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Case report

Immunoglobulin A vasculitis induced by atypical pneumonia infection with *Chlamydophila pneumonia*

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ABSTRACT

Infections are a common trigger for IgA vasculitis. Among the bacteria that cause atypical pneumonia, *Mycoplasma pneumoniae* infection has strongly been associated with IgA vasculitis, with *Chlamydophila pneumoniae* reported with IgA vasculitis in only one case. Though IgA vasculitis is a self-limiting disease, patients with infection-related vasculitis have shown to benefit from early identification and treatment with antimicrobial therapy. Here, we report a case of IgA vasculitis due to *C. pneumoniae* infection in a 19-year-old male who presented with an acute onset of rash, that was later followed by symptoms of cough and fever.

Introduction

Immunoglobulin A vasculitis (IgAV), previously termed as Henoch-Schönlein Purpura, involves IgA deposition of the small blood vessels and subsequent inflammation in various organs [1]. Though it is the most common pediatric vasculitis, adults can rarely be affected and carry higher risks of more severe presentations and complications [2]. The classic tetrad consists of palpable purpura, arthralgia or arthritis, gastrointestinal involvement, and renal disease [3]. These features may take days to weeks to develop, and the order of presentation is variable, though gastrointestinal symptoms typically appear within a week of rash onset [4]. We describe a case of IgAV in a 19-year-old male with an acute onset of a rash that was followed by cough and fever. Diagnosis of IgAV was confirmed by skin biopsy and the respiratory involvement was found to be due to *Chlamydophila pneumonia* infection on respiratory pathogen panel (RPP).

Case report

A 19-year-old male with an unremarkable medical history presented to an outside hospital with acute-onset of skin rash. Eight days before presentation, he noticed small, red dots on his arms and legs. Over the next week, the rash spread to involve his trunk, face, and scalp. He described it as burning and itchy, and noticeably painful to touch from clothing and shoes. After the onset of rash, he developed a fever, frequent cough, and swelling involving the face, hands, elbows, and ankles. He also endorsed transient abdominal pain and joint stiffness. The patient lived in Missouri for the past 3 months for military training, which involved residing in barracks and spending time outdoors. His last sexual contact was 5 months ago. He denied recent travel outside of Missouri (of note, he previously lived in Michigan), exposure to sick contacts, tick or insect bites, animal exposure, or prior history of skin rashes.

On physical examination at our hospital, he was well-appearing and in no acute distress. His vital signs were as follows: temperature: 36.6 C; heart rate: 63 beats/min; blood pressure: 135/68 mmHg; and respiratory rate: 16 breaths/min. His oxygen saturation was 100% on room air by pulse oximetry. There was mild edema on the right side of the face and left eye. There was no noted oral, mucosal, or conjunctival lesions. The lungs were clear to auscultation bilaterally without wheezes or crackles. Skin examination was pertinent for: erythematous, dusky, targetoid-appearing papules scattered on the posterior scalp and back (Fig. 1), glabella, and abdomen; violaceous to red-brown ecchymoses of left upper eyelid and bilateral antecubital fossa (Fig. 2); scattered violaceous papules, some with overlying hemorrhagic crust and scale, and few with overlying vesicles and bullae on the bilateral legs; pinpoint violaceous non-blanching macules on the feet (Fig. 3).

Laboratory studies included a complete blood count and serum chemistry values, which were unremarkable except for mild leukocytosis (14.62×10^9/l). The urinalysis was normal with no hematuria or proteinuria. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were mildly elevated at 20 mm/hr (normal reference value,

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0.0–15.0) and 3.2 mg/dl (normal reference value, 0.00–0.50), respectively (Table 1). Given the patient's presentation with skin lesions and fevers, multiple differential diagnoses were considered including infective endocarditis, sexually transmitted diseases, tick-borne illnesses, and vasculitis.

Lyme serology was positive. Two sets of blood cultures, rapid plasma regain (RPR) screen, *Chlamydia trachomatis* and *Neisseria gonorrheae* (CT/NG) urine test, human immunodeficiency virus (HIV) antigen-antibody assay, and ANCA-associated vasculitis profile (anti-MPO/PR3 antibodies) were negative and complement C3 and C4 levels were normal. Chest x-ray (CXR) (Fig. 4) and computed tomographic (CT) scan of the chest demonstrated opacities and ground glass nodules in the right lower lobe. CT scan of orbit showed skin thickening and soft tissue edema of the left periorbital region.

