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# Acute PR3-ANCA vasculitis in an asymptomatic COVID-19 teenager

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## ABSTRACT

We present the case of an acute onset ANCA positive vasculitis in an asymptomatic COVID-19 infected teenager, resulting in significant colonic damage. The patient was initially diagnosed with Henoch-Schönlein purpura and presented with worsening symptoms with significant necrosis of her perineum and rectum requiring surgical debridement and diverting colostomy. As a part of her work-up, she tested positive for COVID-19 total IgG/IgM antibodies and ANCA antibodies. This case complements previously reported cases of COVID-19 induced autoimmune disease in children but is novel in describing extensive intestinal disease as a result of an autoimmune vasculitis in a child.

## 1. Introduction

As the COVID-19 pandemic caused by SARS-CoV-2 quickly spread, so did research on the clinical manifestations of the virus. Much of the medical literature published on COVID-19 is focused on adult manifestations of the virus, leaving many unanswered questions about how the virus affects the younger population. Systematic reviews have suggested that most children with COVID-19 present with either mild symptoms of fever, dry cough, and fatigue or were asymptomatic [1–4]. However, recent data describing more severe disease and unique sequelae, as well as the newly defined multisystem inflammatory syndrome in children (MIS-C), has proven that there are yet many unsolved questions about how COVID-19 affects children [5]. Here we present the case of an acute onset ANCA positive vasculitis in an asymptomatic COVID-19 infected teenager, resulting in significant anorectal damage.

## 2. Case

A 13-year-old girl was transferred from a local hospital to a tertiary children's hospital with anemia, exudative pharyngitis, and peri-rectal wounds in the setting of previously diagnosed Henoch Schönlein Purpura (HSP). Brief history prior to transfer indicates the patient had fell ill approximately three months prior with swollen hands and feet, and purpura on the lower extremities and back.

*Abbreviations:* ANA, anti-nuclear antibody; ANCA, antineutrophil cytoplasmic antibody; anti-MPO, myeloperoxidase antibody; anti-PR3, proteinase 3 antibody; CMV, Cytomegalovirus; COVID-19, coronavirus disease 2019; EBV, Epstein-Barr virus; HSP, Henoch Schönlein Purpura; IgG, immunoglobulin G; MIS-C, multisystem inflammatory syndrome in children; NSAIDs, Non-steroidal anti-inflammatory drugs.

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She subsequently developed swollen exudative tonsillitis but tested negative for Streptococcus and Epstein-Barr virus (EBV). She was diagnosed with HSP and Staphylococcus tonsillitis and treated with a course of amoxicillin and high dose Non-steroidal anti-inflammatory drugs (NSAIDs). After a brief improvement, her symptoms returned one month later and rapidly worsened. She was again treated with a course of oral antibiotics and NSAIDs with the addition of oral steroids. After this, the purpuric rash started to evolve into numerous coalescing necrotic wounds. Due to worsening of this necrosis, the patient returned to the Emergency Room at the referring facility and was found to have a low-grade fever, hypertension, exudative tonsillitis, and an extensive purpuric rash with associated necrosis from the tip of the coccyx to the anus (Fig. 1). She was also found at that time to have leukocytes, protein, and blood in her urine.

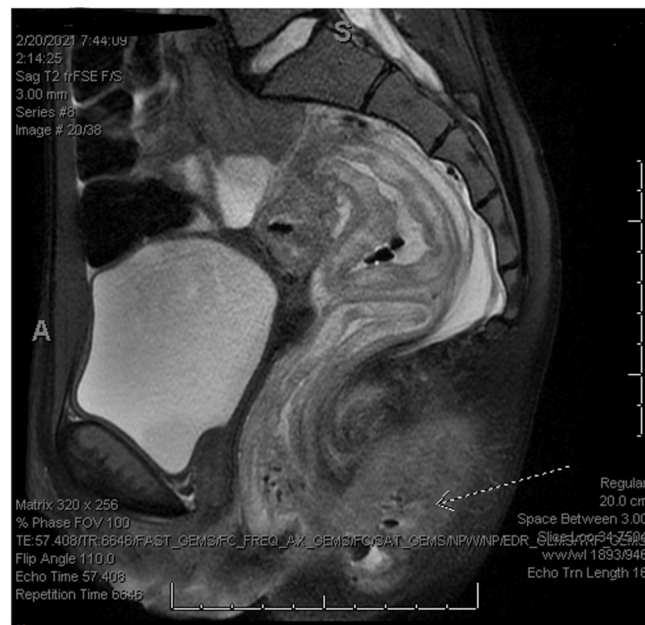
Upon arrival to our facility, the patient was febrile with a temperature of 100.5 °F and hypertensive with a blood pressure of 144/81 mmHg. Physical exam was notable for bilateral exudative tonsillitis and a large peri-anal necrotic area. Labs revealed white blood cells (WBC) 16.09K/ $\mu$ L, total hemoglobin (Hgb) 7g/dL, hematocrit 22.4%, mean corpuscular volume (MCV) 77.8fL, platelet count 465K/ $\mu$ L, and an erythrocyte sedimentation rate (ESR) 47mm/h. The patient had a negative COVID nucleic acid amplification testing (NAAT) nasal swab upon admission however, SARS CoV2 IgG/IgM antibody serology returned positive, indicating prior COVID infection. Clostrid difficile (*C. difficile*) NAAT was positive with a negative toxin antibody. Imaging included an MRI which revealed diffuse bowel wall thickening of the sigmoid colon and rectum with surrounding edema and moderate volume ascites. The more proximal colon and small bowel appeared normal. Additionally, there was an inferior anal sphincter fistula communicating with probable intersphincteric superior abscess and substantial subcutaneous edema with no signs of osteomyelitis (Fig. 2). Renal ultrasound showed increased echogenicity of bilateral kidneys without evidence of artery stenosis.

