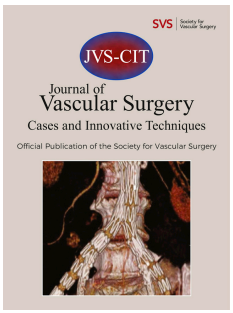

Acute aortoiliac thrombosis and mitral valve regurgitation as acute onset of Eosinophilic Granulomatosis with Polyangiitis (EGPA) in a 26-year-old patient

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TITLE PAGE

MANUSCRIPT TITLE

Acute aortoiliac thrombosis and mitral valve regurgitation as acute onset of Eosinophilic Granulomatosis with Polyangiitis (EGPA) in a 26-year-old patient

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KEYWORDS

Churg Strauss Syndrome, Mitral Valve Regurgitation, Acute Arterial Thrombosis

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The authors have no competing interests.

ABSTRACT

We present a rare case of Eosinophilic Granulomatosis with Polyangiitis (EGPA), involving a 26-year-old woman with a history of asthma and nasal polyps. The patient presented with acute aorto-iliac thrombosis and mitral insufficiency, successfully treated with thrombolysis, aortic thromboendarterectomy and valve replacement. Peripheral hypereosinophilia with eosinophilic infiltration of the heart led to the diagnosis of ANCA-negative EGPA. Treatment with prednisone and Mepolizumab was started, resulting in a positive outcome. This case showcases an unusual manifestation of EGPA with large sized vessel involvement, needing surgical and pharmacological treatment; it highlights the importance of early detection for timely intervention and improved prognosis.

MANUSCRIPT BODY

Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic small vessel vasculitis with a reported incidence ranging from 10.7 to 13 cases per million inhabitants in the general population. [1] [2]

We report a case of acute aortic thrombosis and subsequent acute mitral regurgitation in a patient whose clinical, laboratory and anatomopathological data led to the diagnosis of an atypical presentation of EGPA. The patient was successfully treated with superior mesenteric artery thrombolysis, aorto-iliac thromboendarterectomy, and mitral valve replacement. The patient has consented to the publication of this case report.

Case presentation

A 26-years-old woman was referred to our Emergency Department (ED) due to 8-hour increasing distal lower extremities rest pain , intermittent episodes of bilateral forefoot paresthesia and minimal sensory loss. Vital signs and body temperature were normal. She had a history of Graves' disease and nasal polyposis associated with bronchial asthma and turbinate hypertrophy. Furthermore, 3 months prior, she had been hospitalized for acute pericarditis and idiopathic pneumonia with non-fixed ground glass infiltrates.

On clinical examination the absence of peripheral pulses of both lower limbs was noticed. Duplex ultrasound (DUS) showed a bilateral monophasic post-stenotic doppler waveforms in the femoral district with no arterial flow below the knee and an ankle-brachial index of 0,8. Computer tomography angiography (CTA) demonstrated a complete thrombotic occlusion of the abdominal aorta extending from the inferior mesenteric artery (IMA) to the right common iliac artery (CIA) and the left external iliac artery (EIA). Complete thrombosis of the origin of the superior mesenteric artery (SMA) and partial sub-occlusive thrombosis of the right renal artery were also noticed, despite no sign of visceral and kidney injury. (Figure 1A) No specific periaortic or aortic wall signs of inflammation were noticed, but significant hypereosinophilia (4800 x109 cells/L) and mild neutrophilia (12.000 x109 cells/L) with elevated C-Reactive Protein (CRP) (35 mg/dL) were observed. A transthoracic echocardiography (TTE) demonstrated moderate

mitral valve insufficiency compatible with a rheumatic degeneration, associated with a mild aortic valve stenosis.

Based on clinical findings, patient young age and on the extension of the disease, a total endovascular percutaneous approach was considered appropriate. (Figure 1B)

An ultrasound-accelerated thrombolysis through the EkoSonic® Endovascular System (EKOS Corporation, Bothell, WA, USA) was attempted. Moreover, an overnight infusion of recombinant tissue plasminogen activator was initiated, along with systemic administration of 25.000 unfractionated sodium heparin units/24h.

The 24-hour control angiography showed partial aortic recanalization with significant residual stenosis of both the left EIA and the origin of the SMA. (Figure 1C, 1D) The partial thrombosis of the origin of the right renal artery appeared unmodified. Recanalization of the SMA was performed sequentially using thromboaspiration with the Penumbra Indigo system (Penumbra Inc., Alameda, CA, USA) and thrombectomy with an Embotrap (Cerenovus, Irvine, California, USA) 6.5x45mm stent retriever system. The final angiography showed persistent thrombosis of the origin of the SMA. No further endovascular treatments were deemed appropriate, and the patient was scheduled for surgical revascularization.

