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Single Case

Bullous Vasculitis in Eosinophilic Granulomatosis with Polyangiitis: A Case Report

Tiraporn Phumwiriya Charussri Leeyaphan

Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Keywords
Eosinophilic granulomatosis with polyangiitis · Anti-neutrophil cytoplasmic antibody-associated vasculitis · Eosinophilia · Bullous vasculitis

Abstract
Introduction: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic vasculitis affecting small- and medium-sized vessels. It is characterized by multiorgan involvement and can lead to severe outcomes if not diagnosed promptly. Cutaneous manifestations are common and typically include palpable purpura and subcutaneous nodules. Widespread bullous vasculitis affecting areas such as the forehead and ear presents an atypical presentation. We report a case of EGPA presenting with bullous vasculitis in an unusual location. ***Case Presentation:*** A 40-year-old woman with a history of late-onset allergic rhinitis presented with a 2-week history of numbness in her right leg, along with multiple erythematous papules and vesicles, some with shallow erosions, located on the forehead and left ear. She also experienced fever, progressive dyspnea, and hemoptysis. She was diagnosed with pneumonitis, alveolar hemorrhage, and mononeuritis of the right leg. Laboratory findings revealed leukocytosis with eosinophilia, and the anti-myeloperoxidase antibody was positive. Histopathological examination of the bullous lesion on the forehead showed intraepidermal separation with necrotic keratinocytes and prominent eosinophil infiltration, along with focal leukocytoclastic vasculitis. The patient was diagnosed with EGPA and started on intravenous steroids and cyclophosphamide. EGPA is a rare disease characterized by multiorgan vasculitis, asthma, and granulomatous eosinophilic inflammation, which are its key hallmarks. While cutaneous involvement is common, bullous vasculitis is rarely observed on the forehead and ear. ***Conclusions:*** EGPA is a challenging diagnosis due to its variable presentation. While cutaneous manifestations are common, widespread bullous vasculitis may be atypical and rare clinical presentation. This case underscores the importance of considering EGPA in the

Correspondence to:
Charussri Leeyaphan, Charussrilee@gmail.com

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differential diagnosis of bullous vasculitis, particularly when associated with systemic symptoms and eosinophilia. Early recognition and treatment are crucial for improving outcomes in this potentially life-threatening condition.

Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare anti-neutrophil cytoplasmic antibody (ANCA)-associated systemic vasculitis that affects small- and medium-sized vessels [1, 2]. Characterized by eosinophilia, granulomatous inflammation, and multiorgan involvement, EGPA can present with a wide range of symptoms, often involving the respiratory tract, cardiovascular system, gastrointestinal (GI) tract, kidneys, and necrotizing vasculitis [3, 4]. Cutaneous manifestations are seen in 40–52% of patients and typically include palpable purpura, subcutaneous nodules, livedo reticularis, vesicles, pustules, urticarial plaques, necrotic ulcers, and erythema multiforme-like lesions [1, 2, 5]. Bullous vasculitis, particularly on the forehead and ear, is an unusual presentation [6, 7]. We describe a case of an adult female presenting with bullous vasculitis on the forehead and ear who was diagnosed with EGPA.

Case Presentation

A 40-year-old female patient with a history of late-onset allergic rhinitis was referred from a private hospital to Siriraj Hospital, Bangkok, Thailand. She presented with a 2-week history of numbness in the right leg, progressively worsening dyspnea, and multiple crops of erythematous papules and vesiculobullous lesions that subsequently ruptured, becoming shallow and ulcerated areas on the forehead and left ear. She had been treated with diclofenac and antihistamines, but there was no improvement. Afterward, she developed fever, worsening dyspnea, and hemoptysis. She was admitted to the intensive care unit due to hypoxic respiratory failure and was diagnosed with pneumonitis with alveolar hemorrhage. She denied any underlying diseases and was not taking any current medications. She had no history of smoking or alcohol use.

