IgA Vasculitis in an Adult Linked to Cryptosporidium and Giardia Co-Infection: A Comprehensive Case Study

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Patient: Male, 51-year-old
Final Diagnosis: IgA vasculitis
Symptoms: A maculopapular rash, arthralgia, and abdominal pain
Clinical Procedure: —
Specialty: Rheumatology

Objective: Unknown etiology
Background: Immunoglobulin A (IgA) vasculitis is a small-vessel vasculitis characterized by the deposition of IgA immune complexes primarily in the skin, kidneys, and gastrointestinal tract. While it predominantly affects children, cases in adults are associated with more severe manifestations. Evidence suggests that infectious triggers play a pivotal role in its etiology. Often, it follows a self-limiting course and doesn't necessitate intervention.

Case Report: We present the case of a 51-year-old man who presented with a maculopapular rash, arthralgia, and abdominal pain. An examination revealed a purpuric rash on lower extremities and abdomen. A lower extremity duplex ultrasound identified deep vein thrombosis (DVT) in the right leg. Skin biopsy of the rash confirmed the diagnosis of IgA vasculitis, demonstrating perivascular neutrophilic infiltrate and IgA complex deposition. Stool studies revealed co-infection with Cryptosporidium and Giardia. The patient was treated with a prednisone taper with significant improvement in symptoms.

Conclusions: This case highlights the potential role of Cryptosporidium as a trigger for IgA vasculitis. The presence of concurrent infections underscores the complex interplay between infections and the development of IgA vasculitis. The co-infection with Giardia suggests that a secondary infection may be involved, further complicating the disease's etiology. The observation of DVT suggests a possible link between IgA vasculitis and a prothrombotic state. This report serves to expand the knowledge of IgA vasculitis triggers and associated complications, guiding clinicians in diagnosing and managing similar cases while emphasizing the importance of vigilance in adults with these symptoms.

Keywords: Autoimmune Diseases • Cryptosporidium • IgA Vasculitis • Vasculitis

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Background

Immunoglobulin A (IgA) vasculitis, previously known as Henoch-Schönlein Purpura, is a small-vessel vasculitis characterized by the deposition of IgA complexes primarily in the skin, kidneys, and gastrointestinal (GI) tract. Patients commonly present with palpable purpura, arthritis/arthralgia, abdominal pain, and kidney disease [1-3]. Children are more commonly affected than adults [2]. When occurring in adults, disease frequency increases in the fifth and sixth decades of life, and there appears to be a male predominance of approximately 1.5: 1 that is not noted to occur in children [1,4]. Developing IgA vasculitis as an adult is associated with more severe disease manifestations and poorer outcomes [5]. Additionally, there is a notable seasonal fluctuation in the incidence, with a higher prevalence during the winter and fall months. It’s worth noting that this seasonal variation is more pronounced in children than in adults [4,6,7].

While the etiology and pathophysiological mechanisms remain incompletely understood, evidence suggests that abnormal immune responses triggered by environmental factors, particularly infections, may play a crucial role [7]. In the present report, we present a compelling case implicating Cryptosporidium and Giardia co-infection as a potential trigger for IgA vasculitis.

Case Report

A 51-year-old man with no past medical history presented to the emergency room with a 1-day history of diffuse maculopapular rash, arthralgia, and epigastric abdominal pain. The patient was a truck driver and former tobacco user (2 packs of cigarettes/day). He denied new medications or international travel prior to the development of symptoms. A physical exam noted a rash on the bilateral upper and lower extremities, and the patient reported lower extremity pain. Bilateral lower extremity duplex ultrasounds revealed deep vein thrombosis (DVT) in the right lower extremity, which was treated with a heparin drip and then transitioned to apixaban twice daily. To address the rash, the patient received a single dose of methylprednisolone 125 mg intravenously (IV). Following treatment, the patient reported improvement in symptoms and was discharged.