Aortic embolectomy was performed through a longitudinal infrarenal incision, . Given the absence of macroscopic signs of aortic wall degeneration or atherosclerosis, we opted for primary closure, albeit with a Teflon reinforcement strip, thus providing suture additional support and reducing bleeding. [3] [4] Direct AMS thrombectomy was also performed, and complete mesenteric and peripheral vessels revascularization was obtained. DUS examination of visceral and iliac arteries showed triphasic doppler waveforms following surgery. (Figure 2A) The postoperative course was uneventful, and the patient was discharged after 8 days.

However she was readmitted one month later for progressive shortness of breath and fever, along with hypotension, tachycardia andoxygen desaturation. Blood test showed persistent hypereosinophilia, elevated CRP, and increased pro-B type natriuretic peptide. (Table 1)

Chest X-Ray revealed signs of bilateral pulmonary congestion consistent with pulmonary oedema while TTE showed a dilated left ventricle with an ejection fraction of 60% and a significant progression of the mitral valve regurgitation. (Figure 2B) Due to the progressive hypoxemic respiratory failure, veno-venous extracorporeal membrane oxygenation (V-V ECMO) was initiated.

The patient underwent urgent mitral valve replacement the following day. The histological examination of the right atrial appendage showed subacute pericarditis with focal hypereosinophilia. (Figure 2C, 2D, 2E) The postoperative course was unremarkable. Based on clinical presentation and persistent

hypereosinophilia, an underlying hypereosinophilic vasculitis was suspected and investigated with a dosage of serum primary systemic vasculitis autoantibodies.[5] . Despite the absence of detectable serum antibodies, the patient was classified as being affected by eosinophilic granulomatosis with polyangiitis following the 2022 Classification Criteria for Antineutrophil Cytoplasmic Antibody-Associated Vasculitis; the criteria matched by the patient include: obstructive airways disease, nasal polyps, blood eosinophil count >1 x 10^9/liter, extravascular eosinophilic predominant infiltration. [6]

Due to the reproductive age of the patient, [7] a treatment with prednisone 25 mg bid and Mepolizumab 300 mg subcutaneous injection every 4 weeks, anticoagulant (unfractioned heparin) and cardioaspirin 100 mg die was started. The patient was discharged from the hospital after 15 days. The 3-month follow-up was negative for recurrences, and eosinophils count returned to normal.

Discussion

EGPA is a rare multisystem autoimmune disorder mostly affecting small to medium sized vessels. Although large vessels involvement has been already reported, [8] to date there has been no report of EGPA-related massive aortic thrombosis leading to an acute aortoiliac disease.

EGPA is a progressive disease that may eventually lead to an increased risk of arterial thromboembolic manifestations, due to the development of progressive granulomatous necrotizing vasculitis. [9] [10] [11]

The hyperexpression of eosinophil-derived factor such as eosinophil cationic protein, membrane basic protein, and eosinophil peroxidase, [12] [13] has been associated with an inhibitory effect on multiple levels of the natural anticoagulant pathways. [14] [15] Moreover, negative p-ANCA EGPA is associated with a higher eosinophilic tissue infiltration that determines a higher risk for thrombosis [16] [17] Cardiac valvular involvement is still rarely observed in EGPA patients, however, mitral and tricuspid regurgitation are the most commonly reported. [18] An early diagnosis of vasculitis might be extremely important in the clinical course of the disease; additionally a prompt and proper medical therapy can prevent the progression to a more severe stage [19]

In fact, a retrospective analysis of the patient's medical history shows that asthma, hypereosinophilia, allergies, non-fixed lung infiltrates, and nasal polyposis were present before hospitalization.

To date, there is no consensus regarding the most effective strategy to manage acute aortic vasculitis-related large vessel thrombosis. [20] [21]

Despite the absence of large case series exploring outcomes, endovascular procedures may carry fewer risks avoiding extensive manipulation of potentially inflamed aortic tissue. [22] [23]

However, open surgery may be chosen in case of large vessel acute thrombosis with high risk for distal embolization [24] or after failure of endovascular treatment. In our case, in an urgent setting and facing an extensive disease, we first opted for a less invasive treatment. Afterwards, considering the residual disease extension and patient's fitness for surgery, we chose an open approach as a rescue therapy.

Conclusions

Acute systemic EGPA clinical presentation is extremely variable and can involve large vessels including the aorta. Our case underscores the importance of a timely diagnosis, considering its possible unusual clinical appearance. A prompt diagnosis and tailored management could be crucial in preventing severe complications including major thrombotic events and cardiac involvement.

