Case Report

Steroid-Dependent Recurrent IgA Vasculitis in a 19-Year-Old Woman

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Abstract

Background
Immunoglobulin A (IgA) vasculitis is common in children and typically resolves spontaneously. However, when presenting in adults, it is more likely to be severe and recurrent.

Case Presentation
We present the case of a 19-year-old female patient with recurrent steroid-dependent IgA vasculitis. She had a history of a prolonged episode of IgA vasculitis in childhood. She presented to our hospital with proteinuria and a painful, palpable purpuric rash on her bilateral lower extremities. She was treated with high-dose intravenous steroids. When steroids were tapered, the patient had a recurrence of her painful rash. Over several months, she developed steroid-induced hyperglycemia and worsening proteinuria.

Conclusion
Recent studies have shown that corticosteroids have limited effect on long-term outcomes in IgA vasculitis, but steroid-sparing agents have potential for the treatment of recurrent steroid-dependent IgA vasculitis.

Keywords
immunoglobulin A; IgA; corticosteroids; prednisone; methylprednisolone; drug therapy; adults; case reports

Introduction
Immunoglobulin A (IgA) vasculitis, formerly called Henoch-Schönlein purpura, is the most common form of vasculitis in children, with greater than 90% of cases occurring in patients less than 10 years old.[1] IgA vasculitis is a small-vessel vasculitis mediated by IgA and its complexes in the vessel walls, though pathogenesis remains poorly understood.[2] A diagnosis requires the mandatory criteria of purpura or petechiae with lower limb predominance and a minimum of 1 out of 4 other criteria: diffuse abdominal pain with acute onset, histopathology showing leukocytoclastic vasculitis or proliferative glomerulonephritis with predominant IgA deposits, acute onset arthritis or arthralgia, or renal involvement with proteinuria or hematuria.[3] While the disease is typically self-limiting, relapses can occur, with infection being a common trigger. Presentations of recurrent IgA vasculitis typically involve the skin, but arthralgias, renal damage, and gastrointestinal symptoms are also common. Hypertension can be present at disease onset or during recovery. Nephritis at presentation is indicative of an increased risk of hypertension over the following years.[1] Treatment is typically supportive care with hydration and oral acetaminophen or nonsteroidal anti-inflammatory drugs for arthralgias as 89% of cases in adults resolve spontaneously; however, renal involvement necessitates further consideration. While high-dose intravenous (IV) steroids are used for glomerulonephritis and severe renal disease, recent evidence suggests steroids have a

greater effect on extrarenal symptoms than on renal manifestations.[1,3] The role of steroid-sparing immunomodulatory drugs is currently under investigation, and some reports indicate these drugs can successfully decrease steroid use in IgA vasculitis. Here we present a case of a young woman with recurrent IgA vasculitis and renal involvement who required continuous steroid use to prevent relapse.

Case Presentation

A 19-year-old woman was diagnosed 4 years prior with IgA vasculitis. At 15 years old, she presented with a rash starting on her legs that progressed to other areas of her body. She also had lower extremity swelling, arthralgias, and abdominal pain. A skin biopsy confirmed the diagnosis of IgA vasculitis. She required 5 days of hospitalization, treatment with high-dose steroids, and continued steroid injections after discharge. The steroid tapering proved difficult as the rash would return when steroids were tapered too quickly.

On admission to our hospital at age 19, the patient presented after 2 days of painful, pruritic papular rash, which began on her bilateral ankles and lower calves, spread up her calves, and developed background erythema. Her pain initially improved with ibuprofen but later became uncontrolled. Associated symptoms included arthralgias, severe bilateral achy headache, weakness, fatigue, chills, nausea, and diffuse crampy abdominal pain. She had an episode of diarrhea 3 days prior as well as a minor cold.

Upon physical examination, she had dark red, palpable purpura and a confluence of background erythema over her bilateral lower extremities below the knee with excruciating pain on palpation (**Figure 1**). Her abdomen was soft and nondistended with diffuse tenderness to palpation. Her vitals were within normal limits.

Her bloodwork was significant for leukocytosis of 11.6 x 10^3/µL. Although her creatinine was normal at 0.7 mg/dL, she had trace proteinuria and moderate hematuria. Nasal swabs were negative for influenza and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Her computed tomography (CT) scan of abdomen and pelvis was without acute findings. Further autoimmune workup included negative antinuclear antibody, c-antineutrophil cytoplasmic antibody, p-antineutrophil cytoplasmic antibody, proteinase 3, myeloperoxidase antibody, and reticulin IgG antibodies. Complement 3, complement 4, erythrocyte sedimentation rate, and c-reactive protein were within normal limits.