The patient returned to the emergency room 6 days later, reporting worsening of the rash, joint pains (now with intermittent swelling of his elbows, knees, and wrists), and worsening epigastric pain. The patient reported that the rash now covered his torso and had spread to his back. It was nonpruritic. He reported epigastric pain, which was aggravated with eating, the onset of which coincided with the onset of the rash. He also noted mild diarrhea, with two episodes of dark stools since the onset of symptoms. He denied hematuria.

In the emergency department, the patient was hypertensive at 150/94 mmHg, tachycardic at 113 beats per minute, and afebrile. Physical examination was notable for numerous scattered, non-blanching purpuric papules and macules ranging from bright pink to violaceous in color on the abdomen, flanks, lower back, and bilateral upper and lower extremities (Figure 1). Scaly, erythematous plaques with scattered excoriations with blood crusting encircling the right lower leg were also noted. Labs on admission were significant for leukocytosis (white blood cell count 14.04×10^3 cells/µL), hyponatremia (sodium 134 mmol/L), elevated C-reactive protein at 129.4 mg/L, mildly elevated blood urea nitrogen at 26 mg/dL (lab reference range, 8-21 mg/dL), serum creatinine at 0.74 mg/dL, and estimated glomerular filtration rate (GFR) >90 as reported by our lab. Urinalysis noted proteinuria, 50 mg/dL, and 12 red blood cells per high power field in the sample. In addition, the patient

Figure 1. Skin findings on patient presentation in the hospital. (A) Abdomen with many scattered, non-blanching purpuric papules and macules ranging from bright pink to violaceous in color. (B) The patient’s ankles with non-blanching purpuric papules and macules. (C) Medial aspect of lower extremity with purpuric rash.
underwent computed tomography (CT) of the abdomen/pelvis with IV contrast, which was notable for mucosal wall thickening and fatty deposition within the distal ileum. The patient was admitted for further workup, with rheumatology and dermatology consulted due to concern about vasculitis.

Dermatology performed a punch biopsy of the rash and pathology demonstrated perivascular neutrophilic infiltrate and damage to vessel walls with hemorrhage and mild leukocytoclasis consistent with IgA vasculitis (Figure 2). Direct immunofluorescence showed predominant IgA deposition, as well as C3, and fibrin in the papillary vessel walls. Rheumatology evaluated the patient, and he was started on methylprednisolone 48 mg IV. Screening tests for antinuclear antibodies (ANA), complement levels, antineutrophil cytoplasmic antibody (ANCA) titers, and cryoglobulin were all negative. The urine protein-to-creatinine ratio was within normal limits. Serum IgA and other immunoglobulins were not measured. The patient’s normal creatinine and GFR levels, coupled with minimal proteinuria and hematuria, provided reassurance that renal involvement was mild. Given these findings and the confirmed diagnosis of IgA vasculitis through a skin biopsy, the decision was made to forego a renal biopsy.

The patient reported subjective improvement in rash and joint pains with the administration of methylprednisolone; however, abdominal upset persisted, and the patient had an episode of bright red blood per rectum. The patient was started on a proton pump inhibitor, and gastroenterology was consulted. The patient underwent esophagogastroduodenoscopy (EGD) and colonoscopy, which demonstrated significant necrosis in the terminal ileum with a clear transition of friable inflamed mucosa and unremarkable colonic mucosa. There were also multiple non-bleeding ulcers in the duodenum. These findings are consistent with small-vessel vasculitis involving the GI tract. The patient underwent workup for infectious GI etiologies, including stool culture, Campylobacter, and Cryptosporidium/Giardia antigen testing, with Cryptosporidium/Giardia returning with a positive result for both. Further speciation of Cryptosporidium and Giardia was not obtained.

Figure 2. (A-D) Skin biopsy of purpuric lesions which demonstrate IgA vasculitis, showing a typical finding in skin, with leukocytoclastic vasculitis. Prominent inflammatory infiltrate including neutrophils was present in the dermal capillaries, and marked, extravasated red blood cells were seen in the dermis.
The patient continued to improve and was discharged on a prednisone taper to be completed over 6 weeks starting at 60 mg daily. He was recommended to follow up with GI, dermatology, rheumatology, and nephrology. At subsequent rheumatology appointment one month after discharge, he denied any return of symptoms and creatinine and GFR remained within normal range.

