Arthropod Bite and Churg-Strauss Syndrome

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To the Editor:

I read with great interest the article titled "Eosinophilic Granulomatosis With Polyangiitis Triggered by an Arthropod Bite and Complicated by Renal and Hepatic Infarction and Pulmonary Embolism: A Case Report" by Yu et al [1].

Eosinophilic granulomatosis with polyangiitis (EGPA), previously Churg-Strauss syndrome, is a rare antineutrophil cytoplasmic antibody (ANCA)–related vasculitis characterized by the triad of eosinophilia, asthma, and granulomatous/vasculitic involvement of several organs [2]. Yu et al [1] based their diagnosis on a cumulative score, as defined by the American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) in 2022 [1]. Although the diagnosis appears to meet the criteria for EGPA, the absence of key elements, such as asthma and findings of systemic vasculitis, casts doubt on the accuracy of the diagnosis. According to the 1990 ACR, Lanham, Grayson, 2012 Chapel Hill Consensus, and ACR/EULAR 2022 criteria, asthma is a sine qua non for EGPA [3].

EGPA is generally known to develop in 3 distinct phases [2]: the prodromic "allergic" phase, which may continue for a few years and is characterized by asthma; the eosinophilic phase with eosinophilia and end-organ involvement; and the vasculitic phase, which is characterized by clinical symptoms owing to small vessel vasculitis [2]. In the report by Yu et al [1], data on the history, laboratory tests, and medications used during the allergic phase (which lasted a very long time) were insufficient. In the usual clinical progression, many years may pass between the onset of pulmonary symptoms, persistent hypereosinophilia, and obvious vasculitis [3]. Although the time between the arthropod bite and the diagnosis of EGPA was not given, it seems that it was not as long as expected.

The biopsy taken from the necrotic lesion that developed after the bite revealed cutaneous eosinophilic vasculitis. Eosinophilic granulomatous infiltrates and ANCA-negative necrotizing vasculitic involvement in other involved end organs were not satisfactorily demonstrated [1]. A computed tomography scan of the chest showed a scattered shadow in both lungs, probably due to embolism, whereas patchy bilateral infiltrates would be expected. In Supplementary Figure 2, eosinophilic panniculitis, which is considered a sign of arthropod-related systemic vasculitis (extravascular eosinophil-predominant inflammation), may be a reaction to an arthropod bite that developed locally at that time and place [4].

Tissue eosinophilia in the form of an avascular, perivascular, or interstitial dermal pattern is a common finding in the skin lesions of EGPA, with or without vasculitis [2]. The eosinophilia and skin tissue inflammation in this case could be a reaction to the arthropod bite rather than systemic EGPA. Necrotizing eosinophilic vasculitis, as revealed by biopsy in this case, has been reported in other arthropod reactions, such as those induced by bites from bedbugs and *Candidatus Neoehrlichia mikurensis* [5,6]. Transient eosinophilic reactions (eg, drug-induced reactions and viral/bacterial/parasitic infection–induced reactions) occur as small-vessel localized cutaneous vasculitis that usually follows a short course without systemic involvement, eg, a single episode of purpura of the lower extremities [3].

ANCA, generally against myeloperoxidase (MPO), are detected in ~40% of EGPA cases. Vasculitic features such as glomerulonephritis, peripheral neuropathy, and purpura are more common in ANCA-positive cases, whereas in the case reported by Yu et al [1], hematuria and purpura were present, despite negative ANCA values. In addition, while I am not sure what exactly is meant by normal ANCA in the article [1], I understand it to be negative. Eosinophilic manifestations such as cardiac involvement and gastroenteritis have been reported to be more common in ANCA-negative patients, although these were not thoroughly investigated in the case reported. Again, some issues remain to be clarified, for example, why infarctions and embolisms developed and whether they were related to a coagulation system disorder rather than vasculitis [7]. In addition, first-line tests (pulmonary function tests, echocardiography, abdominal ultrasonography, urinalysis, 24-hour proteinuria, urine protein-creatinine ratio, and fecal occult blood) and second-line tests (troponin, lactate dehydrogenase, tryptase, vitamin B12, B-type natruretic peptide, antiphospholipid antibodies) should be performed to determine other end-organ involvement [2].

The differential diagnosis is with small-vessel vasculitides and eosinophilic diseases. If extrapulmonary organ involvement with eosinophilia is present, as in the case reported, idiopathic hypereosinophilic syndrome (HES) and IgG4-related disorder can be important differential diagnoses [3]. The presence of necrotizing vasculitis, akin to other ANCA-related vasculitides, is both characteristic of EGPA and differential between HES

and EGPA. Specific disease features, such as asthma, nasal polyps, glomerulonephritis, and mononeuritis multiplex, are more representative of EGPA than HES [3]. Although there were imaging and biopsy findings of eosinophilic cutaneous vasculitis in the case report [1], systemic vasculitis and related organ involvement could not be adequately demonstrated. Eosinophilic vasculitis may be a primary/idiopathic process or secondary to a systemic disease, for example, connective tissue/inflammatory bowel disease, infectious or drug-induced vasculitis, and parasitic infestations. Differentiating these disorders from EGPA can be challenging, especially in patients with no evident presentations of vasculitis and positive ANCA values for whom histopathologic examination and/or serum IgG4 levels are missing [8].

As a minor concern, the ANCA status was stated to be negative, although it was not stated whether the antibody was c-ANCA or p-(MPO)-ANCA. Different allergens and environmental factors (drugs such as warfarin, montelukast, and high-dose inhaled corticosteroids) have been blamed for the etiology of EGPA [9]. Similarly, it was not stated whether the patient received montelukast or the topical and/or inhaled corticosteroid treatment required in EGPA patients [1]. To investigate possible etiologies other than arthropods, the patient should also have been screened for additional parasites (*Toxocara canis*) and viral (HIV) infection. The patient's occupation was not mentioned, as environmental factors such as exposure to smoke, silica, organic solvents, and farming have been related to an augmented risk of EGPA. Moreover, the etiology of thrombocytopenia (30×10^9/L) was not discussed [1]. Thrombocytopenia is not a finding of EGPA and should raise doubts about malignancy (eg, chronic eosinophilic leukemia). The findings in the case report (ie, organ infarcts and embolism) should have enabled the authors to rule out imitations of vasculitis (pseudovasculitis), such as antiphospholipid antibody syndrome, purpura fulminans, warfarin necrosis, cholesterol embolization, infective endocarditis, and thrombotic thrombocytopenic purpura [10].

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Conflicts of Interest

The author declares that he has no conflicts of interest.

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