Concurrent pulmonary coccidioidomycosis and immunoglobulin A vasculitis with hemorrhagic bullae

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INTRODUCTION

Immunoglobulin A vasculitis (IgAV), formerly known as Henoch-Schönlein purpura, is a small-vessel vasculitis characterized by histopathologic features of IgA1-predominant immune complex deposition primarily in the small-vessel walls of the skin, gastrointestinal tract, and kidneys.[1,2] This pattern of multiorgan system involvement manifests clinically with classic IgAV presenting as palpable purpura, abdominal pain, hematuria, and arthralgias.[3] IgAV is considered rare among adults, with an estimated annual incidence of 1-1.5/100,000.[3] Antecedent respiratory infection is commonly described and considered a precipitating risk factor for IgAV.[3,4] The occurrence of IgAV following a fungal infection has not been well documented in the literature or has been underreported. The fungal species of the genus *Coccidioides* is the pathogenic cause of pulmonary coccidioidomycosis and endemic to southwestern United States.[5] Here, we report a unique presentation of IgAV in an adult patient with extensive hemorrhagic bullae and concurrent pulmonary coccidioidomycosis.

Abbreviation used:

IgAV: immunoglobulin A vasculitis

CASE REPORT

A 58-year-old Caucasian man with a history of untreated ankylosing spondylitis presented to an outside emergency department with a 1-week history of dry cough, mild fever, and painful skin lesions. Two days prior, he had reported the onset of a rash on the upper portion of his thighs, which spread distally to the lower portion of his legs. At presentation, he was afebrile, hemodynamically stable, and mildly tachycardic (107 beats/min). Initial laboratory studies revealed an erythrocyte sedimentation rate of 26 mm/h, a high-sensitivity C-reactive protein level of 170.87 mg/L, a white blood cell count of 5800/μL, a platelet count of 287,000/μL, a creatinine level of 1.17 mg/dL, and a hemoglobin-A1c level of 9.3%. Results of his urinalysis revealed a red blood cell count of 5-10 per high power field and 3+ glucosuria. Computed tomography imaging of his chest demonstrated a 26-mm intrapulmonary abscess in the upper portion of the right lobe (Fig 1). Due to concern for necrotizing pneumonia, he was initiated on empiric antibiotics and admitted for further evaluation. On day 2 of his hospitalization, severe colicky abdominal pain developed in the patient, with distention and obstipation. Abdominal computed tomography imaging demonstrated dilated small bowel loops and distal small bowel-wall thickening. He was transferred to our tertiary hospital on the third day of admission for dedicated specialty evaluation.

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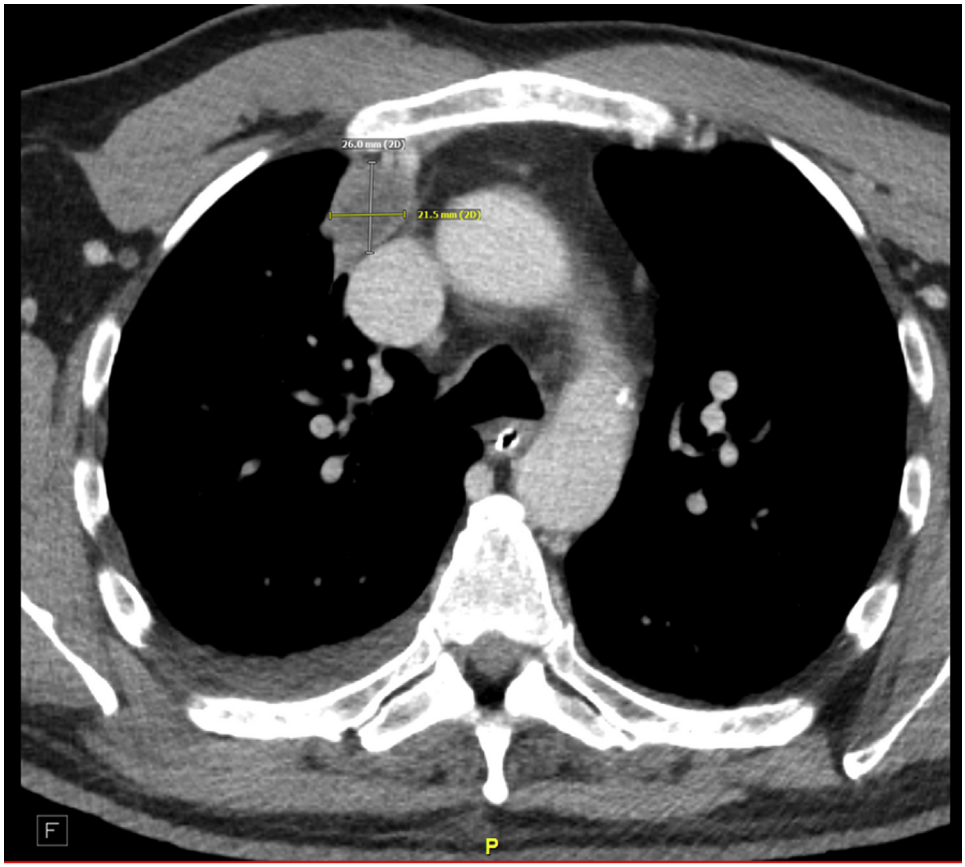

