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Case report

Life-threatening gastrointestinal haemorrhage requiring surgical resection caused by SARS-CoV-2 induced ANCA associated vasculitis: A case report☆

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ABSTRACT

Introduction and importance: SARS-CoV-2 infection has been linked to the *de novo* diagnosis of various autoimmune conditions as well as flares in pre-existing disease. With such high prevalence of SARS-CoV-2 in the community, it is important to consider rare manifestations of autoimmune conditions when patients present with severe symptoms. Multi-specialty care is required to ensure optimal outcomes and prompt diagnosis.

Case presentation: A 28-year-old male presented to our tertiary referral centre with progressive debilitating polyarthritis, a purpuric rash on both flanks and aphthous ulcers 6 weeks after infection with SARS-CoV-2. On the second day of admission, he developed severe gastrointestinal haemorrhage requiring multiple blood transfusions. Attempted angioembolisation failed to identify a site of active haemorrhage. On failing trial of conservative management, the decision was made to perform an exploratory laparotomy. The small bowel was found to have an extensive vasculitis requiring resection to control haemorrhage. Autoimmune serology revealed c-ANCA positivity with anti-PR3 antibodies.

Clinical discussion: Patients presenting with acute vasculitic pathologies related to SARS-CoV-2 have the potential to rapidly progress to severe life-threatening gastrointestinal haemorrhage. Prompt surgical management is appropriate in selected cases.

Conclusion: In the current era of COVID-19, the differential diagnosis of SARS-CoV-2 induced ANCA vasculitis must be considered for such cases with gastrointestinal haemorrhage. Compilation of similar cases and further studies are required to determine an optimal management pathway for these patients.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has had an immense impact on the provision of global health care. At the time of writing the World Health Organisation reported 535,863,950 confirmed cases and 6,314,972 deaths [1]. The majority of mortality and morbidity are related to respiratory complications, however, it is being increasingly recognised that SARS-CoV-2 can cause flares in, or induce *de novo,* autoimmune pathologies with a variety of clinical manifestations [2]. One autoimmune process that can arise from the immune dysregulation caused by SARS-CoV-2 is anti-neutrophil cytoplasmic autoantibodies (ANCA) associated vasculitis (AAV) [2].

AAV is a small to medium vessel vasculitis with two main subgroups comprising eosinophilic granulomatosis with polyangiitis (eGPA) and granulomatosis with polyangiitis (GPA). eGPA is associated with p-ANCA reactivity and MPO antibodies while GPA is associated with c-ANCA reactivity and PR3 antibodies. GPA in particular can affect multiple organ systems, especially ear, nose, lungs and kidneys [3]. A rare manifestation that carries a high mortality is an involvement of the gastrointestinal (GI) tract [4]. GI involvement can lead to severe life-threatening haemorrhage and often requires prompt surgical management [5–7]. Currently, there are no specific standards of care or

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guidelines to guide decision making for these patients.

We report a case of GI haemorrhage secondary to SARS-CoV-2 induced ANCA associated vasculitis. This is a novel presentation associated with SARS-CoV-2 infection and contributes to the ongoing understanding of various ways the virus can cause pathology. The case also contributes to the literature by demonstrating the successful treatment of GI haemorrhage due to AAV with laparotomy and surgical resection. It has been reported in line with the SCARE criteria [8].

2. Case description

A 28-year-old, previously healthy, Caucasian male self-presented to our hospital emergency department with a purpuric rash on both flanks, polyarthralgia and multiple painful aphthous ulcers. These symptoms had initially developed one day after Sars-CoV-2 diagnosis, and progressively worsened until the patient became unable to cope at home. During history taking, it was revealed that one week prior to this presentation the patient had presented to a peripheral hospital for the workup of right upper quadrant pain with polyarthralgia. An abdominal computed tomography (CT) performed during that admission revealed no intra-abdominal pathology except for non-specific right sided abdominal wall fat stranding (Fig. 1). This was deemed to be due to minor trauma from a car accident earlier in the week, and he was discharged until presenting to our facility. The other significant history noted during his presentation at our centre was the development of a purpuric rash in the same distribution following his second BNT16B2b2 (Pfizer) COVID-19 vaccination 3 months prior to this infection. The rash at that time resolved in 3 days after vaccination. Initial laboratory results at the time of his presentation included a mildly elevated CRP (75 mg/L) and leukocyte count (15.1 × 10.9/L).

The patient was admitted for complete work-up with the differential diagnoses including SARS-CoV-2 induced multi-system disease with a reactive arthritis component, vasculitis, and inflammatory bowel disease with extra-intestinal manifestations. Due to the non-specific nature of his symptoms, arriving at the correct diagnosis at presentation was difficult until further investigations were performed. The patient was initially treated supportively, with intravenous fluid therapy and analgesia.