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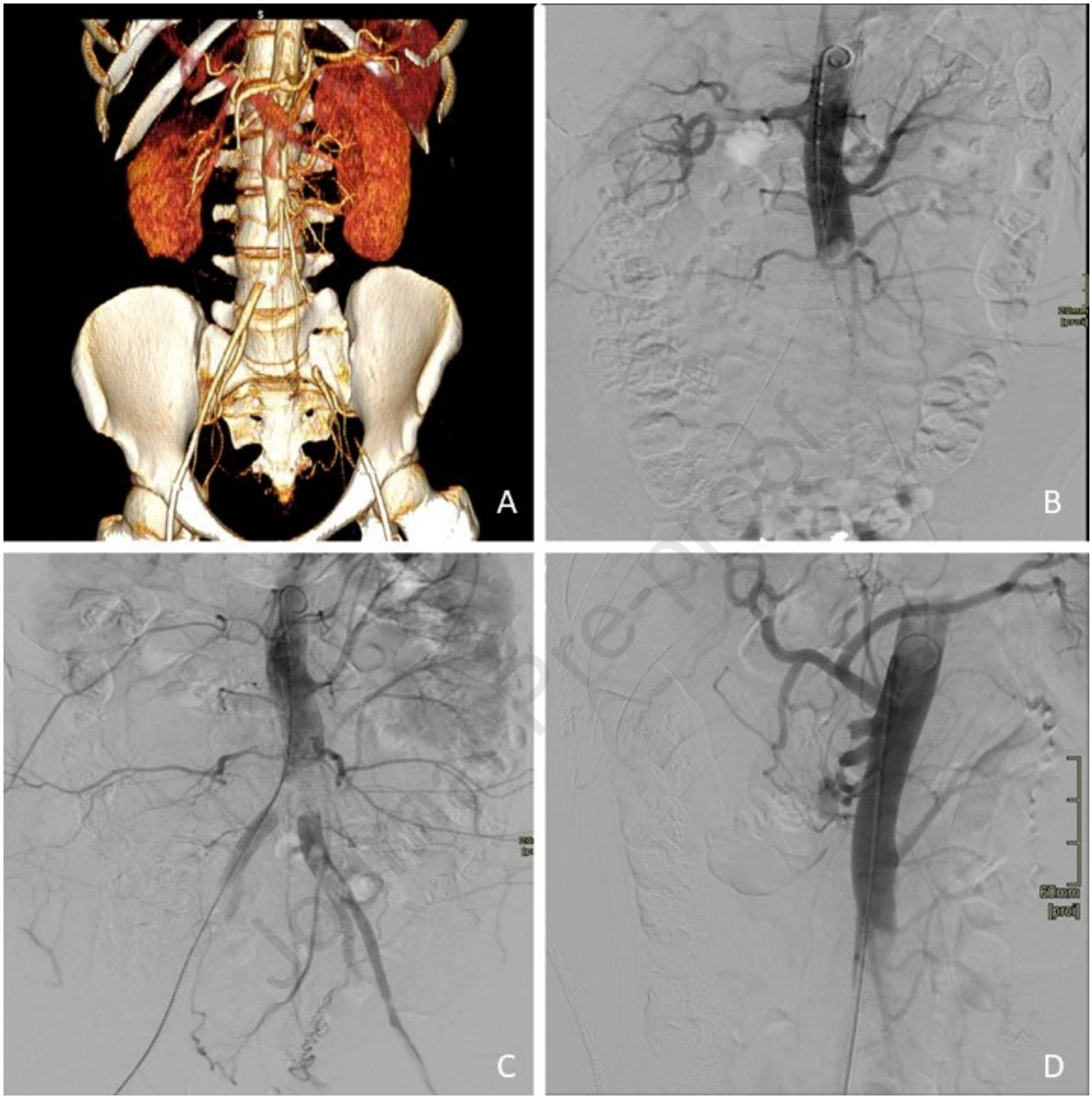
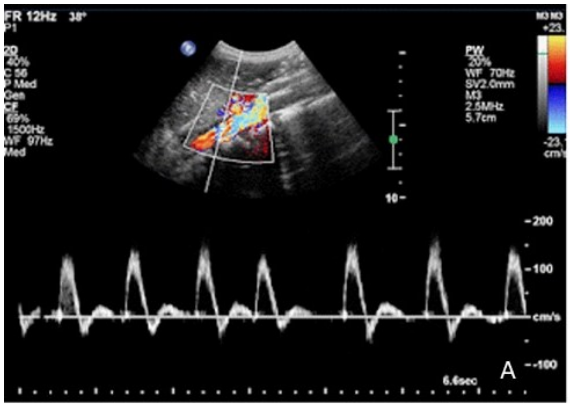
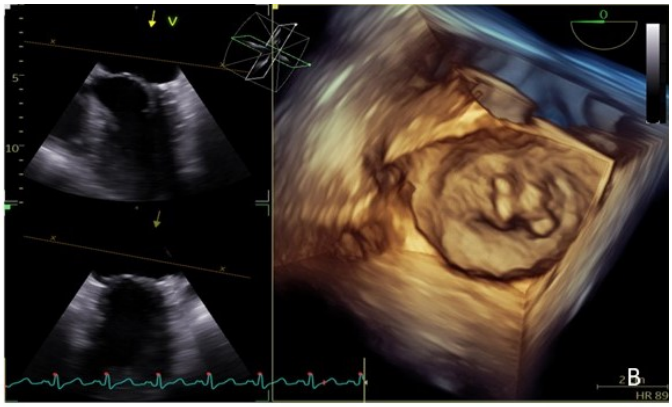
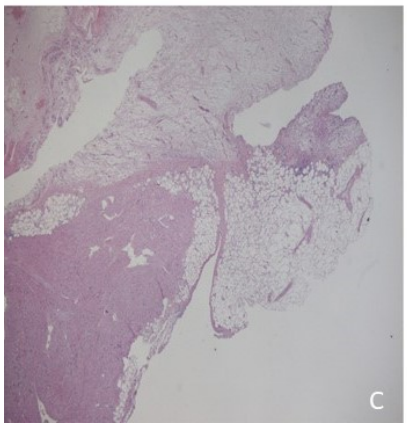
Table 1