Fig 1. Contrast-enhanced computed tomography of the chest revealing an intrapulmonary rim-enhancing abscess (26 × 21.5 × 24 mm) observed in the medial aspect of the upper portion of the right lobe, adjacent to the anterior mediastinum.

Upon our evaluation, skin examination revealed nonblanching palpable purpura and petechiae on the lower portion of his back, arms, and legs. From the proximal aspect of his thighs, the palpable purpuric lesions coalesced distally into contiguous erythematous plaques with interspersing ecchymoses and ulcerations, which were most prominent on the lower portion of his legs (Fig 2, *A* to *C*). Scattered upon this ecchymotic and erythematous base were numerous tense red bullous lesions sized 1-3 cm, actively draining sanguineous fluid (Fig 3). Dermatology was consulted for an evaluation of his skin lesions. A skin punch biopsy was obtained. The dermatopathology evaluation revealed extravasated red blood cells, neutrophilic infiltration, and fibrin deposition within vessel walls (Fig 4). Direct immunofluorescence revealed granular deposition of immunoglobulin A within superficial cutaneous vessel walls.

An extensive infectious disease and rheumatology workup was completed. Enzyme immunoassay serology test results for anticoccidioidal IgM and IgG were positive. Percutaneous fine-needle aspiration of the lung abscess yielded a specimen, whose culture was found to be positive for the growth of *Coccidioides* spp., without species differentiation (eg, *Coccidioides immitis* or *Coccidioides posadasii*). Results from a referring facility revealed negative urine serology test results for *Legionella* antigen, whereas serum serology test results using indirect immunofluorescence were positive for *Legionella pneumophila* serogroup 1 (IgM titer of 1:256 and IgG titer of 1:1024). Test results for *Streptococcus pneumoniae*, methicillin-resistant *Staphylococcus aureus*, *Mycoplasma pneumoniae*, *Pneumocystis jiroveci*, influenzae A and B, parvovirus B19, HIV, hepatitis B virus, and hepatitis C virus were negative. A bronchoscopy performed prior to transfer produced a nondiagnostic bronchoalveolar lavage culture. A comprehensive rheumatologic workup result was positive for HLA-B27 antigen. Negative antibody titers were reported for antinuclear antibody, antineutrophil cytoplasmic antibody, anti-double-stranded deoxyribonucleic acid, rheumatoid factor, anti-Sjogren's Syndrome-A, anti-Sjogren's Syndrome-B,

