Case report

A fatal eosinophilic granulomatosis with polyangiitis case presenting intracerebral hemorrhage and thrombocytopenia

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We report the case of a patient with eosinophilic granulomatosis with polyangiitis and unexplained thrombocytopenia that culminated in a fatal intracerebral hemorrhage. Because vessel damage associated with thrombocytopenia could be the leading cause of fatal hemorrhage, more urgent treatment of thrombocytopenia should be performed in such cases. (J Allergy Clin Immunol Global 2023;2:100148.)

A 26-year-old male had a medical history of allergic rhinitis, unknown history of bronchial asthma, and no history of receiving coronavirus disease 2019 (COVID-19) vaccine. Three days before admission, the patient presented with generalized myalgia, especially in the lower limb muscle groups, arthralgia of the hips and knees, numbness, and quadriparesis. The numbness and weakness of his limbs increased gradually. He was admitted to the hospital in a normal state of consciousness, with muscle pain and a temperature ranging from 37.5°C to 38°C. He had asymmetric bilateral paresis. His numbness and sensory abnormalities were predominantly distal. He had normal bowel function. We detected thrombocytopenia with a platelet count of 127×10^9/L (Table I), and we ordered a wide range of diagnostic tests (Table II).

On the third day after admission, his symptoms tended to worsen. He had a rising temperature, reduced muscle power, more severe myalgia of the extremities, and arthralgia. He had a bronchospasm that was quickly relieved after use of a bronchodilator. Some purpura fulminans appeared on both of his legs. His platelet count was 32×10^9/L. Our initial diagnosis was possible systemic inflammatory disease. He was treated with methylprednisolone, 80 mg per day, beginning on day 3.

Abbreviations used
CNS: Central nervous system
EGPA: Eosinophilic granulomatosis with polyangiitis

His platelet count reached its lowest value (32×10^9/L) on day 3 and gradually increased in the following days (Table I). A platelet count less than 20×10^9/L has been proved to be indicative of a major risk of bleeding in immunologic diseases.[1] Because we did not find any appropriate causes of his thrombocytopenia, we delayed platelet transfusion and treatment for that condition.

A skin biopsy was ordered at the site of purpura fulminans on day 4. After the result (Fig 1) had been obtained, the patient was diagnosed as having eosinophilic granulomatosis with polyangiitis (EGPA) according to the 2022 diagnostic criteria[2]; and his Birmingham Vasculitis Activity Score (version 3)[3] indicated that the disease was in an active phase.

From day 4 to day 8, the patient's fever and myalgia improved and he was able to walk with a walker. On day 9, he suddenly fell into a coma. Brain computed tomography showed massive intracerebral hemorrhage in the left temporal lobe and extravasation of blood into the subarachnoid space and ventricles (Fig 2). He died on day 10 with a platelet count of 46×10^9/L.

DISCUSSION

EGPA or Churg-Strauss syndrome is a rare systemic necrotizing vasculitis that affects small- to medium-size vessels and involves the respiratory tract. It is usually associated with antineutrophil cytoplasmic autoantibodies.[2]

Peripheral nerve damage due to the disease is quite common, affecting 50% to 98% of patients, whereas central nervous system (CNS) involvement is rare, with an prevalence of only 4% to 17%.[4] The lesions predominantly present as cerebral infarction, reversible posterior circulation syndrome, spinal cord, or medulla involvement, and ischemic stroke is the most prevalent type. Intracerebral hemorrhage is extremely, rare with some isolated case reports; however, it is the leading cause of death due to CNS lesions in EGPA.[4]

The pathogenesis of hemorrhage is not fully understood.[4] In 1 research study, 26 patients in France and 62 patients in other countries were found to have lesions in the CNS.[5] Of those patients, 9 had intracerebral hemorrhage and 13 had intracranial

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The caregiver understood the purpose of the case report, the potential risks and benefits of publication, and any risks of harm or embarrassment that may result from the publication. The caregiver granted permission for the case report and accompanying visual elements to be published. We have written entirely original works, and the work and words of others have been appropriately cited.