The patient was treated with intravenous (IV) methylprednisolone of 60 mg every 8 hours. Nephrology was consulted and determined

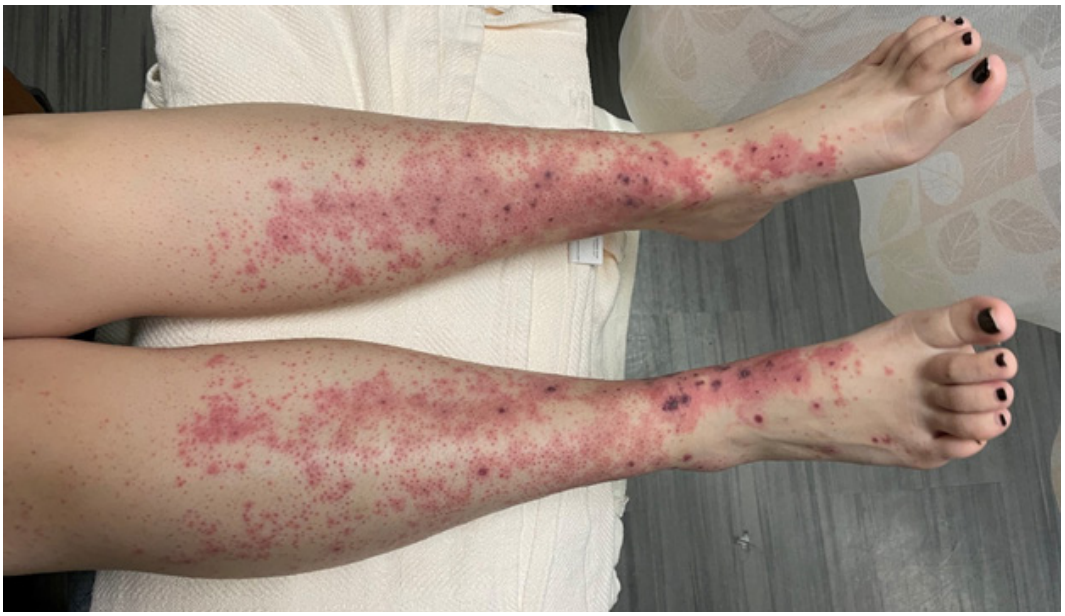

Figure 1. Findings on a physical exam of the patient's legs showed dark red palpable purpura and a confluence of background erythema over the bilateral lower extremities below the knee.

that microscopic hematuria was most likely glomerular in source secondary to IgA involvement. Rheumatology was consulted and recommended oral prednisone 40 mg twice daily until her follow-up in a week. No biopsy was warranted given the prior diagnosis with a skin biopsy. Her hospitalization lasted 5 days. On discharge, she had trace proteinuria and trace hematuria. Her creatinine was 0.6 mg/dL. Her rash was very mild and located only on the bilateral lower extremities.

The patient returned to the hospital 9 days later with a worsening rash that had spread to the plantar aspect of the bilateral feet and to the posterior bilateral upper extremities. Upon examination, she had bilateral lower extremity non-blanching palpable purpura with blistering and ulceration noted to medial aspects of lower extremities, and the coalescing of the rash on the soles of her feet. Her abdomen was non-tender. Her respiratory rate and oxygen saturation were within normal limits, but she was tachycardic and had a blood pressure of 132/72 mmHg. Her white blood cells were 18.2 x 10^3/µL. While her creatinine remained within normal limits at 0.8 mg/dL, her urinalysis showed 100 mg/dL proteinuria, and 500 mg/dL urine glucose. Cryoglobulins were added to her previous workup and were negative.

The patient was initially treated with a methylprednisolone IV of 60 mg every 8 hours for 3 days. An attempted transition to oral prednisone 40 mg twice daily was stopped due to increased pain despite visual improvement in the rash. She was continued on a hydrocortisone IV of 60 mg every 8 hours until discharge. She had 2 blood glucose readings over 200 mg/dL and a glycosylated hemoglobin of 5.9%. Therefore, she was started on metformin for steroid-induced hyperglycemia. She was discharged on oral prednisone 40 mg twice daily, 500 mg metformin twice daily, with a plan to follow up with rheumatology in 2 weeks for management of possible steroid-sparing medications. However, she did not follow up with a rheumatologist, and her IgA vasculitis was managed by her primary care provider.

Two months later, the patient presented to the ED after 3 days of painful pruritic purpuric rash over her lower extremities, nausea, vomiting, diarrhea, headache, and abdominal cramping. She had run out of prednisone a few days prior. SARS-CoV-2 testing was positive. A CT scan of her abdomen and pelvis showed no acute findings, but some mild hepatomegaly was noted. Urinalysis showed greater than 300 mg/dL protein, greater than 50 red blood cells per high-powered field, 5-10 white blood cells per high-powered field, and a few bacteria noted. She received a single dose of methylprednisolone IV 62.5 mg and was discharged with prednisone, an antiemetic, and an antibiotic for a possible urinary tract infection.