Based on these imaging results and presence of a necrotizing perianal wound, the patient was taken to the operating room for debridement and a rectal exam under anesthesia. The rectum was found to be friable and had extensive full thickness ulcerations. Multiple biopsies of the affected colonic tissue were obtained, and a diverting distal colostomy was placed. Skin biopsies of the purpuric lesions and a kidney biopsy was also obtained.

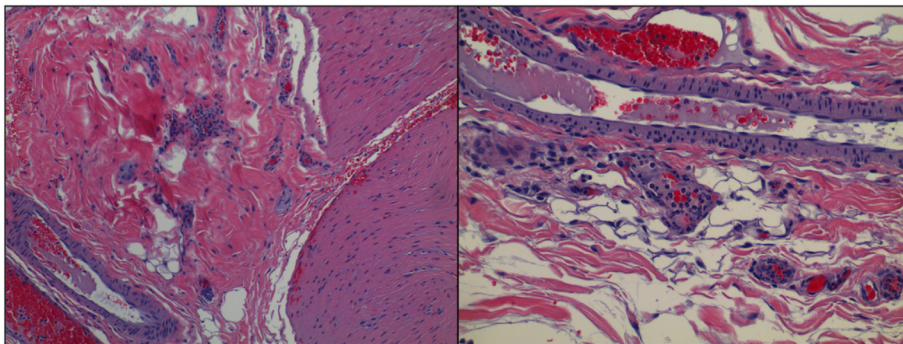
With concern for vasculitis, pediatric rheumatology and nephrology were consulted and an array of immunology labs were obtained. Results were positive for proteinase 3 (anti-PR3) antibody, with an anti-PR3 antineutrophil cytoplasmic antibody (ANCA) titer of 1:640 and decreased C4 complement. Anti-nuclear antibodies (ANA) screening and myeloperoxidase antibody (anti-MPO) ANCA were negative, anti cardiolipin IgG/IgM/IgA, Beta 2 glycoprotein 1 IgG/IgM, dRVVT lupus anticoagulant negative and C3 complement were normal. Also, EBV and Cytomegalovirus (CMV) panels were negative for acute infection. Upon analysis of the rectal and colonic tissue biopsies, pathology reported a leukocytoclastic vasculitis involving small vessels which was negative for immunofluorescent IgA staining (Fig. 3). The renal biopsy demonstrated no evidence of IgA nephropathy or immune mediated glomerular disease by light microscopy or immunofluorescence. Electron microscopy confirmed normal glomerular capillary basement membranes without evidence of glomerular disease. Based on these results, she was diagnosed with PR3-ANCA vasculitis and treated with high dose methylprednisolone and rituximab. She has subsequently had an excellent recovery with resolution of her skin rashes and perineal wound healing.



Fig. 1. Necrotic lesion surrounding anus extending up into the coccyx and down to the labia (left). Extensive purpuric lesions of lower extremities (right).



**Fig. 2.** MRI pelvis with contrast revealing marked bowel wall thickening of the sigmoid and rectum with surrounding edema and moderate volume ascites. Inferior anal sphincter fistula at the 6 o'clock position communicating with probable subcutaneous superior abscess at the 1 o'clock position (indicated by white arrow). Substantial subcutaneous edema with likely small abscesses from inferior and sphincter fistula to the right and left gluteal clefts.



**Fig. 3.** H&E staining of colonic subserosal tissue demonstrating a leukocytoclastic small vessel vasculitis (capillaritis) with sparing of larger vessels (left-100x, right-200x magnification).

### 3. Discussion

This is the first report of new onset anti-PR3 ANCA vasculitis in a COVID-19 antibody positive patient. We cannot be certain that this is a case of COVID-19 induced vasculitis or if our patient has a primary autoimmune vasculitis. However, COVID-19 has previously been linked to cutaneous vasculitis and Kawasaki-like vasculitis in patients with minimal or no lung involvement. The underlying mechanisms for this association has yet to be elucidated [6]. A similar case of a new onset anti-MPO vasculitis with positive COVID-19 IgG antibody was recently reported in a child, however that patient did not have any cutaneous or intestinal manifestations. Rather, they presented with pulmonary hemorrhage [7]. Of note, studies have linked gastrointestinal complications in a small subset of adult patients with COVID-19 [8,9]. Additionally, a surveillance report of MIS-C supported by the CDC showed the gastrointestinal tract to be one of the most commonly involved organ systems, affecting up to 92% of patient with MIS-C [10].

### 4. Conclusion

Our case supports the previously published hypothesis that COVID-19 may serve as an immune trigger for autoimmune conditions [11,12]. Ultimately, there is a need for more studies on the spectrum of sequela that may result from COVID-19 in children.

### Patient consent

Consent to publish the case report was obtained. The report does not contain any personal information that could lead to the identification of the patient.

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**Declaration of competing interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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