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TABLE I. Thrombocytopenia status and results of tests to find causes

Test index		Result	Normal range
Platelet count ($\times 10^9$/L)	Day 1	127	140-350
	Day 3	32	
	Day 4	39	
	Day 5	39	
	Day 6	46	
	Day 7	46	
	Day 9 (after hemorrhage)	43	
Dengue virus status	Nonstructural protein 1 antigen (NS1Ag)	Negative	
	Dengue IgM	Negative	
	Dengue IgG	Positive	
Peripheral blood smear		No red blood cell fragments and percentage of reticulocyte < 1%	
Renal function	Urea level (mmol/L)	5.42	3.3-8.3
	Creatinine level (μmol/L)	48	62-106
D-Dimer level (ng/mL)		6572	<500
Thrombosis status	Abdominal ultrasound	Normal	
	Lower extremity arteriovenous ultrasound	Normal	
	Echocardiogram	Normal	
	Chest computed tomography scan	Normal	

TABLE II. Antibody serostatus and other test results

Test index		Result	Normal range
Thyroid function test	Free thyroxine level (pmol/L)	15.93	12-22
	Thyroid-stimulating hormone level (μIU/mL)	4.23	0.27-4.2
Viral infection status	Hepatitis B virus	Negative	
	Hepatitis C virus	Negative	
	HIV	Negative	
	Coronavirus PCR	Negative	
Cerebrospinal fluid analysis	Cell count (cells/mm^3)	2	< 5
	Protein level (g/L)	0.34	0.1-0.25
	Glucose level (mmol/L)	4.8	
	EBV, CMV, HSV, tuberculosis bacilli	Negative	
Antibody serostatus	Antiphospholipid antibodies (IgM, IgG)	Negative	
	Anticardiolipin antibodies (IgM, IgG)	Negative	
	Anti-beta-2 glycoprotein I antibodies (IgM, IgG)	Normal range	
	cANCA, pANCA	Negative	
	ANA anti-dsDNA	Negative	
Head computed tomography and angiography		Normal	
Nerve conduction studies	Polyneuropathy		

ANA, Antinuclear antibody; *c-ANCA*, cytoplasmic antineutrophil cytoplasmic antibody; *CMV*, cytomegalovirus; *dsDNA*, double-stranded DNA; *HSV*, herpes simplex virus; *p-ANCA*, perinuclear antineutrophil cytoplasmic antibody.

hemorrhage, mainly subarachnoid hemorrhage. There was only 1 case related to cerebral aneurysm and 1 case related to infarction, but no detailed information was provided. The study's authors suggested that vasculitis appeared to be the major cause of bleeding.[5] Another study indicated that almost all of the EGPA cases with intracerebral hemorrhage presented in the active phase of the disease with vasculitis.[6] Patients with EGPA also had general risk factors for primary or secondary intracranial hemorrhage such as vascular abnormalities, use of anticoagulants or antiplatelet agents for treatment or prevention of thrombosis, and hypertension after using fibrinolytic drugs or hemorrhagic transformation of intracerebral infarction.[6]

Our patient had a previous normal cerebral angiogram that excluded aneurysm or cerebral arteriovenous malformation. He did not use anticoagulation or antiplatelet agents before or during the admission. His coagulation function (Table III) and blood pressure were normal. Therefore, we ruled out those risk factors and suggest that vasculitis might be the cause of the hemorrhage.

Thrombocytopenia is not a symptom of EGPA, but it is mentioned in some isolated reports.[7] The causes may be related to thrombotic microangiopathies,[8] hemolytic uremic syndrome,[9] heparin-associated thrombocytopenia, or thrombosis.[7] Thrombocytopenia due to Dengue virus was ruled out in our patient despite his living in endemic areas. A peripheral blood smear showed no red blood cell fragments and a reticulocyte count less than 1% (Table I); therefore, thrombotic microangiopathies were excluded. Tests for ADAMST13 were not performed because of their unavailability in our country. A diagnosis of hemolytic-uremic syndrome was also deemed inappropriate because of the patient's normal renal function. He had not taken heparin before.

