CLINICAL IMAGE

Crohn disease complicated by IgA vasculitis during therapy with tumor necrosis factor-α inhibitor

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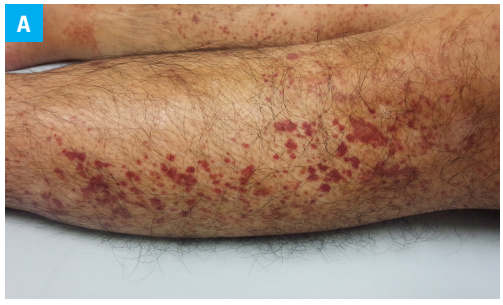
A 50-year-old man with a 26-year history of ileocolonic Crohn disease (CD) presented with purpura and ankle joint pain. He had been treated with the maintenance dose (40 mg) of self-injected adalimumab (tumor necrosis factor-α [TNF-α] inhibitor) fortnightly for 3 years. This treatment had been well tolerated, resulting in a favorable remission. Physical examination revealed stable vital signs and palpable purpura on both legs (FIGURE 1A), along with ankle joint edema. Complete blood cell counts showed white blood cell count of 8000/mm^3, hemoglobin level of 11.2 g/dl, and platelet count of 247 000/mm^3. Biochemical tests showed elevated levels of C-reactive protein (1.92 mg/dl; reference range, <0.14 mg/dl), erythrocyte sedimentation rate (104 mm/h; reference range, 2–10 mm/h), creatinine (1.17 mg/dl; reference range, 0.65–1.07 mg/dl), immunoglobulin A (IgA) (1636 mg/dl; reference range, 93–393 mg/dl), and D-dimer (28.5 μg/ml; reference range, <1 μg/ml). Tests for antinuclear antibodies and antineutrophil cytoplasmic antibodyies were negative. Urinalysis revealed proteinuria and microscopic hematuria. A biopsy of the purpura disclosed leukocytoclastic vasculitis of the dermis, consistent with IgA vasculitis (formerly Henoch–Schönlein purpura) (FIGURE 1B and 1C). Crohn disease complicated by IgA vasculitis was then diagnosed. A renal biopsy was performed, which showed mesangial proliferative glomerulonephritis (FIGURE 1D). Immunofluorescent staining reveled mesangial deposition of IgA and complement component 3, further confirming IgA vasculitis with nephritis. Adalimumab was discontinued and intravenous pulse methylprednisolone, 1 g/d, was administrated for 3 days, followed by oral prednisolone, 30 mg. IgA vasculitis–related manifestations resolved and



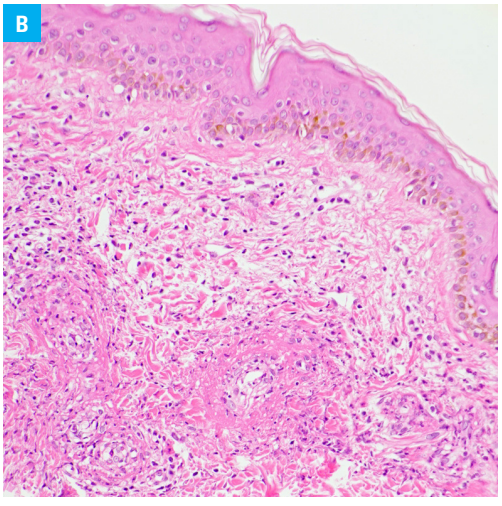


FIGURE 1 **A** – palpable purpura on both legs; **B** – biopsy of the purpura revealing leukocytoclastic vasculitis of the dermis (hematoxylin and eosin staining, magnification ×20)

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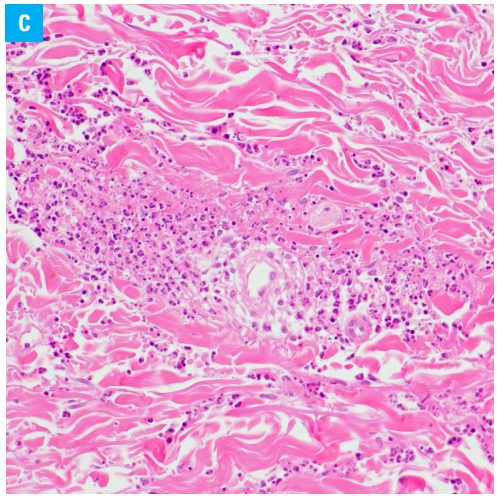
Received: January 14, 2019.
Revision accepted: January 31, 2019.
Published online: February 8, 2019.
Pol Arch Intern Med. 2019;
129 (4): 283-284
doi:10.20452/pamw.4435



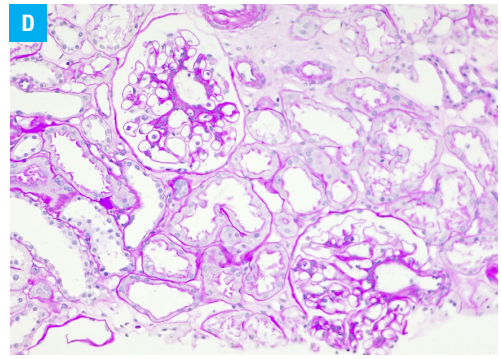


FIGURE 1 **C** – a high-power view showing perivascular neutrophilic infiltrate with nuclear dust and focal fibrinoid necrosis (hematoxylin and eosin staining, magnification ×40); **D** – renal biopsy showing mesangial focal proliferative glomerulonephritis (periodic acid–Schiff staining, magnification ×40)

prednisolone was tapered. Two years later, another TNF-α inhibitor, infliximab, was administered intravenously to treat CD-related diarrhea, with the informed consent. However, palpable purpura reappeared after a routine induction regimen with infliximab, 300 mg, at weeks 0, 2, and 6. Infliximab was then discontinued and the purpura resolved. The patient was treated conservatively with additional elemental diet therapy of Elental® (EA Pharma Co., Ltd., Tokyo, Japan], 1200 kcal/d).

Various types of vasculitis can occur as an extraintestinal manifestation of inflammatory bowel diseases (IBDs) including ulcerative colitis and CD. A large case series reported that these vasculitides include large-vessel vasculitis, cutaneous vasculitis, and antineutrophil cytoplasmic antibody–associated vasculitides.[1] Although TNF-α inhibitors have been widely applied to IBD with dramatic clinical effectiveness, they can induce various adverse effects including vasculitis, thromboembolic events, lupus-like syndrome, and other autoimmune manifestations.[2] There have been several reports of IBD complicated by IgA vasculitis following therapy with TNF-α inhibitors, such as infliximab and adalimumab.[3-5] Although the mechanisms of this adverse effect remain unclear, several hypotheses have been suggested to explain this link: deposition of TNF-α inhibitor and TNF-α immune complexes in vessels, direct drug toxicity, autoantibody production, and a shift in T-cell responses from a type 1 helper T cell to a type 2 helper T cell profile.[2,4] A causal link between the drug and adverse effects usually seems to be speculated when a short period exists from the drug initiation to event onset; however, TNF-α inhibitor–related vasculitis can occur over 2 years after starting administration.[2,5] We should also be aware of the potential risk of vasculitis relapse induced by the rechallenge with a different TNF-α inhibitor, as in our patient. Careful monitoring for potential adverse effects is essential.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

HOW TO CITE Hokama A, Sonosaki T, Zamami R, et al. Crohn disease complicated by IgA vasculitis during therapy with tumor necrosis factor-α inhibitor. Pol Arch Intern Med. 2019; 129: 283-284. doi:10.20452/pamw.4435

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