The patient was empirically treated with intravenous (IV) ceftriaxone and oral (PO) azithromycin at the outside hospital for an assumed community-acquired pneumonia given his fever, cough, and CXR findings. He also received prednisone for the rash. Evaluations by rheumatology, dermatology, and infectious disease specialists suggested different explanations for his findings including leukocytoclastic vasculitis and/or a reactive skin eruption secondary to a respiratory infection, including *Mycoplasma pneumoniae* or *Chlamydophila pneumonia*. Further infectious workup included a respiratory pathogen panel (RPP) and mycoplasma IgM/IgG antibodies. The RPP returned positive for *Chlamydophila pneumonia*. Mycoplasma IgM/IgG antibodies results suggested prior exposure with a negative confirmatory test with immunofluorescence antibody (IFA). Dermatology specialists obtained a punch biopsy from a lesion of the right arm, which revealed prominent IgA deposition in the walls of the superficial dermal vessels.

The antibiotic regimen was changed to IV ceftriaxone and PO doxycycline at our hospital. He also received topical triamcinolone and IV methylprednisolone for the rash. Over the hospital course, the patient's symptoms improved on antibiotics and steroids. He was discharged home to complete a prednisone taper and PO doxycycline for a total of 7 days.

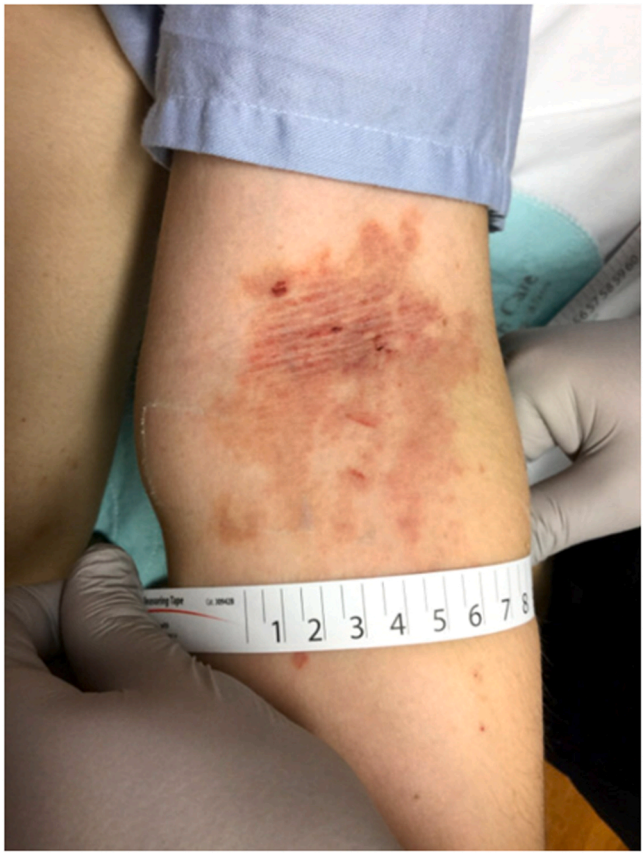

Fig. 2. Violaceous to red-brown ecchymoses of antecubital fossa.

Discussion

Bacterial pathogens that cause atypical pneumonia have been linked to numerous forms of skin manifestations. Both *Mycoplasma pneumoniae*