Physical examination revealed a chronically ill-looking middle-aged woman who was pale and febrile. Bilateral chest crackles were noted, and there was no pedal edema. Cutaneous examination revealed multiple erythematous papules and vesicles with some shallow erosions on an erythematous base located on the forehead and left ear (shown in Fig. 1a, b), as well as multiple well-defined, non-blanchable erythematous patches and papules on both palms and both lower legs. A neurological examination showed decreased pinprick sensation in the right foot, and motor power was grade V/V in all extremities. Examination of the GI and cardiovascular systems was unremarkable.

Laboratory results on admission were as follows: white blood cell count, 20.8 × 10^3/μL; neutrophils, 34.5%; eosinophils, 52.8%; absolute eosinophil count, 10.9 × 10^3/μL; hemoglobin, 10.5 g/dL; platelets, 281 × 10^3/μL; total protein, 6.8 g/dL; serum albumin, 3.6 g/dL; AST, 31 U/L; ALT, 41 U/L; ALP, 96 U/L; serum urea nitrogen, 7.4 mg/dL; serum creatinine, 0.5 mg/dL. Workup for infections, including blood and sputum cultures, was negative. Autoimmune serology demonstrated a positive anti-myeloperoxidase antibody and negative results for antinuclear antibody and anti-proteinase-3 antibody. The chest X-ray showed multifocal alveolar opacities in both the middle and lower lung zones. A CT scan of the chest performed at presentation revealed multifocal consolidations with surrounding ground-glass

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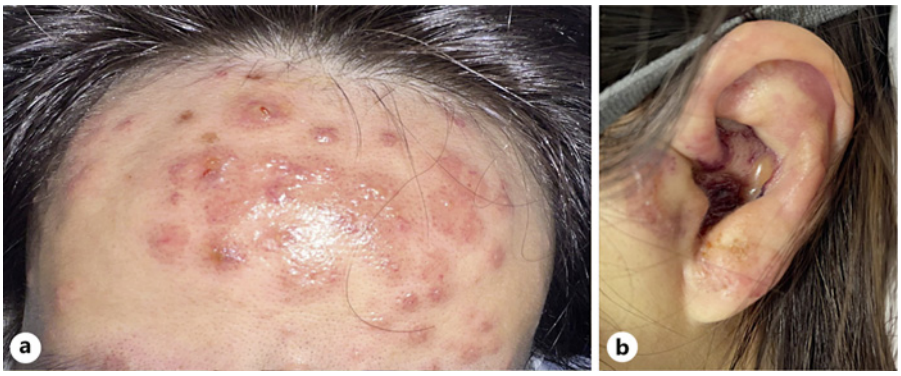

Fig. 1. Multiple erythematous papules and vesicles with some shallow erosions on erythematous base located on the forehead (**a**) and left ear (**b**).

opacities scattered in both lungs, suggestive of diffuse alveolar hemorrhage. Bronchoalveolar lavage was performed, revealing a white blood cell count of 3,500 cells/μL, with neutrophilia (3%), eosinophilia (67%), and numerous red blood cells. Transbronchial biopsy showed eosinophilic pneumonia and marked eosinophilic infiltrates in the bronchial wall tissue, but no vasculitis or granulomas were identified in the tissue sample. A skin biopsy of the forehead revealed intraepidermal separation accompanied by necrotic keratinocytes, with the presence of neutrophils and eosinophils within the vesicle, along with focal leukocytoclastic vasculitis. There was superficial and deep perivascular and interstitial infiltration, predominantly consisting of eosinophils and neutrophils (shown in Fig. 2a, b). Direct immunofluorescence (DIF) was negative. Electromyography showed evidence of multiple mononeuropathies.

