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LETTER TO THE EDITOR

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A rare case of cutaneous vasculitis with diagnostic difficulty in coexistence of serum anti-PR3 antibody and in vivo IgA deposits in the skin

Dear Editor,

Granulomatosis with polyangiitis (GPA) represents a necrotizing granulomatous inflammation involving the upper and lower respiratory tract with necrotizing vasculitis at small- to medium-sized vessels.[1] GPA is also characterized by the presence of serum anti-neutrophil cytoplasmic antibodies (ANCAs), consisting of ANCA-associated vasculitis (AAV). In contrast, IgA vasculitis is an immune complex disease affecting small vessels in various organs, involving

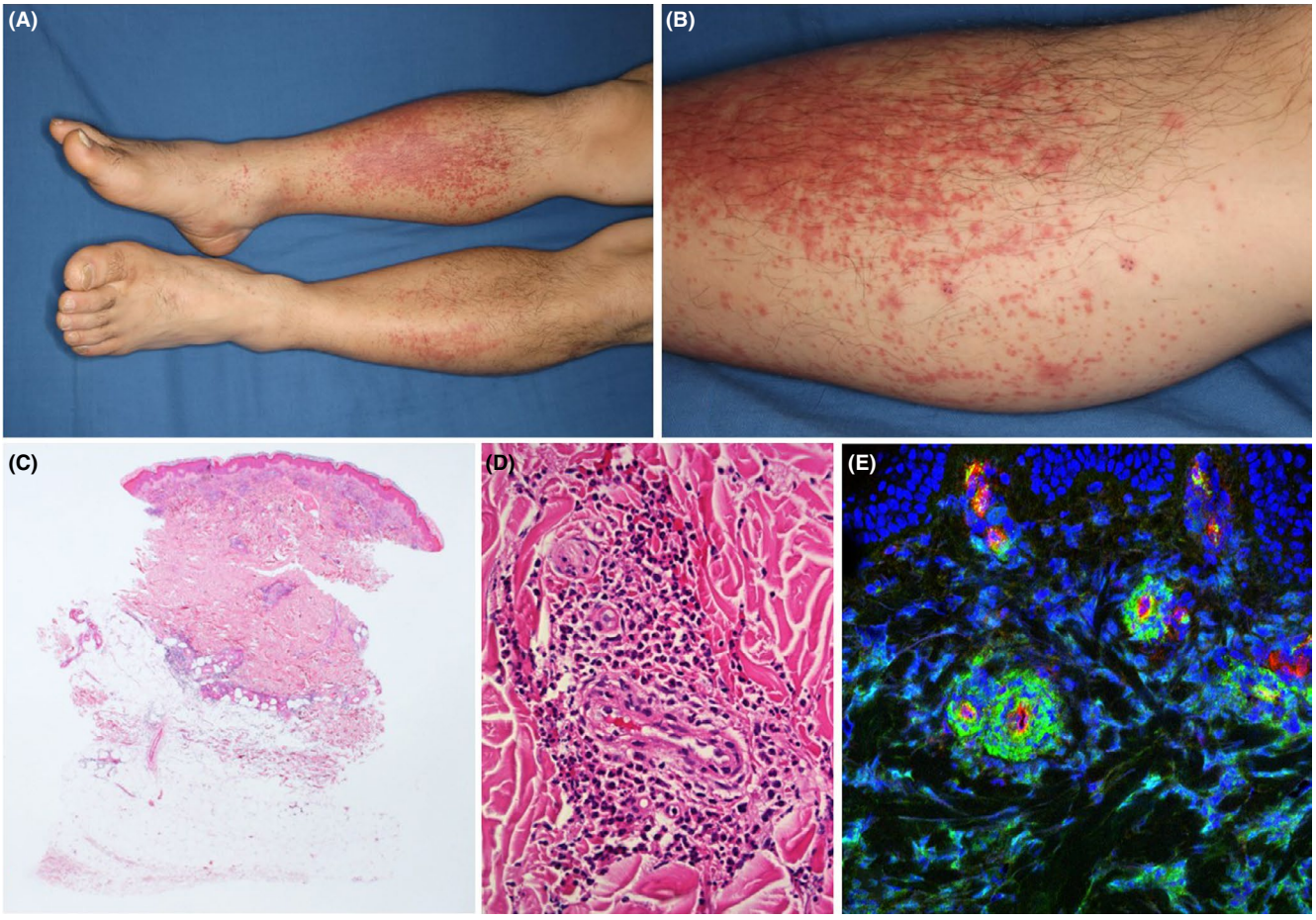

FIGURE 1 A, Multiple small-sized purpura distributed on the lower limbs. B, Palpable purpura and violaceous papules with a tendency of coalescence. C, A low power view of the whole skin section showing patchy, perivascular inflammatory infiltrates that predominate in the upper dermis (HE × 12.5). D, Histopathology showing leukocytoclastic vasculitis without granuloma formation in the upper dermis (HE × 200). E, Immunofluorescence staining of the lesional skin biopsy for CD31 (*red*) and IgA (*green*), counterstained with 4,6-diamidino-2-phenylindole (DAPI, *blue*) (×320)

the skin, gastrointestinal tract, kidneys, and arthritic joints.[1] Both disease phenotypes sometimes overlap and are difficult to discriminate. Here, we report an exemplified case of cutaneous vasculitis with simultaneous positivity for in vivo IgA immunofluorescence in the dermal small vessels and serum antiproteinase 3 (PR3) ANCA.

An otherwise healthy 40-year-old Japanese man presented with high-grade fever, arthralgia, and painful swelling with purpura in bilateral lower limbs 2 days ago. Examination showed multiple small-sized palpable purpura and violaceous, coalescent papules (Figure 1A,B). Histopathology of the lesional purpura showed leukocytoclastic vasculitis without granuloma formation throughout the dermis (Figure 1C,D). Direct immunofluorescence showed IgA deposits at blood vessel walls (Figure 1E). Abnormal laboratory data included an elevated serum PR3-ANCA (89.9 U/mL; ref. <3.5 U/mL). Serum cryoglobulins and renal function were within normal limits. Ophthalmologic examination revealed no abnormalities. Contrast-enhanced computed tomography (CT) detected no granulomas