



## Case report

# Microscopic polyangiitis: Atypical presentation with extensive small bowel necrosis, diffuse alveolar hemorrhage, and renal failure

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## ABSTRACT

Microscopic polyangiitis is an uncommon systemic vasculitis of varying severity that is associated with myeloperoxidase (MPO) and perinuclear antineutrophil cytoplasmic (p-ANCA) antibodies. The most commonly affected organs are the lungs and kidneys. We report on a very unusual case of microscopic polyangiitis presenting with severe mesenteric ischemia in addition to diffuse alveolar hemorrhage and acute renal failure. The patient was initially diagnosed with acute pancreatitis at an outside facility given his severe abdominal pain and elevated pancreatic enzymes. Further investigations after transfer to our facility determined that the patient was actually suffering from a severe exacerbation of previously diagnosed microscopic polyangiitis. He quickly developed diffuse alveolar hemorrhage (DAH) necessitating intubation and acute kidney injury (AKI) requiring dialysis. He subsequently developed mesenteric ischemia and bowel necrosis resulting in emergent laparotomy and extensive small bowel resection. Physicians need to be aware that microscopic polyangiitis can very rarely present with severe involvement of the abdominal viscera and mesenteric vessels. Severe disease necessitates the use of high dose IV steroids, rituximab or cyclophosphamide, and plasma exchange (PLEX).

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## 1. Introduction

Microscopic polyangiitis is one of the pulmonary-renal vasculitides syndromes associated with MPO and p-ANCA antibodies. It typically results in pulmonary and renal involvement characterized by diffuse alveolar hemorrhage (DAH) and acute kidney injury (AKI) respectively; whereas involvement of other organ systems is rare. We report on a rare case of microscopic polyangiitis that presented initially with severe mesenteric ischemic resulting in bowel necrosis. The patient quickly developed multiorgan failure with severe pulmonary and renal dysfunction as described below.

## 2. Case report

A 56 year old male patient with a 2 month history of constitutional symptoms presented to an outside hospital with abrupt abdominal pain and was initially diagnosed with acute pancreatitis (Fig. 1). His respiratory status declined rapidly thereafter necessitating intubation and transfer to our facility. On admission, a chest x-ray (Fig. 2) and chest computed tomography (CT) (Fig. 3) showed diffuse bilateral pulmonary infiltrates, and an EKG revealed new onset atrial fibrillation. Bronchoalveolar lavage performed via bronchoscopy revealed a progressively bloody return indicating DAH. He developed acute kidney injury (AKI) and his serum creatinine eventually peaked at 6.5 mg/dL. Urinalysis showed proteinuria and RBC casts. Further history was subsequently obtained from family members who confirmed that the patient had been previously diagnosed with microscopic polyangiitis via a kidney biopsy and had been put on oral cyclophosphamide by his home nephrologist. However, he had been non-compliant due to financial constraints. His kidney biopsy slides were obtained for review by our pathologists and the diagnosis of ANCA associated vasculitis was reconfirmed. The results of the kidney biopsy in combination with the positive antibodies for MPO and p-ANCA

*Abbreviations:* MPO, Myeloperoxidase; ANCA, Anti-neutrophil cytoplasmic autoantibody; DAH, Diffuse alveolar hemorrhage; AKI, Acute kidney injury; PLEX, Plasma exchange.

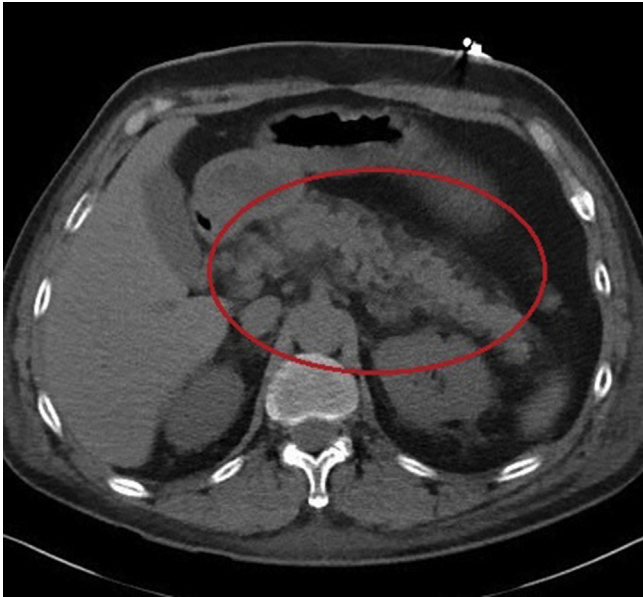
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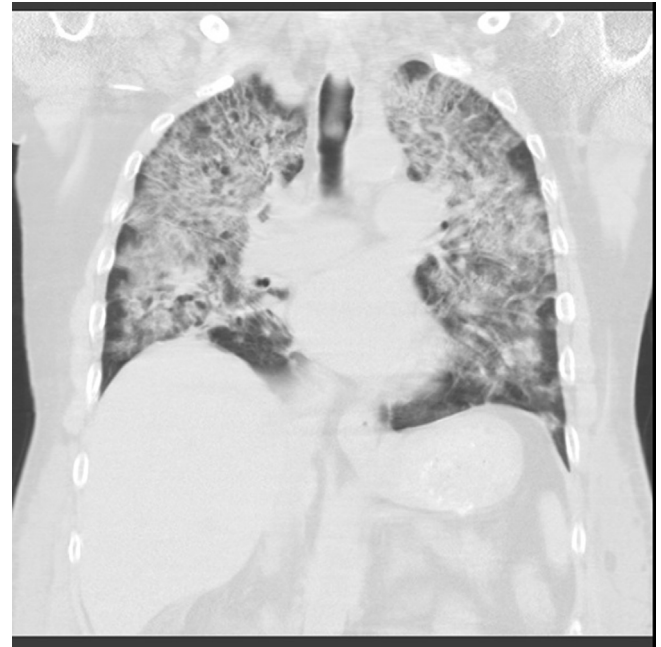