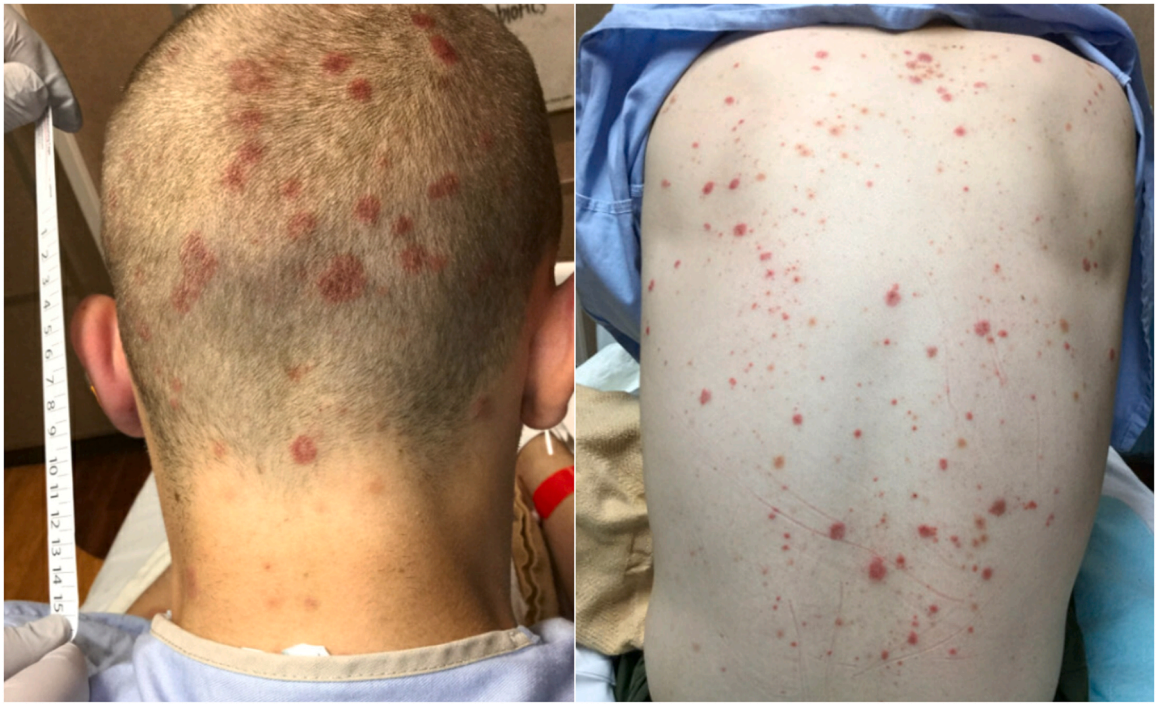

Fig. 1. Erythematous, dusky, targetoid-appearing papules on the posterior scalp and back.

and *Chlamydophila pneumoniae* infection have been reported with erythema nodosum, erythema multiforme, urticaria, the relatively new diagnosis *Mycoplasma*-induced rash and mucositis (MIRM), and various vasculitides [5–9]. Regarding IgA vasculitis (IgAV), infection is a common trigger. It is thought that many types of bacteria and viruses induce abnormal IgA autoimmune reactions and are therefore associated with its pathogenesis [1]. In fact, studies show a 28–73% infection rate in those with IgAV [10]. *M. pneumoniae* is a common cause of respiratory infection in children, which is also the age group with the highest incidence of IgAV [10]. Among the bacterial pathogens that cause atypical pneumonia, *M. pneumoniae* has most often been associated with small-vessel vasculitis, and especially IgAV [10,11]. To our knowledge, *C. pneumoniae* infection has been reported to be the trigger for IgAV in only one other case prior to this [12].

The skin manifestation of IgAV usually starts with petechiae and palpable purpura, which are characterized by non-blanching, hemorrhagic lesions that are slightly elevated from the skin surface [2,3]. Less typically, erythematous, macular, or urticarial wheals, or even target and psoriasis-like lesions may manifest as the initial rash [2,3]. Over time, the initial lesions may coalesce and transform into ecchymoses, petechiae, palpable purpura, bullous or necrotic lesions [3]. The location of the lesions involve gravity-dependent areas and pressure points such as the lower extremities and buttocks, but may also affect the face, trunk, and upper extremities [3]. Our patient presented with both the typical and atypical features of skin rash associated with IgAV, as well as the arthralgia and abdominal pain that is often seen in this disease.

Aside from the clinical features of IgAV, our patient also had respiratory involvement demonstrated by a frequent cough, which was later revealed to be *C. pneumonia* infection. The patient's rash preceded the cough. *C. pneumoniae* infection can cause both upper and lower respiratory tract infections, though most patients are asymptomatic [13]. The incubation period for is 21 days, and there is a biphasic pattern of illness to its course: initially, pharyngitis and hoarseness can last days to weeks and is then followed by lower respiratory symptoms, such as cough [14]. Fever, chills, and myalgias may also be present [13]. Overall, the onset of infection is gradual and recovery is slow, with coughing that can persist for weeks even with appropriate antibiotic therapy [14]. In our case, the patient may have initially had an asymptomatic infection with

Table 1
Lab test results.