On the day following admission the patient developed severe haematochezia causing haemodynamic instability and required ongoing blood transfusion. The decision was made to perform a computed tomography angiogram (CTA). This was favoured over endoscopy as the patient had not received any bowel preparation and it was hoped that embolization could be achieved. CTA revealed an arterial blush in the distal ileum consistent with active bleeding (Fig. 2). Angioembolisation was attempted but no active bleeding was visualised during the procedure. Due to ongoing haemorrhage, a second CTA was repeated 24 h later with no active bleeding visualised. The patient continued to have intermittent haematochezia requiring ongoing transfusions and the decision was made to proceed to exploratory laparotomy. This occurred three days after initial GI haemorrhage. The operation was performed by a high-volume colorectal surgeon at our tertiary referral centre. During the operation, the small bowel was found to have frequent patchy vasculitis throughout its entirety. This was worse in the terminal ileum (Fig. 3). Due to the extent of the vasculitis in the terminal ileum it was deemed non-viable, and the decision was made to perform a small bowel resection with an end ileostomy (Fig. 4). Post-operatively, the patient was commenced on pulsed intravenous methylprednisolone (1 g/day for 3 days), followed by high dose corticosteroids (50 mg prednisolone). They received routine post-operative care on the ward. Their post-operative course was benign with no recurrence of haematochezia or any post-operative complications.

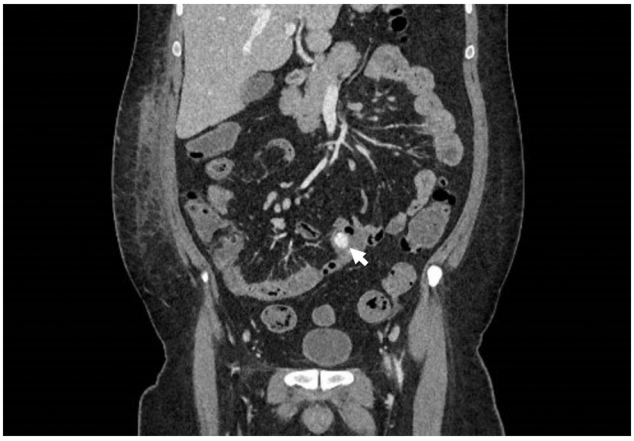

Fig. 2. Computer topography angiogram demonstrating arterial blush in the distal ileum.

Macroscopic examination of the resected terminal ileum specimen revealed multiple punch-out ulcers throughout the bowel segment (Fig. 5). The microscopic sections showed demarcated ulcers with no evidence of chronicity or granuloma in the surrounding mucosa. Vasculitis was present at the small and medium-sized arteries within the ileal mucosa and submucosa, with a transmural infiltrate of neutrophils, eosinophils and histiocytes and fibrinoid necrosis (Fig. 6). Interestingly, no vasculitis was seen within subserosa and ileal mesentery. The serology studies for vasculitis returned during the recovery. It showed the presence of c-ANCA reactivity at a titre of 1:1280 and anti-proteinase 3 (PR3) was elevated at 271 IU/mL. The combination of clinical,

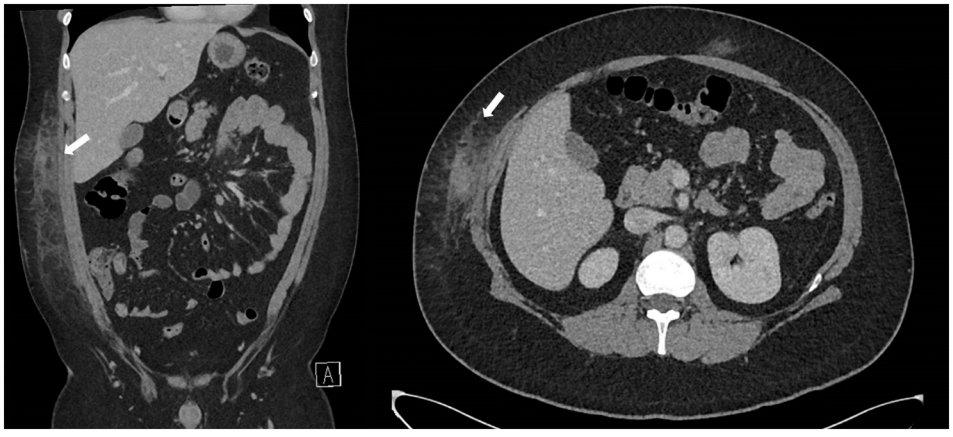

Fig. 1. Computed topography from the patient's initial presentation at a peripheral centre demonstrating non-specific fat stranding within the abdominal wall (white arrow).

