



A Very Rare Case of Immunoglobulin A Vasculitis in an Adult with Alcoholic Liver Cirrhosis

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Keywords

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Abstract

Immunoglobulin A vasculitis, formerly known as Henoch-Schönlein purpura, is an IgA-mediated small-vessel vasculitis that predominantly affects children with an incidence of 10-20 per 100,000 per year. It is very unusual in adults; however, cirrhosis has been associated with immunoglobulin A vasculitis because of the cirrhotic liver's inability to metabolize circulating IgA complexes, resulting in systemic deposition particularly in the skin and kidney. In cirrhosis, the most common causes of acute kidney injury are those of prerenal azotemia including hepatorenal syndrome followed by intrarenal causes. Our very rare case of kidney injury in a cirrhotic patient is due to deposition of circulating IgA complexes. We present a very rare case of palpable purpura and acute kidney injury consistent with immunoglobulin A vasculitis in an adult with alcoholic cirrhosis. This patient's skin and renal findings improved with oral prednisone.

Case Presentation

A 56-year-old male presented with a two-week history of bilateral lower limb swelling with scattered pruritic, palpable purpura. He denies fever, upper respiratory symptoms or other infectious symptoms. Past medical history was significant for alcoholic liver cirrhosis and a two-month history of asymptomatic rise in creatinine from 0.76 mg/dL to 1.84 mg/dL. The patient denies recent illness, allergic reaction, or change in medication. Physical examination of the lower extremities revealed numerous 5 mm non-blanching, palpable purpura with 3+ pitting edema. Abdomen was soft, distended with a positive fluid wave, and non-tender to palpation. Complete blood count revealed thrombocytopenia (30,000 platelets/ μ L), and complete metabolic panel revealed creatinine of 2.23 mg/dL and estimated glomerular filtration rate (eGFR) of 31 mL/min/1.73 m², measured by MDRD study equation (Modification of Diet in Renal Disease).

Diagnosis & Treatment

Laboratory values showed deteriorating renal function. 24-hour urine protein showed nephrotic range proteinuria (3328 mg/24 hour), and urinalysis indicated 3+ hemoglobin with numerous red blood cells with red blood cell casts. Given the purpuric rash and hematuria with proteinuria, vasculitis was high on the differential diagnosis. Nephrology was consulted, but renal biopsy was deferred because of the risk of bleeding from thrombocytopenia.

Hepatitis B surface antigen, hepatitis C virus polymerase chain reaction, hepatitis C virus antibody, and human immunodeficiency virus antibody were all negative. ANA, anti-dsDNA, anti-MPO, and