**Discussion**

IgA vasculitis is characterized by a constellation of symptoms commonly involving the skin, kidneys, and GI tract. These symptoms are secondary to IgA immune complex deposition within the small vessels of these organs [2]. Biopsies of affected tissues, often skin as it is easiest to obtain, will histologically show leukocytoclastic vasculitis in postcapillary venules with IgA deposition. Palpable purpura, most notably on the lower extremities, and arthralgia/arthritis are the most common presenting symptoms in adults [1]. Renal involvement includes a spectrum ranging from mild renal abnormalities including microscopic hematuria to more severe manifestations, including nephritis and renal failure. GI symptoms such as abdominal pain, nausea, and vomiting are also common [1,2].

Our patient presented with findings consistent with classic IgA vasculitis, including a diffuse purpuric rash on bilateral lower extremities accompanied by abdominal pain, diarrhea, and migratory polyarthralgia that began a few hours after the rash developed. His renal function was normal with urinalysis being positive for microscopic hematuria. In addition, the autoimmune panel, including ANA, complement levels, ANCA titers, and cryoglobulin, were all negative, which is also consistent with IgA vasculitis. The diagnosis was then confirmed with skin and GI biopsies demonstrating the leukoclastic vasculitis pattern in small vessels with IgA complex deposition.

It is essential to acknowledge the well-established role of infectious triggering events in the development of IgA vasculitis, as substantiated by multiple studies. For instance, in a study involving 219 children with IgA vasculitis, an infectious trigger was identified in approximately 37% of cases [7,8]. Evidence of seasonal fluctuations in the incidence of IgA vasculitis further underscores the association between infections and this condition. Both adult and pediatric cases exhibit a notable increase during the winter and fall months, with a subsequent decline during the summer months. Although there is a larger body of data supporting infectious triggers in children, evidence suggests that adults are not immune to such triggers. A Korean study involving 160 patients with IgA vasculitis, including 48 adults and 112 children, noted an increased incidence of the condition during the spring and winter months in both age groups [7-9]. The distinct seasonality of this phenomenon, especially among children, may be linked to the increased prevalence of respiratory infections during the winter, as suggested by a French cohort study examining the impact of the COVID-19 pandemic on IgA vasculitis epidemiological data. It is worth noting that while there was less seasonal variation in adults, the excess risk during the winter period was elevated in both adults and children [4].

In addition, numerous case reports have identified various preceding infections as potential triggers for IgA vasculitis [7,9-11]. These infectious agents encompass a wide array of microbes, including group A Streptococcus, human parvovirus, and *Giardia*, which are commonly associated with bacterial, viral, and protozoal infections, respectively [7]. They are typically pathogens associated with respiratory or GI infections [7,10]. One aspect to consider is the abundant production of IgA in the gut-associated lymphoid tissue (GALT), making the digestive tract a significant source of IgA antibodies. A hypothesis suggesting that a dysregulation of the digestive lymphoid organs, possibly incited by the activation of the innate immune response of the digestive mucous membranes due to microorganisms, might play a pivotal role in the development of IgA vasculitis. This hypothesis was suggested in a review of IgA vasculitis authored by Pillebout and Sunderkötter. This hypothesis highlights the significance of exploring GI infections and pathogens as potential contributors to IgA vasculitis [10].

Our patient reported no prior upper respiratory symptoms or recent sick contacts. In addition, a respiratory panel including influenza, coronavirus, mycoplasma, respiratory syncytial virus, adenovirus, rhinovirus, parainfluenza, and chlamydia was negative. This makes the possibility of a respiratory source as the triggering event unlikely. Other common triggers of IgA vasculitis in adults include medications, vaccinations, and malignancy. Our patient denied recent vaccine administration, reported no new medication use, and had no overt signs of malignancy. Given this, the patient underwent further infectious testing as well as colonoscopy and EGD. Stool studies revealed a positive result for *Cryptosporidium* and *Giardia*. Although our patient only reported mild diarrhea, this is likely due to his immunocompetent state.