**Fig. 1.** CT Abdomen showing pancreatitis with diffuse peripancreatic edema.



**Fig. 2.** Chest X-ray showing diffuse bilateral interstitial and fluffy (alveolar) type infiltrates in both lung fields.

confirmed the diagnosis of microscopic polyangiitis. High dose intravenous steroids, Rituximab, plasma exchange (PLEX), and hemodialysis were initiated with considerable and rapid improvement allowing for extubation. On day 6, however, he developed acute abdominal distention and respiratory distress leading to reintubation. Abdominal CT showed extensive small bowel ischemia (Fig. 4). An emergent laparotomy was performed and resulted in removal of 60% of the terminal small intestine, placement of an end ileostomy, and initiation of total parenteral nutrition. Mesenteric surgical pathology revealed microthrombi but no evidence of vasculitis. His abdomen was temporarily closed and he underwent subsequent end ileostomy revision and abdominal washout. He continued to improve and was ultimately discharged after a prolonged hospital stay including 2 weeks in the ICU and one



**Fig. 3.** Coronal Chest CT scan image with diffuse bilateral ground glass infiltrates and focal areas of consolidation.

month of dialysis. Specific microscopic polyangiitis treatment included a total of 6 days of high dose IV methylprednisolone, 7 sessions of PLEX, and 4 doses of Rituximab. This was followed by a 1 mg/kg/day oral prednisone taper with rheumatology and nephrology outpatient follow-up.

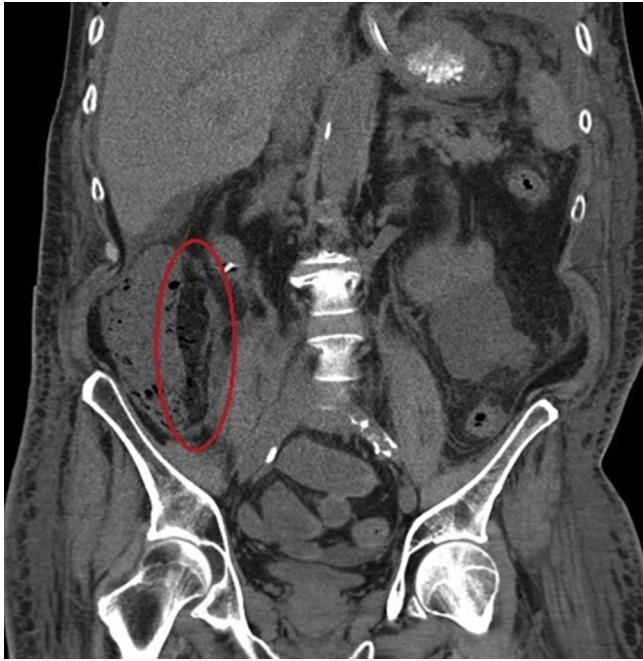
### 3. Discussion

Microscopic polyangiitis is a pauci-immune, ANCA-associated systemic vasculitis that affects small blood vessels. It typically involves the lungs and kidneys, with rare potential to involve any organ. Manifestations in the lungs typically include interstitial pneumonitis or DAH. The kidneys can develop necrotizing crescentic glomerulonephritis with subsequent acute renal failure [1,2].

Microscopic polyangiitis initially presents with non-specific symptoms like fever, fatigue, arthralgia, cough, and hemoptysis, with renal failure being a late manifestation. ANCA tends to be detectable at symptom onset making it useful for early diagnosis and treatment. Persistent or intermittent ANCA detection is an independent risk factor for relapsing disease but treatment for asymptomatic disease is controversial [3].

The etiology of anti-neutrophil cytoplasmic antibodies (ANCA) is thought to be caused by antigenic mimicry from multifactorial triggers. Some of the more common associations and hypothesized triggers include infections like Coxsackie B3 and parvovirus B19, silica, and medications like PTU, hydralazine, and allopurinol [3]. ANCA targets antigens found in the cytoplasmic space of polymorphonuclear (PMN) leukocytes. C-ANCA has cytoplasmic fluorescence reactivity to proteinase 3 (PR3), whereas P-ANCA has perinuclear fluorescence reactivity to myeloperoxidase (MPO). P-ANCA and MPO are most associated with microscopic polyangiitis [3].