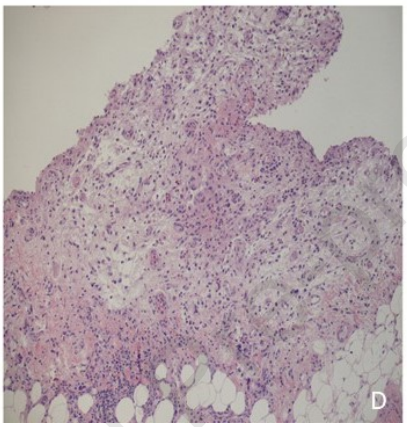
Test / Conventional Units	Result	Reference Range
WBC (white blood cells) x 10^3/µL	23,5	4-11,0
Neutrophils x 10^3/µL	9,1	2,5-8,0
Lymphocytes x 10^3/µL	3,1	1,5-7,0
Monocytes x 10^3/µL	2,7	1,0-4,0
Eosinophils x 10^3/µL	8	0,05-0,5
Basophils x 10^3/µL	0,6	0,025-0,1
PLT (platelet count) x 10^3/µL	400	142-450
ESR (erythrocyte sedimentation rate) mm	45	<20
Glucose mg/ml	105	70-100
Urea mg/ml	32	20-45
Creatinine mg/ml	0,95	0,72-1,05
CRP (C-reactive protein) mg/dl	19	<0,5
Hemoglobin g/dl	11	10,5-13,5
ALT U/L	35	10-34
AST U/L	20	10-45
NT-proBNP pg/mL	10250	< 125
Partial thromboplastin time (aPTT) sec	25	25-36
Prothrombin time (PT) sec	12	10-13
Fibrinogen mg/dl	480	130-330











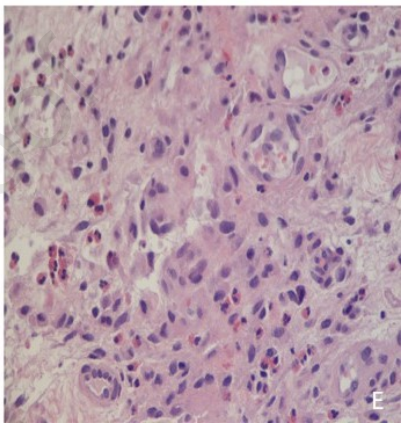


Figure 1. (A) 3D reconstruction of the angioCT at first ER access. (B) Angiography view of visceral and aorto-iliac thrombosis. (C) and (D) Final angiography with residual renal, mesenteric and iliac thrombosis.

Figure 2. (A) Color Doppler view of SMA after surgery. (B) Cardiac Doppler echocardiography at readmission. (C), (D) and (E) Eosinophil infiltration in the histological sample from the right atrial appendage.

Table 1. Results of blood tests at readmission