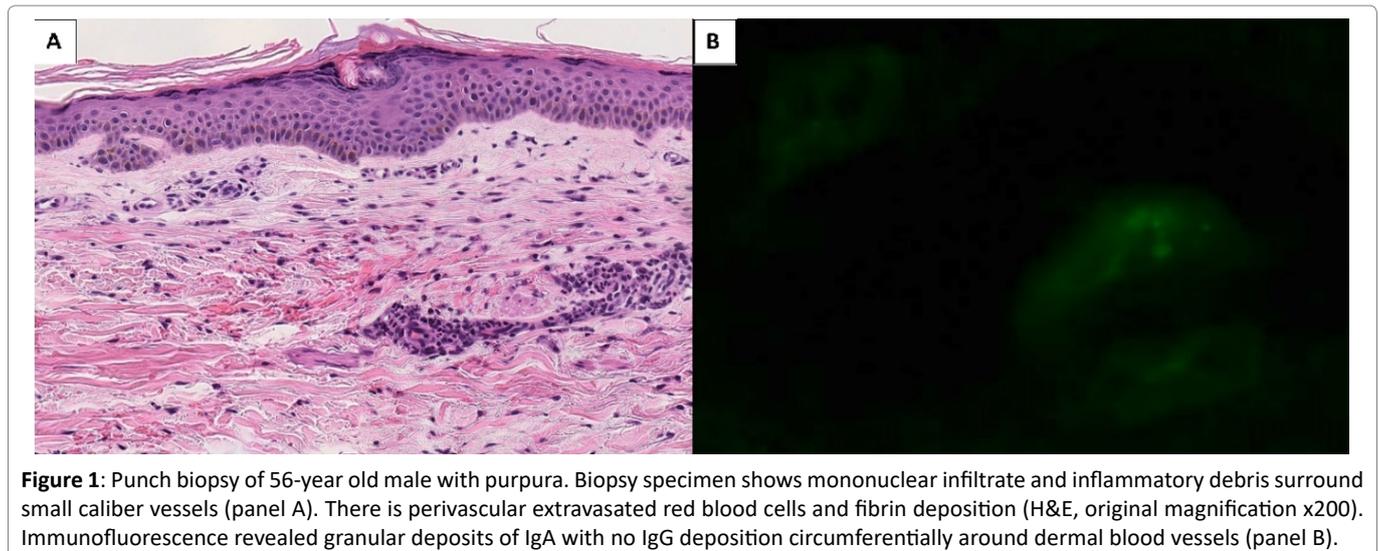


Figure 1: Punch biopsy of 56-year old male with purpura. Biopsy specimen shows mononuclear infiltrate and inflammatory debris surround small caliber vessels (panel A). There is perivascular extravasated red blood cells and fibrin deposition (H&E, original magnification x200). Immunofluorescence revealed granular deposits of IgA with no IgG deposition circumferentially around dermal blood vessels (panel B).

anti-PR3 were negative. The serum C3 level was 101.2 (normal 87-200) mg/dL and serum C4 level was 22 (normal 19-52) mg/dL.

Punch biopsy of the purpura showed extravasated erythrocytes, polymorphonuclear cells, and nuclear debris surrounding microvasculature in the dermis with sparse superficial perivascular lymphocytic infiltrate. Immunofluorescence revealed granular deposits of C3, C5b-9, C4D, IgM, and IgA with no IgG (Figure 1).

The latest criteria for diagnosing immunoglobulin A vasculitis in adults is the European League Against Rheumatism/Paediatric Rheumatology International Trials Organisation/Paediatric Rheumatology European Society (EULAR/PRINTO/PRES). This criterion has a sensitivity of 99.2% and specificity of 96% in adults^[1].

This criterion includes purpura or petechiae and one of the following four:

1. Abdominal pain.
2. Arthritis/Arthralgia.
3. Renal involvement.
4. Leukocytoclastic vasculitis with predominant IgA deposits or proliferative glomerulonephritis with predominant IgA deposits.

Our patient's purpura, renal involvement, and skin biopsy meet the diagnosis of immunoglobulin A vasculitis. The patient was started on prednisone 60 mg oral tablet daily, and his rash resolved within two weeks. At two weeks, his creatinine decreased to 1.84 mg/dL, and his eGFR rose to 38 mL/min/1.73 m². After 7 months' post-discharge, his creatinine decreased to 0.83 mg/dL, and his eGFR rose to >60 mL/min/1.73 m². Prerenal differentials like hepatorenal syndrome are less likely because of his skin findings and improvement in kidney function with prednisone.

Discussion

Cirrhosis prevalence is approximately 630,000 people in the United States^[2] and is expected to rise because of rising 5-year survival rates. Prerenal azotemia like hepatorenal syndrome is high on the differential for acute kidney injury in cirrhosis. Intrarenal causes like immunoglobulin A vasculitis is a rare manifestation of cirrhosis and has been reported in only thirteen cases. Each case presented with varying levels of dermal, renal, and gastrointestinal involvement (Table 1). The causes of cirrhosis in twelve cases include viral hepatitis, primary biliary cirrhosis, alcohol, and medication use. Cirrhosis leads to decreased clearance of serum IgA and results in dermal, renal mesangial and gastrointestinal IgA deposition^[3]. Coexisting cirrhosis and IgA glomerular deposition can be unrelated; however, the incidence of glomerular IgA deposition is up to 50%-100%, arguing for a possible association between the two diseases^[4]. In addition, animal models show liver injury leads to increased serum IgA, IgA immune complexes, and IgA deposition in mesangial deposition^[5]. To date there are no treatment guidelines for adults with immunoglobulin A vasculitis.

The differential for rash in our patient includes thrombocytopenic petechiae, immunoglobulin A vasculitis, or cryoglobulinemia. Biopsy showed dermal extra-capillary IgA deposition consistent with immunoglobulin A vasculitis. Van de Wiel et. al. reported 68% of cirrhosis patients presented with immune complex deposition in the dermis; however, very few presented with purpura. 87% of those with measurable IgA-containing immune complexes (CIC) in serum demonstrated IgA skin deposits, whereas 53% of those without IgA CICs in serum had IgA skin deposits^[6]. Of the thirteen reported cases of immunoglobulin A vasculitis in cirrhosis patients in literature, twelve cases presented with a purpura and one presented with a non-descript skin rash. Patients often seek medical care because of acute skin changes

Table 1. Reported cases of immunoglobulin A vasculitis in patients with liver cirrhosis.