There are conflicting studies looking at the possible pathogenic role of ANCA, but the evidence that supports the theory of ANCA's pathogenicity include animal models showing that P-ANCA may induce vasculitis in immunodeficient mice, ANCA titers correlating



**Fig. 4.** Coronal abdominal CT scan image consistent with bowel wall thickening and pneumatosis intestinalis.

with disease activity, ANCA binding to PMNs altering their function, ANCA binding to endothelium leading to cell injury, and increased surface expression of PR3 in neutrophils correlating with disease activity. Factors that speak against the pathogenicity of ANCA include lack of placental transfer, passive transfer of ANCA in animal models does not induce vasculitis, rat models exposed to human MPO develop ANCA but no vasculitis, and high titers of ANCA can be found in patients who do not have vasculitis [3].

ANCA-associated vasculitis (AAV) patients are at increased risk for VTE including deep venous thrombosis (DVT) and pulmonary embolism (PE). Several studies have looked at the increased risk of VTE in AAV patients while accounting for more classic VTE risk factors (immobilization, trauma, surgery, malignancy, pregnancy, oral contraception/hormone replacement, smoking, atrial fibrillation, family history, obesity, and thrombophilia) [4–6]. The increased VTE risk ranged between 1.8/100–7/100 person-years compared to 0.3/100 person-years in the healthy population [4–6]. It is important to remember that while hemoptysis may represent DAH, it could also be a sign of a PE [6]. Increased VTE risk in AAV patients is likely attributed to cytokines, ischemia, and ANCA which play a role in thrombosis from endothelial damage and inflammation [4,6]. Cyclophosphamide and high dose steroids may also contribute to thrombosis [4].

Thrombosis of mesenteric vessels is a rare manifestation of VTE in AAV patients [3–6]. The patient in our case developed acute mesenteric ischemia resulting in emergent laparotomy and resection of the majority of his small bowel. The surgical pathology revealed microthrombi without evidence of vasculitis. The cause for this patient's mesenteric ischemia likely revolves around the hypercoagulable state often seen in patients with microscopic polyangiitis and other kinds of systemic vasculitis. The role of PLEX in promoting a prothrombotic state has also been previously suggested due to differential removal of serum proteins with anticoagulant properties [8].

Treatment for microscopic polyangiitis typically includes the combination of steroids and immunosuppressives like cyclophosphamide or rituximab [7,9,10]. The RAVE and RITUXVAS trials

showed that rituximab is comparable to cyclophosphamide at inducing remission in severe disease [7]. Microscopic polyangiitis used to be an invariably fatal disease prior to the aforementioned therapies, but it is still associated with relapse (50% over 5 years) and significant morbidity including ESRD, DAH, and even death [7,9,10].

Plasma exchange (PLEX) therapy has been used in severe cases of microscopic polyangiitis. Proposed benefits of PLEX include removing ANCA, and proinflammatory mediators like activated lymphocytes and macrophages, complement, fibrinogen, TNF, and IL-1 [9,10]. After each PLEX session there is a cellular shift and re-equilibration necessitating repeated sessions every 24–48 hours [10]. It takes 5–7 PLEX sessions to remove 75% of IgG-like antibodies and is most often performed for 7 sessions [10]. Rituximab is cleared by PLEX thus making it imperative that Rituximab be administered after a PLEX treatment [7]. The combination of these two therapies will need to be further investigated [10]. There have been several studies evaluating the use of PLEX with conflicting results in its utility with AAV [9]. The strongest data to recommend PLEX comes from the MEPEX trial [7]. Because there has been some controversy regarding the use of PLEX in AAV, an ongoing international randomized controlled trial entitled PEXIVAS was designed to evaluate and clarify the effect of PLEX on ESRD, DAH, and mortality [9,10].

In conclusion, we report a case of microscopic polyangiitis in a patient with severe multi-systemic involvement, which is rarely seen in its entirety. What makes our case unique is the atypical presentation with initial pancreatitis followed by DAH, AKI and extensive small bowel necrosis. This report highlights the fact that microscopic polyangiitis can present in an atypical fashion with severe life-threatening complications. It is for these reasons that clinicians should broaden their differential diagnoses to include microscopic polyangiitis in atypical multisystemic organ involvement. Once diagnosed, prompt treatment with high dose IV steroids and either cyclophosphamide or rituximab should be initiated [7]. Patients with microscopic polyangiitis are at higher risk for VTE and therefore clinicians should have a low threshold to evaluate for thrombosis and prophylactic anticoagulation should be considered in the appropriate context [4,5]. PLEX is typically used in severe disease and its role is under investigation in an ongoing clinical trial (PEXIVAS) [9,10].

#### Summary conflict of interest statements

No conflicts of interest to report.

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#### Notation of prior abstract publication/presentation

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