factor (TNF)-α agents have been reported to date (1). IgA vasculitis in patients with Crohn's disease induced by TNF-α antagonists was comprehensively reviewed by Yan et al. (5). According to their report, the median age at onset of IgA vasculitis was 20 years (11 of 16 cases; range: 16 to 69 years). The median duration from the initiation of anti-TNF-α therapy to the onset of IgA vasculitis was 18 months (8 of 16 cases; range: 2 weeks to 3 years). The male-to-female ratio was 1.75:1, with 7 males and 4 females.

Ustekinumab is a relatively new therapeutic agent (6), positioned as a safe and effective treatment for Crohn's disease (7). Including the present case, a total of 7 cases of leukocytoclastic vasculitis associated with ustekinumab therapy for Crohn's disease have been documented in the literature to date (3, 6, 8–10) (**Table I**). Among these, only 2 were specifically diagnosed as IgA vasculitis. In these cases, the median age of the patients was 29 years (range: 20 to 70 years). Vasculitis developed at a median of 6 weeks following initiation of ustekinumab (range: 36 days to 3 years). The male-to-female ratio was 1:6 (1 male and 6 females), indicating a predominance of female patients. When compared with TNF-α-induced vasculitis (5), there was no significant difference in the age of onset or age range. However, the interval between the initiation of ustekinumab and the onset of vasculitis appears to be shorter than that observed with anti-TNF-α therapy.

The mechanisms underlying the development of IgA vasculitis during treatment with biological agents, including anti-TNF-α agents and ustekinumab, remain to be elucidated. Several hypotheses have been proposed, including the possibility that antibody therapy may induce a shift from a Th1-dominant to a Th2-dominant immune response (1). At present, no clear distinctions can be drawn between ustekinumab and anti-TNF-α agents in this regard. In the present case, it is likely that the underlying Crohn's disease contributed to increased susceptibility to IgA vasculitis during ustekinumab therapy.

In conclusion, clinicians should be aware of the potential risk of IgA vasculitis associated with the use of biologics in the management of inflammatory bowel disease.

The authors have no conflict of interest to declare.

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