*Cryptosporidium* is an intracellular parasite that can cause cryptosporidiosis [12], a condition characterized by watery diarrhea, occasional nausea, vomiting, fever, and cramp-like abdominal pain [13]. Multiple species of *Cryptosporidium* exist, with *Cryptosporidium parvum* being the most common species affecting humans. While waterborne transmission is a major route, it can also be transmitted through food, anthroponotic means, and inhalation of oocysts [14-16]. Infections can range from asymptomatic shedding of oocysts to severe disease, particularly in immunocompromised individuals, while immunocompetent individuals typically experience self-limiting symptoms.
Generally, immunocompetent individuals do not require specific therapy, and supportive care is usually all that is necessary [17].

Protozoal infections, including *Giardia*, have been proposed as a trigger for IgA vasculitis [7,9]. However, our patient lacked evidence suggesting chronic giardiasis. Similarly, our patient did not have overt symptoms of cryptosporidiosis. Therefore, it is reasonable to hypothesize that neither *Giardia* nor *Cryptosporidium* alone are sufficient to trigger IgA vasculitis. We hypothesize that *Giardia*, in combination with a concurrent or superimposed additional GI infection, such as *Cryptosporidium*, led to the IgA complex formation and deposition. This is also illustrated in a case of a 73-year-old man who was diagnosed with biopsy-confirmed IgA vasculitis and subsequently tested positive for both rotavirus and *Giardia* [9]. Similarly, in our patient’s case, there was a positive presence of *Giardia* as well as *Cryptosporidium*. While it is well-established that infectious triggers can induce IgA vasculitis, there is currently no reported case of *Cryptosporidium* being identified as a trigger for this condition [7]. In addition, our patient furthered the hypothesis that additional co-infection may be required when *Giardia* is proposed as the trigger.

In addition to our patient’s presentation of *Cryptosporidium* and *Giardia* infection as a potential trigger for his vasculitis, he interestingly exhibited DVT. Notably, the patient, being a truck driver, had immobility as a known risk factor. However, the initial visit to the emergency room was prompted by a lower extremity purpuric rash, and incidentally, a DVT in the right tibial vein was discovered during the evaluation. Although thromboses are rare complications of IgA vasculitis, evidence suggests a potential link between IgA vasculitis and a prothrombotic process in genetically susceptible adults [18]. Several case reports in adults have documented the development of thromboses after developing IgA vasculitis [19-21]. This has also been observed in children as well, indicating a link between prothrombic states and IgA vasculitis [22]. These instances highlight the possibility of thrombotic events occurring in conjunction with IgA vasculitis, and further investigation is warranted to understand this association better.

Finally, most cases of IgA vasculitis are self-limited and resolve without intervention [23]. Treatment is typically supportive and includes acetaminophen or non-steroidal anti-inflammatory medications such as naproxen for arthralgias. It was previously thought that a course of corticosteroids could be used to prevent renal complications; however, a 2015 Cochrane review concluded that there was not enough evidence to support that theory [24]. The decision to treat our patient with a corticosteroid taper was based on the severity of his polyarthralgia, persistent abdominal pain, and diffuse rash. He noted rapid improvement in rash and arthralgias while abdominal pain was slower to respond.

**Conclusions**

This case report provides insight into a typical presentation of IgA vasculitis in an adult with concurrent *Cryptosporidium* and *Giardia* infection. This study highlights the relationship between infections and the development of IgA vasculitis. Notably, we present the first documented occurrence of *Cryptosporidium* with *Giardia* as potential triggering factors for this condition. Additionally, the fact that our patient exhibited acute DVT further emphasizes the significant morbidity experienced by patients affected by this condition.

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**References:**