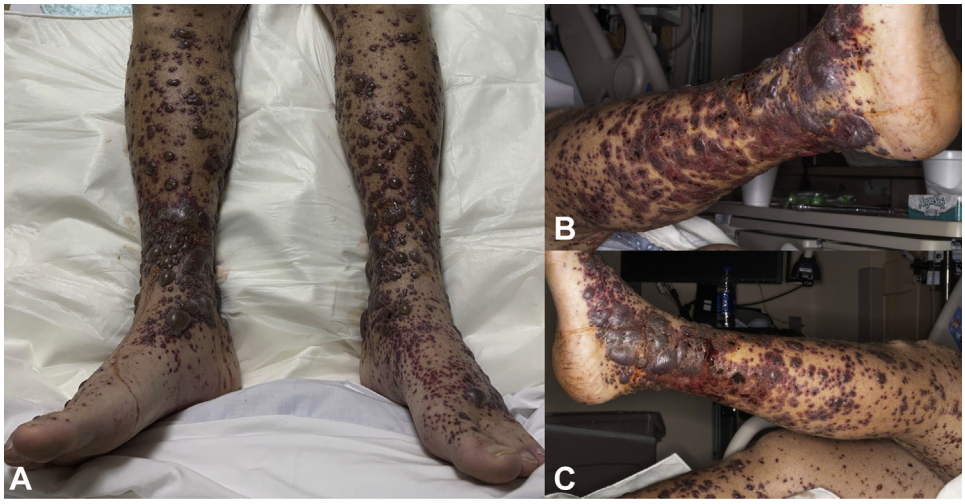

Fig 2. **A**, Diffuse purpuric lesions and hemorrhagic bullae on the lower extremities. **B**, Right lower extremity. **C**, Left lower extremity.

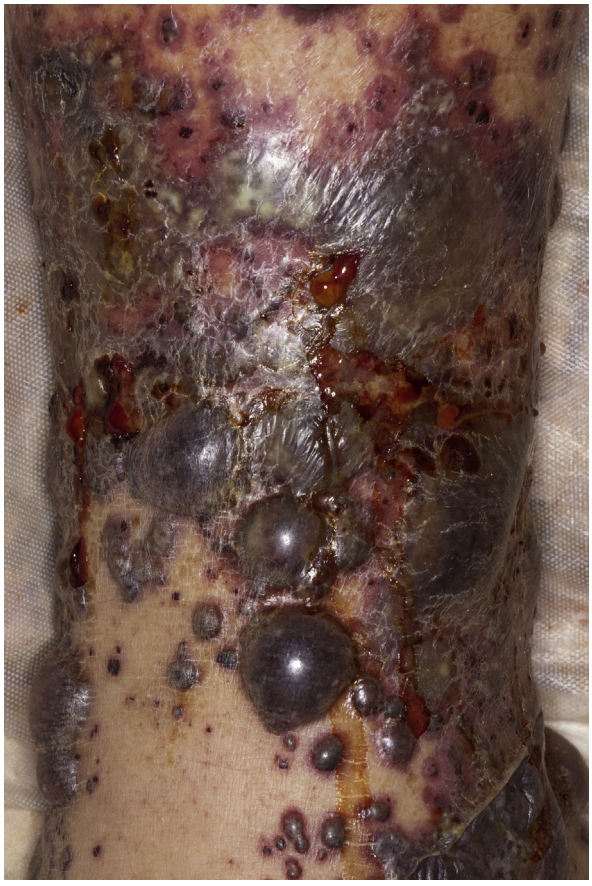

Fig 3. Right lower extremity showing ulcerating hemorrhagic bullous lesions with active drainage of sanguineous fluid.

cryoglobulins, anti-desmoglein-1, and anti-desmoglein-3. Serum immunoglobulin and complement concentrations were within normal limits.

The patient was initially treated empirically with piperacillin-tazobactam and vancomycin for necrotizing pneumonia. Since the results of the cultured lung lesion specimens were pending, antimicrobial coverage was de-escalated to doxycycline and fluconazole for *Legionella* and coccidioidomycosis, respectively. He was started on high-dose methylprednisolone for the small-vessel vasculitis and transitioned to an oral prednisone taper for 1 month. The lower extremity skin lesions were addressed with wound care. Two weeks after discharge, computed tomography showed that the lung lesion had decreased in size (17 mm), and the adjacent micronodules had resolved. His lungs were otherwise clear, and 6 weeks post discharge, he reported no respiratory symptoms. At 3 months post discharge, chest computed tomography demonstrated continued improvement. Fluconazole treatment continued for 5 months after the discharge. Follow-up renal function studies reported a serum creatinine level of 0.8 mg/dL and no hematuria or proteinuria. He continues to be followed up for infectious disease, rheumatology, and endocrinology for surveillance.