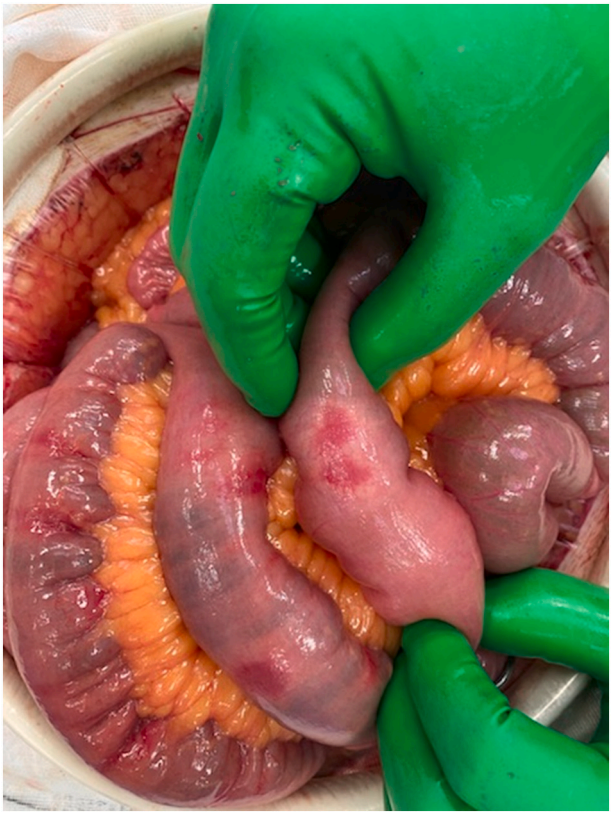

Fig. 3. Patchy areas of vasculitis seen within the small bowel during exploratory laparotomy.

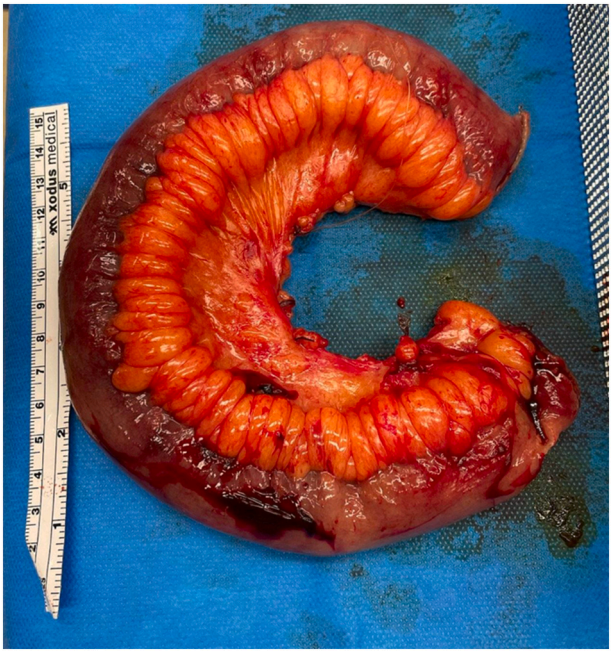

Fig. 4. Resected non-viable bowel with extensive vasculitis during exploratory laparotomy.

laboratory and histopathological findings has made the diagnosis of SARS-CoV-2 associated GPA.

The patient was discharged home two weeks after the operation on a weaning dose of prednisolone (25 mg at time of discharge) and was administered two doses of rituximab as an outpatient. Routine post-

Fig. 5. Macroscopic specimen of resected terminal ileum demonstrating multiple punch-out ulcers.

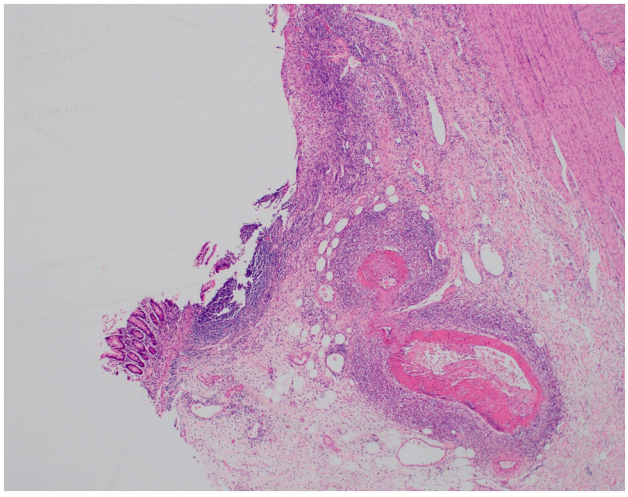

Fig. 6. A microscopic histopathology section demonstrating small to medium vessel vasculitis at the submucosa.

laparotomy and ileostomy instructions were provided. They were followed up in the surgical clinic. The patient reported no further episodes of GI bleeding. Both colonoscopy and gastroscopy are booked for 3 months after the surgery and reversal of the ileostomy is planned for 6 months post the date of surgery.

