CASE REPORT

CE 1.0 Contact Hour

Immunoglobulin A Vasculitis Case Report

Kristin Mannke and Madeleine Maguire

ABSTRACT: Immunoglobulin A (IgA) vasculitis, also known as Henoch–Schönlein purpura, is a type of cutaneous small-vessel vasculitis. IgA vasculitis typically presents with nonblanching, palpable purpura favoring dependent sites and areas of trauma (Bolognia et al., 2014). In some cases, IgA vasculitis is associated with systemic disease—most commonly, kidney injury. Nevertheless, most cases of IgA vasculitis are self-limiting, and the disease resolves over weeks to months (Bolognia et al., 2017).

Key words: IgA Vasculitis, Palpable Purpura, Small-Vessel Vasculitis, Vasculitis

CASE REPORT

A 22-year-old woman developed red macules on the trunk and lower extremities after completing a course of dicloxacillin for mastitis. The patient was evaluated at an outside emergency department where serum laboratory markers were unremarkable and urinalysis suggested a urinary tract infection despite lack of symptoms. She was prescribed cephalexin and was referred to dermatology for further evaluation.

At dermatology, the patient presented with numerous, 2- to 9-mm purpuric papules and plaques, the largest lesions with central bullae or necrotic crusts. Most of the purpuric papules and plaques were distributed over the lower legs and ankles and involved pressure points such as the elbows and sock line. There was also mild involvement of the proximal thighs and abdomen and sparing of the neck, face, palms, and soles. The buccal mucosa and gingiva were clear, and there was no exudate or edema of the pharynx. There was one solitary vesicle on the right upper palate.

Upon review of systems, the patient reported mild abdominal pain and diarrhea since onset of the rash. She also reported atraumatic left ankle pain and swelling but denied any other joint involvement. She denied nausea, vomiting, fever, chills, cough, shortness of breath, dysuria, hematuria, or sick contacts. She did endorse recent mastitis and asymptomatic urinary tract infection.

Her past history was unremarkable with no history of kidney or liver disease and no personal or family history of autoimmune disease. Her only recent medications were dicloxacillin and cephalexin, both of which were started at the onset of the rash. She did not use any topical treatments

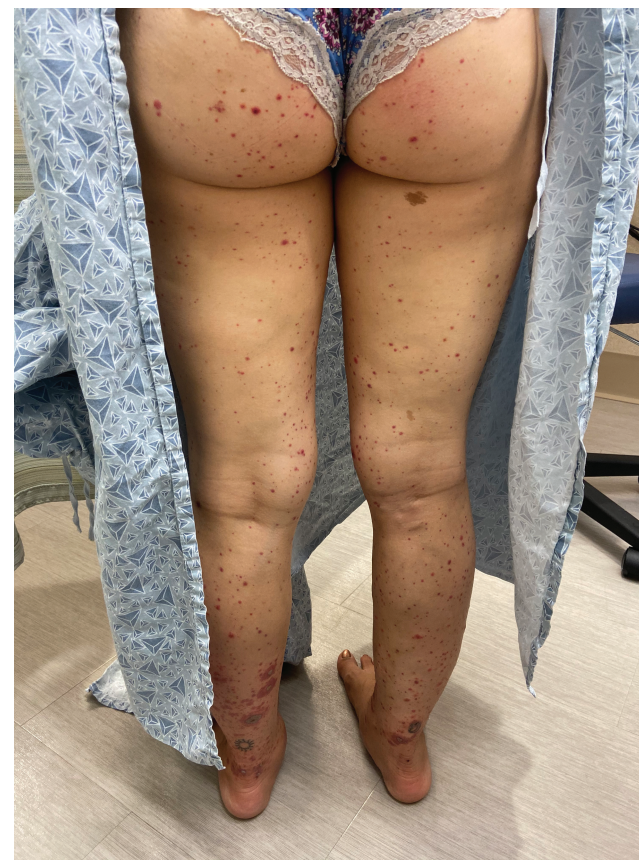

FIGURE 1. Palpable purpura.

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FIGURE 2. Palpable purpura distributed over pressure points of the sock line.

for the rash. She works as a server in a diner and lives with her boyfriend and her two young children. She is not currently pregnant and continues to breastfeed her 1-year-old.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for this case include small-vessel vasculitis, small-to-medium vessel vasculitis, and medium-vessel vasculitis as well as infectious causes. Given the hallmark finding of palpable purpura, which is characteristic of small-vessel disease, the favored diagnosis in this case is a small-vessel vasculitis. Small-vessel vasculitides present as nonblanching, red-to-purple papules that favor dependent sites and areas of trauma (e.g., Koebner phenomenon or pressure from tight clothing). However, lesions may initially be nonpalpable, partially blanching or urticarial macules, which are often asymptomatic but may be associated with pruritus, burning, or pain (Bolognia et al., 2014). Types of small-vessel vasculitides include leukocytoclastic vasculitis (LCV), IgA vasculitis or HSP, urticarial vasculitis, microscopic polyangiitis, and erythema elevatum diutinum.