First Author	Age	Sex	Cause of Cirrhosis	Presenting Symptoms	Treatment	Outcome
Ogawa et. al. (1995) ^[12]	56	M	Hepatitis C Virus	Purpuric rash + proteinuria and hematuria	Plasmapheresis + corticosteroids	Deceased
Madison et. al. (2002) ^[13]	63	M	Hepatitis C Virus	Purpuric rash + hematuria + abdominal pain	Corticosteroids	Deceased
Akizue et. al. (2017) ^[14]	62	M	Hepatitis B Virus	Purpuric rash + proteinuria and hematuria + abdominal pain	Corticosteroids	Resolved
Aggarwal et. al. (1992) ^[15]	63	F	Not specified	Purpuric rash + hematuria, proteinuria, and oliguria	Hemodialysis	Unresolved
Fleischman et. al. (2017) ^[16]	52	M	Not specified	Purpuric rash + oliguria and proteinuria + abdominal pain	Corticosteroids	Progressive kidney failure
Miret Mas et. al. (2003) ^[17]	46	M	Alcohol	Purpuric rash + proteinuria, hematuria, proteinuria	Not specified	Not specified
Jung et. al. (2016) ^[18]	54	M	Alcohol	Skin rash + proteinuria + abdominal pain	Hemodialysis	Resolved
Gweon et. al. (2019) ^[19]	42	M	Alcohol	Petechial rash + proteinuria and hematuria + abdominal pain	Corticosteroids	Resolved
Gupta et. al. (2015) ^[3]	58	M	Alcohol	Purpuric rash + proteinuria and hematuria + abdominal pain	Corticosteroids + hemodialysis	Deceased
Gatselis et. al. (2007) ^[20]	71	F	Primary Biliary Cirrhosis	Purpuric rash + proteinuria and hematuria + abdominal pain	Corticosteroids	Resolved
	72	F	Primary Biliary Cirrhosis	Purpuric rash	None	Resolved
Mu et. al. (2018) ^[21]	12	M	Drug-Induced	Purpuric rash + abdominal pain	Corticosteroids + umbilical cord-derived Mesenchymal Stem Cell transplant	Resolved with transplant
Kitamura et. al. (2006) ^[22]	66	M	Hepatitis C Virus	Purpuric rash	Corticosteroids	Resolved

*Robeva, Joerg, Korting, Bolliger, Galeone have published work regarding immunoglobulin A vasculitis in cirrhosis patients as well.

since many other symptoms of immunoglobulin A vasculitis, including hematuria, proteinuria, and abdominal pain, can be missed, misattributed to cirrhosis, or non-descript.

Hepatic disease is associated with glomerular lesions, most commonly membranous nephropathy, crescentic glomerulonephritis, proliferative and exudative glomerulonephritis, and hepatic IgA glomerulonephritis. Hepatic IgA glomerulonephritis results from IgA deposition; however, it rarely produces nephritic urinary sediment unlike primary or purpuric IgA glomerulonephritis^[7]. Our patient has demonstrated marked hematuria and proteinuria in addition to skin involvement. The severity of IgA nephropathy in immunoglobulin A vasculitis varies widely; however, severity of renal involvement is the most important long-term prognostic factor^[8]. Immunoglobulin A vasculitis nephritis with nephrotic syndrome is more likely to progress to end-stage renal disease and has a worse outcome than immunoglobulin A vasculitis nephritis alone^[9]. Ten cases reported hematuria, proteinuria, or oliguria consistent with immunoglobulin A vasculitis nephropathy. Eight of the ten cases presented with hematuria, seven of which exhibited concomitant nephrotic syndrome. In this patient with proteinuria and hematuria, immunoglobulin A vasculitis caused a prolonged acute kidney injury, one that began three months prior to admission without any respiratory illness and ended seven months after admission.

While this patient did not report gastrointestinal (GI) symptoms, the presence of gastrointestinal disease, including perforation and hemorrhage is the most important determinant of length of hospital admission^[10]. Eight cases presented with GI complaints.

Immunoglobulin A vasculitis is a self-limiting disease with average symptom duration of 4-6 weeks. Early use of glucocorticoids has not been shown to reduce the risk of renal or gastrointestinal involvement; however, use of prednisone has been shown to help resolve abdominal pain and rash in a previous case report^[11]. In patients with cirrhosis and immunoglobulin A vasculitis, five of the eight patients treated with corticosteroids had resolution of symptoms; other patients did not survive because of their decompensated gastrointestinal pathology.

Conclusion

Cirrhosis is commonly associated with purpuric rash and usually attributed to thrombocytopenic petechiae. In the presence of renal insufficiency with hematuria and proteinuria, a clinician should consider immunoglobulin A vasculitis in the differential diagnosis even in the absence of any respiratory illness.

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