DISCUSSION

The presentation of nonthrombocytopenic palpable purpura in the adult patient was a diagnostic challenge due to the constellation of clinical features shared among the small-vessel vasculitis syndromes. A complete patient history and physical examination may reveal the patterns of multiorgan system dysfunction, which will be helpful in narrowing initial differential diagnosis. The most common clinical characteristics in adult IgAV have been

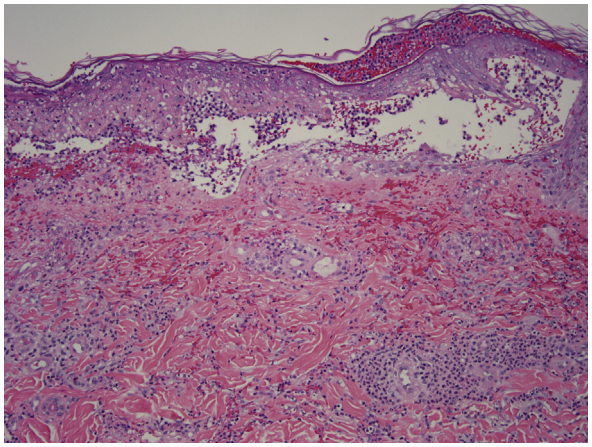

Fig 4. Perivascular neutrophilic dermal inflammation and a subepidermal bulla filled with neutrophils. Notable leukocytoclastic vasculitis (nuclear debris from polymorphonuclear leukocytes) with visible vascular wall damage, RBC extravasation, and fibrinoid change. (Hematoxylin-eosin stain; original magnification: ×100.) *PMN*, Polymorphonuclear leukocytes; *RBC*, red blood cell.

retrospectively reported to be palpable purpura (99.4%), proteinuria (55.2%), microscopic hematuria (46.6%), arthralgia (37.9%), abdominal pain (33.9%), and a history of recent infection (42.0%).[4] The urine analysis should be completed quickly due to the poor prognosis and increased mortality associated with hematuria and proteinuria in adult vasculitis patients.

In this biopsy-proven adult IgAV case, the patient reported abdominal pain, which prompted laboratory evaluation for cryoglobulinemic vasculitis, granulomatosis with polyangiitis, and microscopic polyangiitis. The negative antineutrophil cytoplasmic antibody titer was not consistent with antineutrophil cytoplasmic antibody-associated granulomatosis with polyangiitis and microscopic polyangiitis vasculitis syndromes. The negative hepatitis C virus screen result and undetectable serum cryoglobulin virtually made cryoglobulinemic vasculitis an unlikely diagnosis. A punch biopsy revealing infiltrating granulocytes with leukocytoclastic features is useful in establishing the presence of vasculitis but has limited value in differentiating between vasculitis syndromes or specific IgAV-associated etiologies. The diagnosis of IgAV was confirmed by positive direct immunofluorescence result demonstrating IgA deposition in the small-vessel walls of the biopsy specimen. The presence of hemorrhagic bullous lesions in IgAV has been reported to occur in 10.9%-14.1% of biopsy-proven adult IgAV cases.[4,6] Biopsied specimens of hemorrhagic lesions demonstrate histopathologic features of red blood cell extravasation, neutrophilic infiltration, and edema.

The causal pathogenic mechanisms of IgA vasculitis remain unknown. A recent infection is considered a precipitating risk factor, and this classic feature has been reported retrospectively in 42.0% of adults diagnosed with IgA vasculitis.[4] The *Streptococcus* species is the most common microbial pathogen associated with IgAV.[2,3] In this case report, the lung abscess specimen cultures were found to be positive for *Coccidioides* spp. While positive *Legionella* titers were reported in this patient, there have been no reports of IgA vasculitis secondary to *Legionella* infection, and a single positive serology test result with no finding of *Legionella* in the specimen cultures is inconclusive. Cavitary lung lesions, including active pulmonary coccidioidomycosis, are relatively common in *Coccidioides*-endemic Arizona. Additionally, histopathologic features of vasculitis have been documented in case reports of *Coccidioides* meningitis.[7] This unique case appears to be a rare presentation of concurrent pulmonary coccidioidomycosis and biopsy-proven IgAV.

This case of biopsy-proven IgAV in an adult man describes the unique presentation of palpable purpura with extensive hemorrhagic bullae and concurrent pulmonary coccidioidomycosis. This case report aims to inform clinicians of the possible association of IgAV with pulmonary coccidioidomycosis and of the diagnostic utility of direct immunofluorescence of a biopsy specimen in adults presenting with palpable purpura.

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