The patient was diagnosed with EGPA based on a history of eosinophilic pneumonitis, pulmonary vasculitis, eosinophilic bullous vasculitis, mononeuropathies, eosinophilia, and positive anti-myeloperoxidase antibodies. She was treated with intravenous methylprednisolone 500 mg/day for 3 days and a single dose of intravenous cyclophosphamide 800 mg (0.52 g/m^2), followed by a switch to oral prednisolone 30 mg/day. The skin lesions gradually improved, developing post-inflammatory hyperpigmentation, and her oxygen requirements showed improvement. Subsequently, she was discharged on oral steroids with a plan to infuse cyclophosphamide once a month for induction of remission. Four months after diagnosis, the patient progressed to GI vasculitis with bowel ischemia, ileal perforation, and subsequent death from gram-negative bacilli septicemia.

Discussion

EGPA is a rare ANCA-associated cutaneous and systemic vasculitis. The cardinal features include asthma, pulmonary infiltration, eosinophilia, granulomatous eosinophilic inflammation, and necrotizing small- to medium-sized vasculitis [1, 2]. Diagnosis requires both clinical and histopathological findings to meet the diagnostic criteria [3, 8]. EGPA is described as having three phases: a prodromal allergic phase, an eosinophilic phase, and a vasculitis phase [3, 4]. Cutaneous manifestations are common, occurring in 40–52% of patients, and include palpable purpura, subcutaneous nodules, livedo reticularis/racemosa, vesicles, pustules, urticarial plaques, necrotic ulcers, and erythema multiforme-like lesions [1, 2, 5]. These lesions are frequently distributed bilaterally over the extensor surfaces of the lower extremities [6]. Bullous vasculitis is distinctive but not pathognomonic for EGPA and is uncommon on the forehead and ear [6, 7]. In addition, bullous vasculitis can indeed be a

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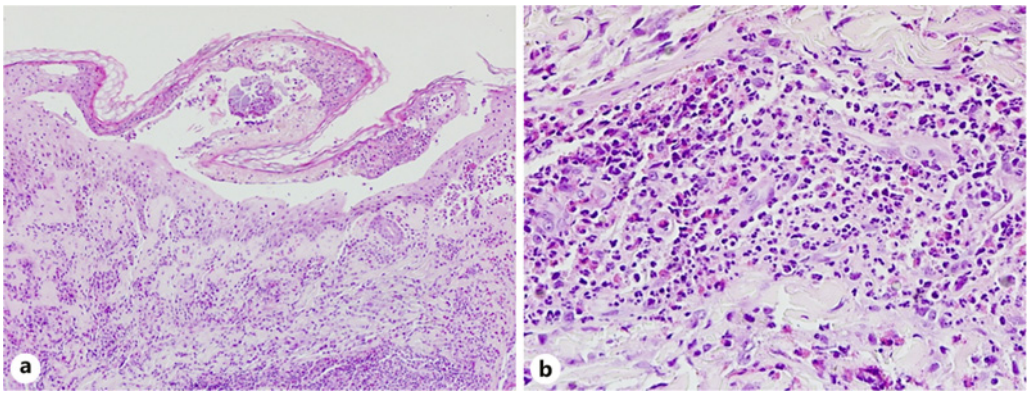

Fig. 2. Skin biopsy specimen showing intraepidermal separation accompanied by necrotic keratinocytes and presence of neutrophils and eosinophils within the vesicle (hematoxylin and eosin staining, original magnification, ×40) (**a**), superficial and deep perivascular and interstitial infiltration, predominantly consisting of eosinophils and neutrophils (original magnification, ×400) (**b**).

symptom of several different conditions, such as IgA vasculitis, other ANCA-associated vasculitis, and bullous systemic lupus erythematosus. It may be the first and only manifestation of the disease or part of a systemic condition. A typical initial evaluation includes a skin biopsy to confirm vasculitis. The biopsy results must be correlated with DIF data, medical history, physical examination, laboratory findings, and radiological findings to reach the correct diagnosis [9].