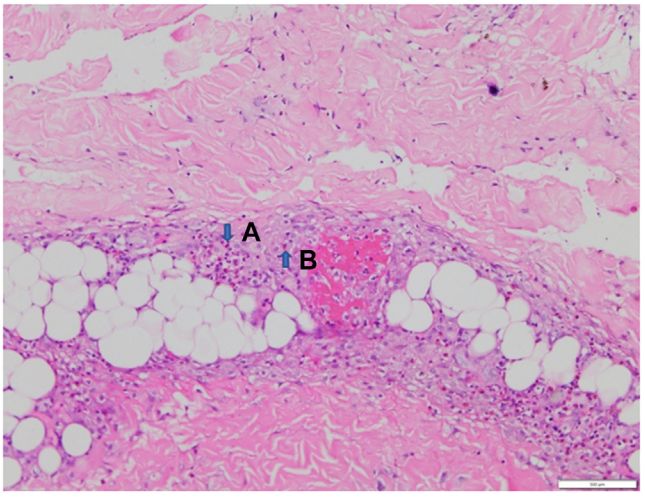

FIG 1. Biopsy specimen of purpura fulminans on the lower limb showed the eosinophilic infiltrates (**A**) and fibrinoid necrosis of vessel wall with eosinophilic infiltrates in the dermis and subcutaneous fat magnification (**B**). Hematoxylin and eosin staining; original magnification, ×20.