Mixed or small-to-medium vessel vasculitides include the antineutrophil cytoplasmic antibody (ANCA)-positive vasculitides such as Wegener's granulomatosis, Churg–Strauss syndrome, and microscopic polyangiitis (Alikhan & Hocker, 2017). Mixed vasculitis presents with a mixture of small-vessel vasculitis and medium-vessel disease. Clinical presentation includes livedo reticularis, retiform purpura, ulcers, and subcutaneous nodules. Mixed vasculitis should be considered especially if there is renal and/or pulmonary involvement. Medium-vessel vasculitides include polyarteritis nodosa and Kawasaki's disease. Clinical features include subcutaneous nodules, livedo reticularis, retiform purpura, and ulcers (Alikhan & Hocker, 2017). This patient did not have clinical findings suggestive of mixed or medium-vessel pathology.

Finally, consideration of an infectious cause of purpura, such as meningococcemia or Rocky Mountain spotted fever, is warranted given the significant morbidity and mortality associated with these diseases. Meningococcemia presents with palpable purpura, often of the lower legs, in a toxic-appearing patient. Classically, Rocky Mountain spotted fever presents with petechial rash of the palmar hands (Bolognia et al., 2014).

INVESTIGATIONS

The goals of the workup for small-vessel vasculitis are to elucidate the underlying cause and evaluate for systemic involvement. Hematoxylin and eosin and direct immunofluorescence tissue biopsies, as well as serum laboratory studies, are obtained. The biopsy specimen is evaluated for the presence of perivascular neutrophilic infiltrate within the small vessels, and direct immunofluorescence examines for specific immunoglobulin and complement deposition within

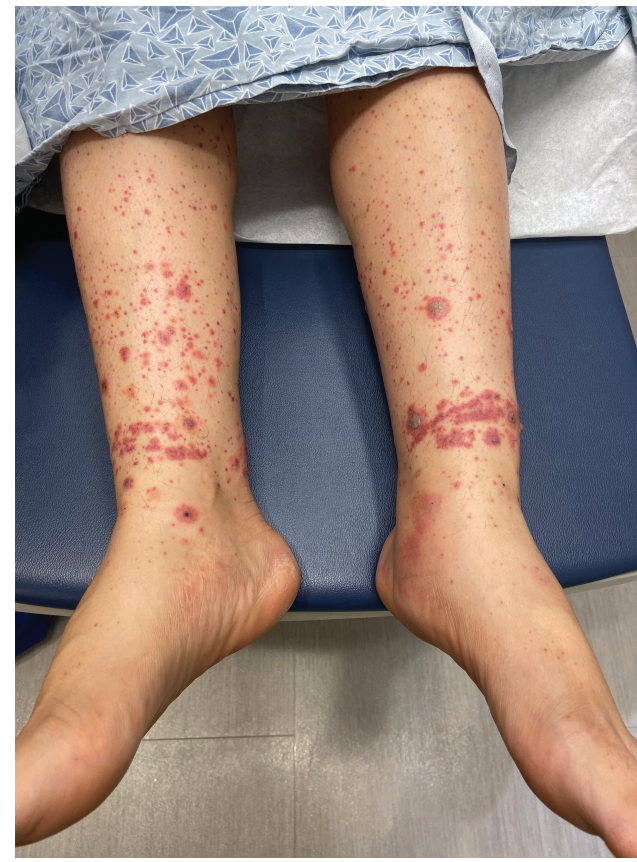

FIGURE 3. Palpable purpura with overlying bullae.

the vessel walls. In IgA vasculitis, there is IgA predominance (Bolognia et al., 2017), whereas complement component 3 (C3) is present in IgA vasculitis, LCV, and urticarial vasculitis. Tissue biopsies are ideally less than 24 hours old, as after 48 hours, pathology may show mononuclear cells rather than neutrophils within the infiltrate, rendering the tissue specimen nonspecific (Alikhan & Hocker, 2017). Interestingly, an absence of eosinophils on skin biopsy in adult patients with IgA suggests a threefold increase in the risk of renal involvement (Poterucha et al., 2013).

In 50% of cases of small-vessel vasculitis, the cause is idiopathic. However, the remaining 50% of cases are triggered by secondary causes such as infection, inflammation, autoimmune disease, drug reaction, or neoplastic disorder (Alikhan & Hocker, 2017). Therefore, serum laboratory investigation is an important adjunct to thorough history, physical examination, and tissue biopsy when suspecting cutaneous small-vessel vasculitis.