Discussion

We present a patient with recurrent IgA vasculitis requiring a slow taper of steroids to prevent relapse. The clinical course of IgA vasculitis in adults has a higher risk of severe symptoms and renal involvement with recurrence happening in approximately 20% of cases.[4,5] Our patient was first diagnosed with IgA vasculitis when she was a 15-year-old pediatric patient with her first recurrence as an adult at 19 years old. She was above the mean age of diagnosis in children, 6 years, and below the median age of onset in adults, 50 years.[4] Thus, it is difficult to determine if she had a relapse of a pediatric presentation or if she had an early-onset adult presentation. Renal manifestations are more common in adult presentations with about 75% of patients having proteinuria, hematuria, or red blood cell casts.[4] While pediatric patients typically require only symptomatic treatment, approximately 11% of adults will require additional treatment, particularly given the higher risk of end-stage renal disease.[3,4]

Corticosteroids are frequently used when IgA vasculitis is not responsive to symptomatic treatment or when glomerulonephritis is present, but recent evidence has called their role into question.[1,3] In 2015, a Cochrane review examined 5 randomized controlled trials on the benefit of corticosteroids in the treatment of renal involvement in IgA vasculitis, with no studies showing any benefit.[6] In our patient, an initial urinalysis showed trace proteinuria and on her subsequent visits she had increased proteinuria, 100 mg/dL 9 days after initial discharge and 300 mg/dL 2 months later, despite near constant corticosteroid use. Although steroid-use improved her pain and her rash, it did not benefit her proteinuria, which supports

prior studies on the utility of corticosteroids treatment of IgA vasculitis.[1,3,4]

Additionally, steroids have significant risks, including hyperglycemia and hypertension.[7] Our patient was seen multiple times with symptom recurrence after stopping or decreasing corticosteroids. Over the course of these visits, she developed leukocytosis, hyperglycemia, and an increase in systolic blood pressure from the 120s mmHg to the 130s mmHg. Her hyperglycemia required treatment with metformin, and her glycosylated hemoglobin was 5.9%, placing her in the pre-diabetic range and at a high risk of developing diabetes mellitus. Her hypertension could be due to either steroid use or a symptom of her IgA vasculitis.

Recent studies have demonstrated potential for the use of steroid-sparing agents in treating severe, recurrent, or steroid-dependent IgA vasculitis, which would provide benefits in decreasing steroid-related side effects. Multiple studies have demonstrated that rituximab is a safe and effective option for treatment of refractory IgA vasculitis, though no studies have compared rituximab directly to corticosteroids. One study examined adults with refractory or relapsing IgA vasculitis who received rituximab followed by no maintenance therapy. At 2 years, 90% of patients had achieved remission and had a significant reduction in proteinuria and in glucocorticoid dose.[8] One retrospective analysis on children with IgA vasculitis concluded that rituximab successfully reduced the number of hospital admissions and corticosteroid burden.[9] A case report on a patient similarly aged to ours, a 20-year-old man with gastrointestinal involvement and multiple relapses, showed treatment with rituximab was able to reduce his prednisone use to 5 mg daily.[10] As our patient was requiring 40 mg twice daily doses of prednisone to maintain remission, a reduction to only 5 mg daily would benefit her significantly. Rituximab shows promise at reducing steroid use and proteinuria, but additional studies are needed to determine if its use can replace steroids or only reduce their dosage.

A potential steroid-sparing agent with less definitive evidence is cyclosporin A. A randomized controlled trial compared cyclosporin A treatment to steroid treatment over 12 months and saw faster improvement in proteinuria in the cyclosporine A group. Additionally, the cyclosporin A group required no additional immunosuppressive treatment after 1 year, whereas 46% of patients in the steroid group required additional treatment.[11] While this trial supports the use of cyclosporin A in place of steroid treatment, all the patients in the study were pediatric with a mean age of 9.4 years. Therefore, more studies are needed to determine the role of cyclosporin A in steroid-dependent IgA vasculitis, particularly in adults.

Other therapies without a significant body of evidence to support their use are cyclophosphamide, mycophenolate mofetil, and azathioprine. A randomized controlled trial on 54 adults with severe IgA vasculitis showed no difference in remission rate or proteinuria level when comparing glucocorticoid use to cyclophosphamide and glucocorticoids together, but individual case reports have shown promise.[12,13] Mycophenolate mofetil may lower relapse rates and proteinuria as demonstrated in 1 retrospective and a single prospective study.[14,15] Observational evidence indicates that azathioprine in combination with glucocorticoids in children may be more effective at achieving clinical remission and reducing proteinuria than glucocorticoids alone, but no studies have been completed in adults.[16-18]

Given the complex and changing landscape of evidence regarding steroid-sparing treatment options, patients with recurrent or steroid-dependent IgA vasculitis would benefit from regular follow-ups with a rheumatologist who can prescribe and manage these medications. Continuous steroid use, particularly at high doses, can lead to many complications and increase patient morbidity. Therefore, thoughtful consideration should be given to continued corticosteroid use even in a patient with seemingly steroid-dependent recurrent IgA vasculitis. Additionally, patients should be assessed to determine if there are any social barriers to care and engage case management to assist in addressing any concerns.

Conclusion

Research on the treatment of IgA vasculitis has been predominantly conducted in children, and this case highlights the need for continued research into the treatment of IgA vasculitis in adults. Adults with steroid-dependent recur-

rent IgA vasculitis are at greater risk of developing renal dysfunction, and corticosteroids have not proven effective at improving renal function. Given the risks associated with continued steroid use including hyperglycemia and hypertension, patients who are being maintained on steroids for recurrent IgA vasculitis would benefit from following up with a rheumatologist for initiation and management of steroid-sparing medications.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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