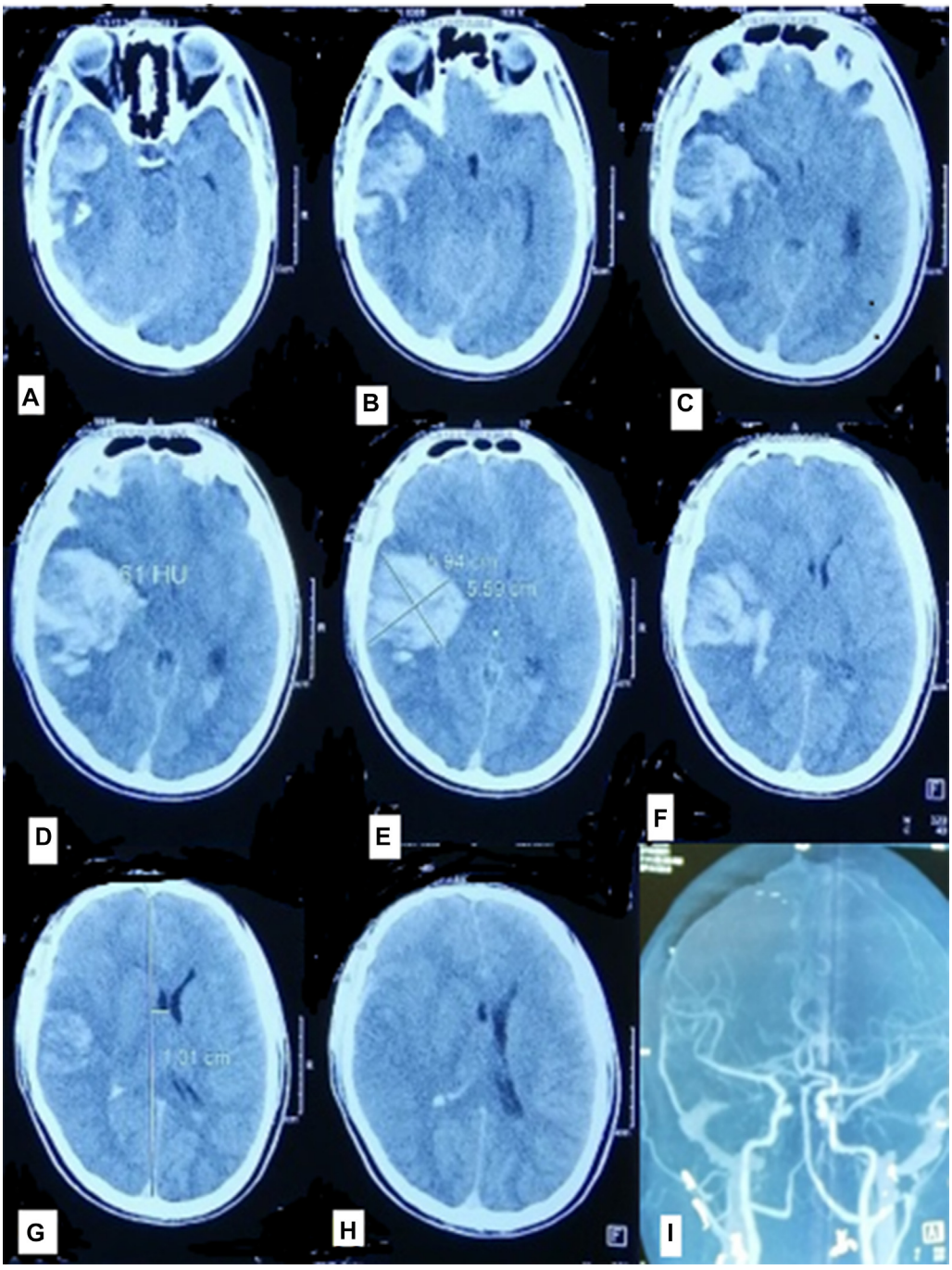

FIG 2. Brain computed tomography scan (**A-H**) showed massive intracerebral hemorrhage in the left temporal lobe and blood in the subarachnoid space and ventricles at day 9 and brain angiogram **(I)** showed no abnormalities at day 1.

Thrombocytopenia has also been reported in patients with EGPA with elevated D-dimer levels.[7] Our patient had an increased D-dimer index (Table I), but examination of his lower extremity vasculature did not reveal any abnormalities associated with venous thrombosis. No clinical symptoms of thrombosis in the hepatic vein, pulmonary artery, or cerebral venous sinus were recorded. Therefore, EGPA could have been the cause of the patient's thrombocytopenia.

The fatal intracerebral hemorrhage in our patient with EGPA suggested that there might be a relationship between intracranial hemorrhage and the condition of thrombocytopenia and vasculitis. Thrombocytopenia could be the major risk of bleeding in patients with vessel damage due to vasculitis. The vessel impairment could increase the risk of hemorrhage in patients with thrombocytopenia even though low platelet count (>20 $\times$ 10^9/L) has been proved to not be a major risk factor in bleeding.

TABLE III. Complete blood count and coagulation test results

Test index	Day 1-2	Day 3	Day 6	Day 9 (after hemorrhage)	Normal range
White blood cell count ($\times 10^9$/L)	10.28	10.6	14.5	22.6	4-10
Neutrophils (%)	61.4	74.8	64.2	86.5	40-74
Lymphocytes (%)	9.2	9.1	14.0	4.3	19-48
Eosinophils (%)	17.2	10.2	12.3	0.2	0-7
Red blood cell count (L)	5.18	5.1	4.73	4.93	4.2-6
Hemoglobin level (g/L)	127	160	147	150	130-170
Prothrombin time (s)		16.6		16.1	10-14
Prothrombin (%)		70		73	70-140
Fibrinogen level (g/L)		5.31		2.92	2-4

In addition, the low platelet count also hindered the emergency surgery to save our patient.

To our knowledge, our patient may be the first reported patient with EGPA accompanied by thrombocytopenia and fatal massive intracerebral hemorrhage. The causes and consequences of thrombocytopenia in EGPA require evaluation in further studies. Thrombocytopenia may be warning signs for early management of thrombocytopenia and could be considered as the risk factors of severe hemorrhage to guide the initial selection of therapy in patients with EGPA to reduce the severe hemorrhage.

DISCLOSURE STATEMENT

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