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CASE REPORT

Acute Pancreatitis as the First Presentation of Wegener's Granulomatosis

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ABSTRACT

Context Wegener's granulomatosis is a systemic vasculitis with prominent involvement of the respiratory tract and kidney. An association between acute pancreatitis and Wegener's granulomatosis is rarely reported and is even rarer as the first presentation. This can result in diagnostic difficulty and may allow severe pancreatitis to develop with potentially poor outcome.

Case report We report a rare case with fatal outcome of vasculitis consistent with Wegener's granulomatosis presenting as acute pancreatitis in a 20-year-old female. The patient was admitted with worsening abdominal pain associated with nausea and loss of appetite. Accepted causes of acute pancreatitis were excluded and granulomatous vasculitis of the pancreas was confirmed from immunological profile, computed tomography and histology. As the disease progressed the patient experienced cutaneous, pulmonary, renal and severe gut involvement. Thirteen months from diagnosis the patient died of multi-organ failure despite appropriate surgical and immunosuppressive therapy.

Conclusion Vasculitic disease of the pancreas is rare but should be considered when other causes have been appropriately ruled out. Careful radiological, immunological and histological diagnosis is necessary and early immunosuppressant therapy in conjunction with advice from immunologists is essential to avoid the poor outcome reported in this and other case reports.

INTRODUCTION

Wegener's granulomatosis is a systemic vasculitis with prominent involvement of the respiratory tract and kidney. An association between acute pancreatitis and Wegener's granulomatosis is rarely reported and is even rarer as the first presentation. This can result in diagnostic difficulty and may allow severe pancreatitis to develop with potentially poor outcome.

CASE REPORT

A 20-year-old previously healthy woman presented with a week history of worsening upper abdominal pain, radiating to the back, associated with nausea and loss of appetite. Apart from urinary tract infection ten days previously, which was treated by her primary care physician with trimethoprim, the rest of her medical history were unremarkable. She drank approximately five units of alcohol per week. On initial examination she was haemodynamically stable, with epigastric tenderness to deep palpation, but no rebound. Initial laboratory investigations showed a white cell count of 15.1 $x10^9$/mL (reference range: 4-12 $x10^9$/mL), carbohydrate reactive protein (CRP) 145 mg/L (reference range: 0-5

mg/L), amylase 20 IU/L (reference range: 36-128) with otherwise normal renal and liver profiles and abdominal ultrasound scan. She was discharged within a few days pain free following a period of conservative management with oral analgesia. A diagnosis of missed late presentation mild pancreatitis was entertained.

Two weeks later she was re-admitted with worsening of her abdominal pain which now involved the right iliac fossa and flank, accompanied by severe nausea and vomiting and swelling in her feet. Ultrasound scan showed trace fluid in the pouch of Douglas. An abdominal CT scan (Figures 1 and 2) showed an oedematous pancreatic tail, with thrombosed splenic vein and a markedly abnormal spleen (from mechanical obstruction to splenic venous outflow from the severely inflamed pancreas). Fluid was also demonstrated in the parietocolonic recess. Biochemical testing again showed normal renal and liver function with raised CRP. Given that acute pancreatitis of unclear aetiology was demonstrated on cross sectional imaging the patient was admitted to the high dependency unit for optimisation of fluid status and closer monitoring for systemic sequelae of the pancreatitis where initially a good symptomatic recovery was made without significant organ dysfunction.

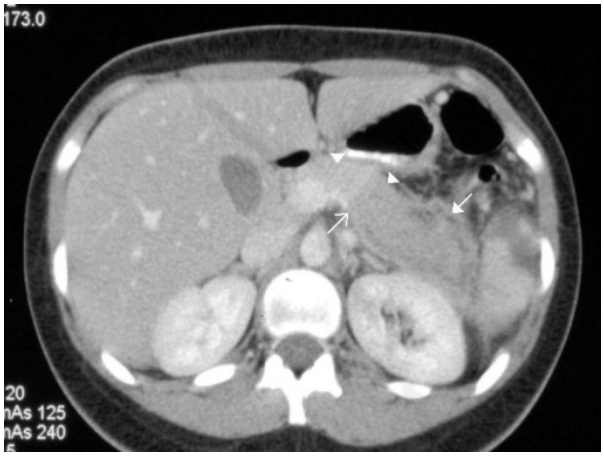

Figure 1. Axial portal venous phase i.v. contrast enhanced CT image through the pancreas. Sharp demarcation between the pancreatic neck/body and tail with reduced enhancement within the tail (arrow heads). There is a small volume of fluid seen within the pancreatic envelope consistent with peripancreatitis (closed arrow), splenic vein occlusion (open arrow).