3. Discussion

Severe GI haemorrhage (GIH) can be a life-threatening surgical emergency requiring bowel resection. There are many known aetiologies for GI haemorrhage, however, this is the first case of SARS-CoV-2 associated ANCA vasculitis leading to severe GIH reported within the literature.

Since the beginning of the SARs-CoV-2 pandemic there has been a substantial increase in the world's health burden. Included in this burden is a significant impact on the provision of surgical services. An impact on these services that is difficult to quantify, is the increase in surgical disease due to complications related to SARS-CoV-2 infection. Currently, there are various reports of patients with SARS-CoV-2 induced GI complications requiring emergency surgery for these pathologies [9,10]. This report highlights another SARS-CoV-2 associated complication requiring surgical bowel resection for definitive treatment.

AAV encompasses granulomatosis with polyangiitis (GPA), microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis.

GPA usually causes pauci-immune glomerulonephritis, alveolar haemorrhage, purpura, peripheral neuropathy, and eye inflammation [11,12]. Due to this potential for multiple organ system involvement, these patients require hospitalisation with the care of several specialities. Currently, routine medical management includes immunosuppression and glucocorticoids though there still remains a high risk of death and adverse events [13]. One potential cause of death is severe gastrointestinal involvement which can manifest as life threatening haemorrhage [14,15]. GPA is usually considered primary with no underlying disease or exposure being identified to have caused the pathology [16,17]. However, when there is an identified trigger, the vasculitis is classified as secondary. One novel and currently poorly defined secondary cause of AAV is SARS-CoV-2.

SARS-CoV-2 associated AAV is a recognised entity with a proposed pathophysiology. Autopsies have revealed that patients affected with SARS-CoV-2 can develop small, medium and large vessel vasculitis within multiple organ systems [6]. This is hypothesised to be caused by a dysregulated autoimmune response trigged by elevated levels of cytokines and immune cell hyperactivity [6]. SARS-CoV-2 has also been found to induce and/or exacerbate various other autoimmunological disease processes [2]. Different phenotypes have been reported in the literature, affecting integumentary, renal, and respiratory systems with a variety of clinical manifestations associated with each [5–7,18]. However, there have been no reported cases of severe GIH caused by SARS-CoV-2 associated vasculitis.

GI manifestations of vasculidities such as AAV are rare. However, they carry immense clinical significance due to GI involvement demonstrating a high mortality rate in these patients [4]. GI manifestations in patients with AAV have a reported incidence of between 6 % to 7 % [12,15]. There exist a variety of non-specific manifestations that can occur is these patients including bowel ischemia, bowel ulceration, bowel perforation, peritonitis, pancreatitis, hepatitis, and GI haemorrhage [14,19]. Of these, abdominal pain and GI haemorrhage are the most common [19]. This indicates the importance of surgeons having an evidenced based approach to managing these more common presentations and symptoms of AAV.

The current literature around decision making for surgical intervention in patients with GI involvement in AAV is scarce. There exist case series including patients requiring bowel resection due to ongoing haemorrhage in the context of AAV [14,15]. However, no higher quality evidence on surgical management of these patients was identified. Despite, the paucity within the literature, surgical resection is the life-saving treatment for these patients when haemorrhage is refractory to medical management. With a high mortality, early diagnosis and expedient management for these patients is paramount for improving outcomes [4].

4. Conclusion

The association between SARS-CoV-2 and autoimmune conditions is becoming increasingly evident in the literature. This case demonstrates the need to consider autoimmune complications of COVID-19 in patients presenting with GI haemorrhage and the role for surgical resection. Further studies are required to develop an optimal management pathway for such cases.

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Ethical approval

N/A.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research registration

N/A.

Guarantor

Dr. Brian Draganic

Provenance and peer review

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Thomas Giles: Writing - original draft and editing, methodology, data collection, project administration

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Brian Draganic – Supervisor, consultant surgeon

Declaration of competing interest

The authors have no competing interests to declare.

This case has not been presented at a conference or regional meeting.

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