Complement levels (including C3 and C4), antinuclear antibodies (ANAs), and rheumatoid factor (RF) are obtained to evaluate for autoimmune causes such as rheumatoid arthritis, Sjogren's syndrome, and systemic lupus erythematosus. If present, results will show hypocomplementemia and positive ANA and RF. A complete blood count is done to examine for peripheral eosinophilia, as in Churg–Strauss syndrome. Urinalysis evaluates for proteinuria and/or hematuria, as in the case of kidney injury. Of note, normal or minimal hematuria or proteinuria is not a sufficient prognostic indicator for the development of long-term renal impairment (Baumrin et al., 2020). Therefore, laboratory should be checked at intervals. Elevated blood urea nitrogen and creatinine indicate kidney involvement. Elevated liver enzymes (such as aspartate aminotransferase and alanine aminotransferase) indicate liver involvement. To rule out the possibility of mixed and medium-vessel ANCA-positive vasculitides, an ANCA is checked. Laboratory markers for Hepatitis B, Hepatitis C, HIV, and a serum titer for streptococcal infection may be checked depending on the degree of suspicion for an infectious trigger. Finally, concern for malignancy warrants a serum protein electrophoresis and urine protein electrophoresis and/or a chest x-ray. In adult IgA vasculitis, underlying malignancy is often hematologic in nature rather than a solid organ tumor. When IgA vasculitis does involve solid organ neoplasm, it is most often lung (Bolognia et al., 2017).

Treatment of cutaneous small-vessel vasculitis involves three main components: treating skin disease, monitoring and treating systemic disease, and decreasing the risk of complications (Bolognia et al., 2014). Patients with mild symptoms can be treated with supportive measures, such as leg elevation and nonsteroidal anti-inflammatory medication for pain (Bolognia et al., 2014). Systemic corticosteroids alone or in combination with azathioprine or cyclosporine are prescribed for abdominal pain, arthritis (which would indicate systemic involvement), and severe nephritis (Alikhan & Hocker, 2017). Many clinicians describe rapid symptomatic improvement in patients treated with oral corticosteroids. However, although glucocorticoids may address inflammation, they do not appear to alter long-term clinical outcomes of IgA vasculitis (Dedeoglu & Kim, 2019) and may not prevent renal disease or its sequelae (Bolognia et al., 2014). In addition, patients treated with corticosteroids for severe abdominal pain require close monitoring because these medications can mask signs and symptoms of internal organ injury associated with IgA vasculitis. Glucocorticoids should be tapered over the course of 4–8 weeks to mitigate adrenal suppression and to prevent rebound of inflammation (Dedeoglu & Kim, 2019).

Alternative treatments for IgA vasculitis include histamine-2 receptor blockers, such as ranitidine, to decrease the severity and duration of abdominal pain. Intravenous immunoglobulin may be considered if glomerulonephritis is rapidly progressing (Alikhan & Hocker, 2017). In patients with recalcitrant IgA vasculitis, treatment with antineutrophilic medications such as dapsone or colchicine may be beneficial (Dedeoglu & Kim, 2019). In adult-onset IgA vasculitis, rituximab appears well tolerated and may induce remission and allow for corticosteroid tapering (Maritati et al., 2018).

DISCUSSION

The biopsy from the left inner thigh revealed IgA vasculitis, evidenced by the deposition of IgA and C3 in a vascular pattern within the papillary dermis (Bolognia et al., 2017). Fortunately, the patient's renal and liver panel, complete blood count, complement levels, and ANCA were within normal limits. On the basis of her uncomplicated history and negative review of systems, laboratory diagnostics including RF, ANA, Hepatitis B and C, HIV, and malignancy testing were omitted from the workup. Surprisingly, her urinalysis did reveal bacteriuria, leukocytes, and leukocyte esterase (despite lack of symptoms and previous treatment with antibiotics), which suggested cystitis. The urinalysis lacked proteinuria or hematuria, which might otherwise heighten concern for nephritis (Baumrin et al., 2020). Because of her ankle arthritis, mild diarrhea, abdominal discomfort, and purpura above the waistline—which suggested systemic involvement— she was prescribed a prednisone taper (safe in breastfeeding), which started at 40 mg per day and decreased to 10 mg per day over the course of 3 weeks (St John et al., 2018).

On the basis of history, physical examination, tissue biopsy, and laboratory workup, this case was consistent with adult IgA bullous vasculitis with mild systemic involvement. The vasculitis was likely triggered by an asymptomatic urinary tract infection. The antibiotic dicloxacillin was considered as a potential trigger, but given that the onset of the rash was the same day as the first dose, this appeared very unlikely. A 5-day course of nitrofurantoin (considered safe in breastfeeding) was prescribed to treat the suspected cystitis. The patient completed the prednisone taper and returned to dermatology 14 days later for follow-up. She denied new lesions within the week and fading of the lesions on

the trunk and lower legs. The patient was then asked to return in 3 months to evaluate for complete resolution of palpable purpura and to reassess kidney function. In roughly 30% of adult patients with IgA vasculitis, there is progression to renal insufficiency (Pillebout et al., 2002); therefore, serial laboratory are almost always warranted.

CONCLUSION

The differential diagnosis of palpable purpura includes (from most common to least common) LCV, IgA vasculitis or HSP, urticarial vasculitis, microscopic polyangiitis, and erythema elevatum diutinum. In cases of IgA vasculitis, identifying potential triggers (such as infection, autoimmune disease, or malignancy) and evaluating for systemic involvement (in particular, kidney involvement) are key components of management. In 90%–95% of IgA cases, the patient will remain disease free (Bolognia et al., 2017). ■

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