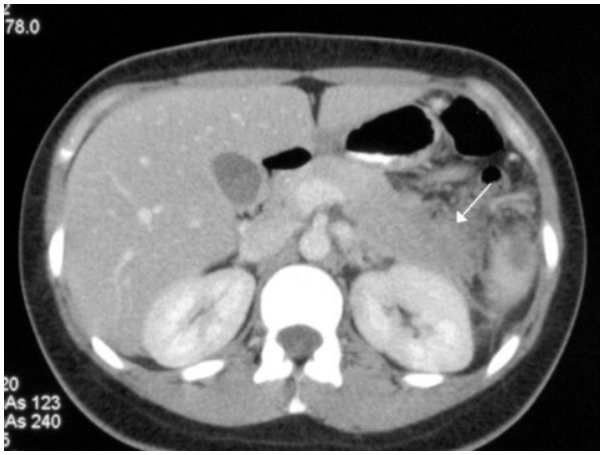

Figure 2. Axial portal venous phase i.v. contrast enhanced CT image through the pancreas. Peripancreatic inflammatory change with congestion in the associated mesenteric fat (arrow).

One month later dry mucous membranes were noted and the right elbow, left knee, left ear, lips and peri-orbital regions became swollen and tender and a vasculitic rash appeared over the trunk and limbs. Blue nail beds, nail fold infarcts, palmer erythema with puffy swollen hands and some splinter haemorrhages were observed. Infectious causes were excluded from serial negative blood and urine cultures, thoraco-abdomnial cross sectional imaging for infective foci and trans-thoracic echocardiography. Autoimmune investigations showed positive C-antineutrophil cytoplasmic antibodies (C-ANCA) with confirmatory proteinase 3 antibodies assay greater than 600 U/mL (reference range 0-9 U/mL). P-ANCA (with myeloperoxidase assay result 1.1 U/mL; reference range 0-9 U/mL) was negative. Further immunological testing in the form of ANA (including extractable nuclear antigen and double stranded DNA antibodies), thrombophilia screening and antiglomerular basement membrane antibodies were all negative. Given the above immunological profile a provisional diagnosis of pancreatic and systemic Wegener's granulomatosis was considered and the patient treated with high dose steroids and cyclophosphamide.

The patient deteriorated further with severe abdominal pain secondary to ischaemic colitis. Laparotomy and subtotal colectomy with ileostomy was performed; signs of pancreatic inflammation with no necrosis

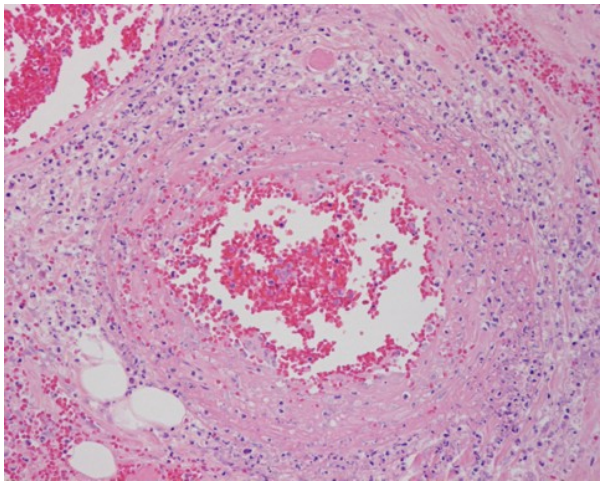

Figure 3. Small bowel resection showing a blood vessel with a leukocytoclastic vasculitis (magnification x400).

were noted. Small and large bowel histology (Figures 3 and 4) showed ischaemic bowel secondary to a vasculitis without granuloma formation but otherwise consistent with Wegener's. A renal biopsy was also taken although no renal impairment had developed at this stage to further confirm the diagnosis and this showed a crescentic glomerulonephritis (Figure 5).

The post-operative course was further complicated by pulmonary haemorrhage and acute renal failure and thrombocytopenia and the patient was transferred to the intensive care unit (ICU) for positive pressure ventilation and immunomodulatory therapy changed to intravenous immunoglobulins and plasmapheresis. Despite this, the patient experienced refractory anaemia and developed clostridial wound infection and streptococcal peritonitis. Appropriate broad spectrum antibiotics were commenced and the patient remained in ICU for several months for haemofiltration and continued ventilatory requirements. After several months in the ICU with sloughed wounds, treated with recurrent debridement, and necrotic leak from a small bowel fistula, she developed sepsis, multiorgan failure and died.

DISCUSSION

Vasculitis of the abdominal viscera is a rare cause of the acute surgical abdomen. Nevertheless in patients suffering from systemic vasculitides abdominal involvement is not uncommon and abdominal pain is the predominant presenting complaint [1]. The dominant vasculitis with abdominal involvement is polyarteritis nodosa especially in association with hepatitis B but patients with Churg-Strauss syndrome, microscopic polyangitis [2] and Wegener's [3, 4, 5, 6] may all experience abdominal crises. Primarily pancreatic involvement of systemic vasculitides however is rare. A case series of 62 vasculitis patients with gastrointestinal involvement [1] suggested that acute pancreatitis was diagnosed in only 3 patients and that features associated with poor outcome included first presentation of Wegener's, bowel perforation or infarction.