or organ involvements, except mild ethmoid sinusitis and pulmonary emphysema. He was initially diagnosed with IgA vasculitis with anti-PR3 ANCA and treated with oral prednisolone 40 mg/d (0.5 mg/kg/d). His fever and arthralgia were subsided, but the purpuric eruption rapidly spread to the trunk. Upon the ongoing oral steroid, a high-dose intravenous cyclophosphamide was added, and the skin lesions improved with concomitant decrease of serum PR3-ANCA titer. Thereafter, the daily dose of oral steroid was tapered to 5 mg/d during 1 year of follow-up, but his symptoms have never relapsed.

Our case poses a diagnostic dilemma in the coexistence of in vivo IgA deposit at the dermal blood vessels and seropositive anti-PR3 ANCA. Moreover, the serum antibody titer was consistent with the clinical course, supporting the provisional diagnosis of GPA rather than IgA vasculitis, albeit no detectable granulomas in any organs. An alternative diagnosis arises the possibility of IgA vasculitis with positive PR3-ANCA. However, there has been a documented case who primarily diagnosed with IgA vasculitis but later developed pulmonary hemorrhage with granuloma and required immunosuppressive therapy[2]. A careful follow-up is hence mandatory for life-threatening complications abruptly activated in GPA.

Antineutrophil cytoplasmic antibody-associated vasculitis has been considered as a pauci-immune condition that is unrelated to immune complex basis.[3] However, an updated case series implicates the possible overlapping of AAV and immune complex vasculitis, as seen in ANCA-associated glomerulonephritis with complement and/or immunoglobulin deposition in kidney.[4,5] The concept is strengthened by observation that the complement depletion completely blocked anti-MPO ANCA-induced crescentic glomerulonephritis in mice.[6] Alternative complement activation may, in part, coexist as the pathogenic modifier of AAV. Combining these with evidence that the tissue-bound complements and immunoglobulins are degraded by locally infiltrating leukocytes,[7] the disease stage-/tissue-dependent activation of immune complex system may aid interpretation of the complex pauci-immunity in AAV.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

INFORMED CONSENT

Obtained.

DECLARATION

Approval of the research protocol: No human participants were included.

Registry and the Registration No.: N/A.

Animal Studies: N/A.

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