Extracutaneous involvement can affect many organs, such as the upper respiratory tract, pulmonary system, cardiac system, renal system, GI tract, central nervous system, and peripheral nervous system. Upper respiratory tract involvement may include paranasal sinusitis, nasal polyposis, allergic rhinosinusitis, and epistaxis. Pulmonary involvement includes asthma, pulmonary nodules, pleural effusion, and alveolar hemorrhage. Asthma in EGPA is a critical and prevalent feature, often presenting severely and preceding other systemic manifestations [1, 10]. Peripheral neuropathy and CNS involvement are significant aspects of EGPA, affecting a substantial proportion of patients. Mononeuritis multiplex is a common presentation of peripheral neuropathy, often involving the common peroneal, tibial, ulnar, and median nerves. Nerve conduction studies are essential diagnostic tools for evaluating and assessing peripheral nerve damage [11, 12]. Cardiac manifestations, which affect 20–50% of patients, can be severe and are associated with significant morbidity and mortality. Cardiac conditions include myocarditis, pericarditis, endocarditis, valvulitis, and coronary vasculitis. Comprehensive evaluation using troponin levels, ECG, echocardiography, and cardiac MRI is essential for early detection and management [5, 10]. Renal involvement, particularly necrotizing crescentic glomerulonephritis, is a serious complication that requires close monitoring and management. Regular assessment of kidney function and early treatment with immunosuppressive therapies are essential to prevent progression of renal disease and improve patient outcomes [10, 11]. GI involvement can lead to significant discomfort and serious complications, including mucosal ulceration, rectal bleeding, bowel obstruction, and perforation. Symptoms may occur before or during the vasculitis phase and require careful management with both medical and surgical approaches [11]. In most cases of EGPA, ANCA is directed against MPO rather than PR3. ANCA-positive patients, who make up 40–60% of cases, are more likely to have cutaneous vasculitis, glomerulonephritis, and peripheral neuropathy, while ANCA-negative patients may present more frequently with cardiac involvement and gastroenteritis [3]. Other laboratory findings include peripheral eosinophilia and elevated IgE and IgG4 levels [1–3]. Histopathological features reveal granulomatous eosinophilic inflammation, leukocytoclastic vasculitis

with fibrinoid necrosis, primarily involving venules. DIF is seen in 50% of cases, showing IgM and/or C3 deposits around dermal small vessels [1, 13].

Management of EGPA is determined based on disease severity and the extent of organ involvement. While no specific treatment exists for cutaneous manifestations alone, effective management of systemic disease can lead to improvement in skin lesions. For the induction of remission in new-onset organ-threatening or life-threatening disease, a combination of glucocorticoids and either cyclophosphamide or rituximab is recommended. Life-threatening conditions may require plasma exchange. For non-organ-threatening conditions, a combination of glucocorticoids and either methotrexate or mycophenolate mofetil can be used. Maintenance therapy includes low-dose glucocorticoids combined with azathioprine, rituximab, methotrexate, or mycophenolate mofetil, depending on the patient's response and tolerability. Continuous monitoring and individualized treatment adjustments are essential to optimize outcomes and manage potential side effects [3, 14, 15].

In addition, EGPA patients with GI involvement present with a distinct clinical profile, characterized by more severe disease activity, higher disease activity scores, and poorer prognostic indicators. These patients tend to have worse long-term outcomes, including lower survival rates, lower remission rates, and higher relapse rates. These findings underscore the critical importance of early detection, careful management, and individualized treatment approaches, particularly for those with GI manifestations [16]. Diagnosing EGPA can be difficult because of its diverse clinical presentation. Although skin involvement is frequent, widespread bullous vasculitis affecting areas such as the forehead and ear is an uncommon and atypical manifestation. This case emphasizes the need to include EGPA in the differential diagnosis of bullous vasculitis, especially when accompanied by systemic symptoms and eosinophilia. Timely identification and intervention are essential for better outcomes in this potentially fatal condition.

The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000544815).

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Tiraporn Phumwiriya and Charussri Leeyaphan: contributions to the design of the work, validation, writing – original draft, and writing – review and editing.

Data Availability Statement

All data used in this article are included under the references section. Further inquiries can be directed to the corresponding author.

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