Unlike polyarteritis nodosa the predominant clinicopathological syndrome in Wegener's is reno-respiratory which makes the case

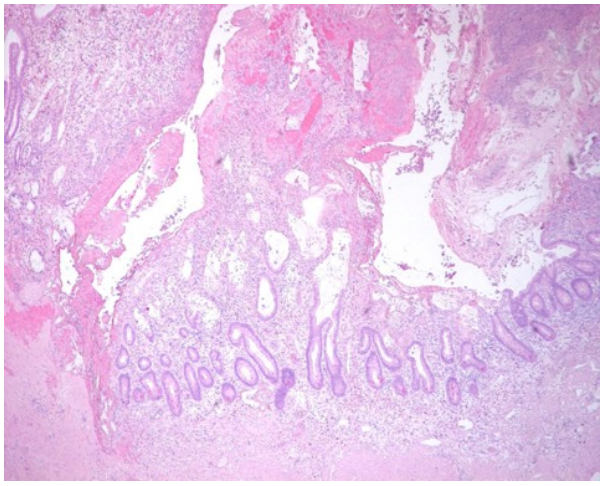

Figure 4. Colonic resection showing ischaemic change with ulceration (magnification x40).

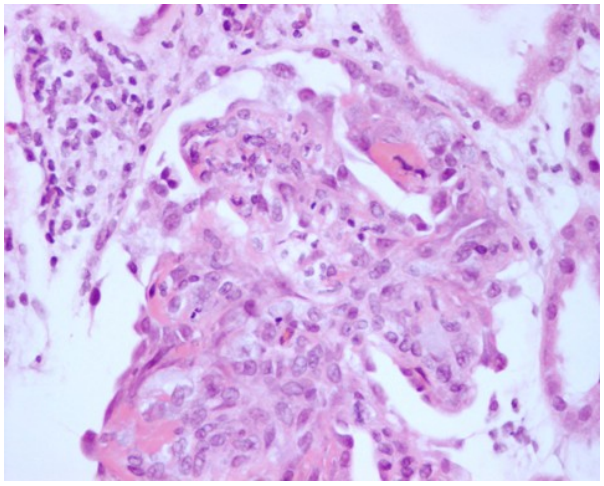

Figure 5. Renal biopsy and shows a crescentic glomerulonephritis (magnification x 400).

presented here more unusual. Wegener's granulomatosis with the onset of acute pancreatitis has been reported, but never at such a young age. An early previous report described recurrent pancreatic involvement in a 57-year-old man previously diagnosed with Wegener's who received early gluco-corticoids during each relapse [3]. Other authors note the difficulty in making a *de novo* diagnosis of Wegener's from pancreatic involvement alone [4] and how fulminant disease can evolve without prompt recognition [5]. A more chronic tumour like syndrome has been described in two reports [4, 6] and functional disease in another [7].

Medical history of the patient excluded ethanol, gallstone, iatrogenic, lipid or trauma induced pancreatitis [8]. Familial pancreatitis was ruled out and extensive laboratory and imaging investigation revealed no other causes of pancreatitis. As a vasculitic picture became clearer it was important to make a definitive diagnosis in order to guide therapy. The main differential was of Wegener's granulomatosis, microscopic polyangitis and polyarteritis nodosa. Polyarteritis nodosa normally affects middle aged men, is associated with hepatitis B infection and while commonly affecting gastrointestinal organs is usually ANCA negative with aneurysms in medium sized arteries. Microscopic polyangitis shares more features with Wegener's although the immune profile is more likely to include myeloperoxidase positivity in comparison with Wegener's where proteinase 3 positivity alone is more common (as in this case). Nevertheless renal involvement in microscopic polyangitis is similar to Wegener's in that crescentic glomerulonephritis can be demonstrated although granuloma formation is usually a hallmark of Wegener's alone. As the disease progressed as described above, it was felt that a diagnosis of Wegener's disease was more likely although microscopic polyangitis remains high on the differential diagnosis [2]. Whether this distinction would have lead to a change in outcome is unclear as immunosup-pressive therapy was instigated when infection had been ruled out and clinical and immunological profile suggested a leucocytoclastic vasculitis consistent with both diseases. This was confirmed on renal biopsy.

Lessons from this case of poor outcome from a young patient with acute pancreatitis as a first presentation of a vasculitis consistent with Wegener's granulomatosis and the case series in the literature are important for the pancreatic specialist. While acute pancreatitis is well recognised and treatment programs are mature vasculitic acute pancreatitis is rare, poorly recognised and standard treatment protocols inappropriate. In patients suffering from vasculitides gastrointestinal pathology may be rapidly associated to the underlying disease but where abdominal syndromes are the first presentations of vasculitic disease, cases inappropriately labelled as idiopathic may have poor outcomes especially where the abdominal syndrome itself has a high mortality as in acute pancreatitis although the majority of idiopathic cases of acute pancreatitis are not vasculitic [9]. Knowledge of these rarer causes, astute radiological observation for key imaging features and appropriate use of readily available immunological screening tests are vital for diagnosis and prompt use of immunosuppressive therapy.

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Keywords Pancreatitis, Acute Necrotizing; Wegener Granulomatosis; Vasculitis

Abbreviations ANCA: antineutrophil cytoplasmic antibodies

Conflict of interest The authors have no potential conflicts of interest

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