Lab test (unit)	Results day 1	Reference value
CBC		
Hb (g/dl)	10.8	13.5–17.5
Hct (%)	33.2	38.8–50.0
MCV (fl)	83.2	81.2–95.1
WBC (x 10^9/l)	14.62	3.50–10.50
ANC (x 10^9/l)	9.44	1.70–7.00
Plt count (x10^9/l)	429	150–450
CMP and miscellaneous		
Creatinine (mg/dl)	0.90	07.– 1.20
BUN (mg/dl	16	6–20
Na+ (mmol/l)	142	136–145
K+ (mmol/l)	4.1	3.5–5.1
Cl- (mmol/l)	106	98–107
HCO3- (mmol/l)	25	22–29
Total bilirubin (mg/dl)	0.20	0.00–1.60
AST (units/L)	22	$\leq$ 40
ALT (units/L)	35	10–50
INR	1.0	0.9–1.1
PT (seconds)	14.4	13.8–15.8
CRP (mg/dl)	3.2	0.00–0.50
ESR (mm/hr)	20	0.0–15.0

Abbreviations: ANC, Absolute Neutrophil Count; ALT, Alanine Transaminase; AST, Aspartate Aminotransferase; BUN, Blood Urea Nitrogen; CBC, Complete Blood Count; CMP, Complete Metabolic Panel; CRP, C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate; Hb, Hemoglobin; Hct, Hematocrit; INR, International Normalized Ratio; Lab, Laboratory; MCV, Mean Corpuscular Volume; Plt, Platelet; PT, Prothrombin Time; WBC, White Blood Cell.

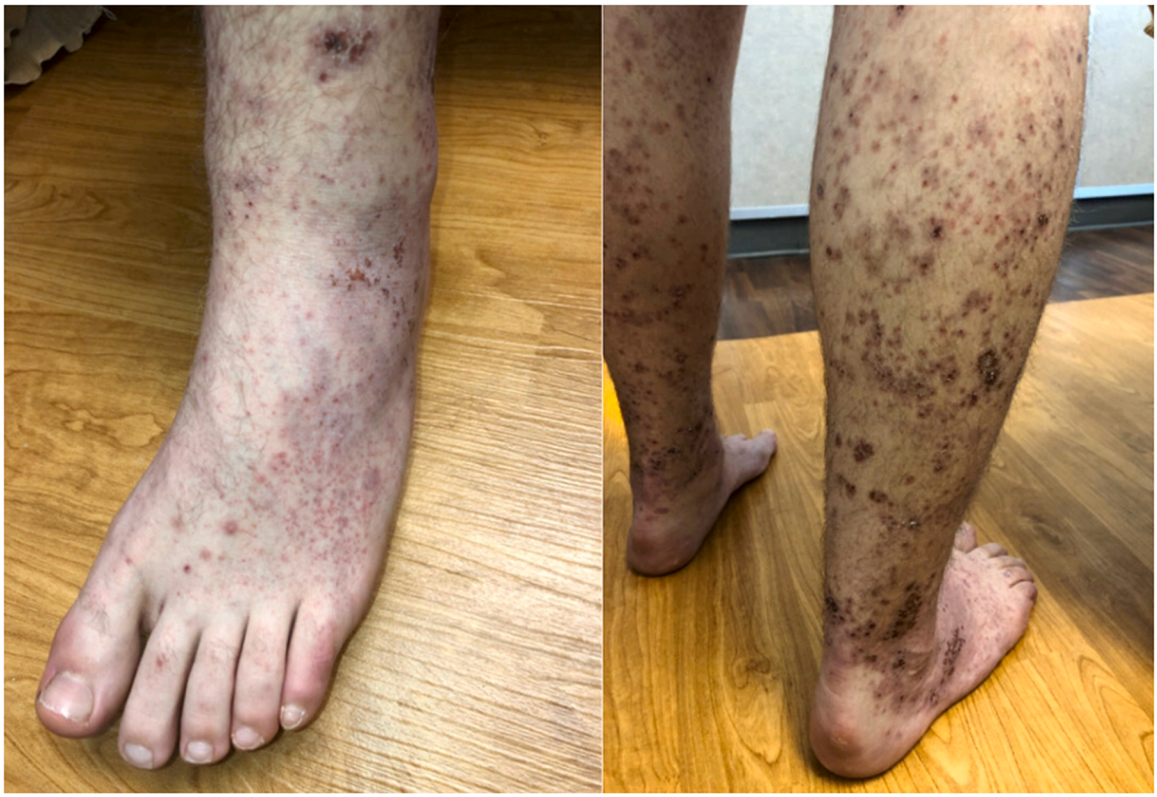

Fig. 3. Pinpoint violaceous non-blanching macules on the feet; scattered violaceous papules, some with overlying hemorrhagic crust and scale, and few with overlying vesicles and bullae on the bilateral legs.

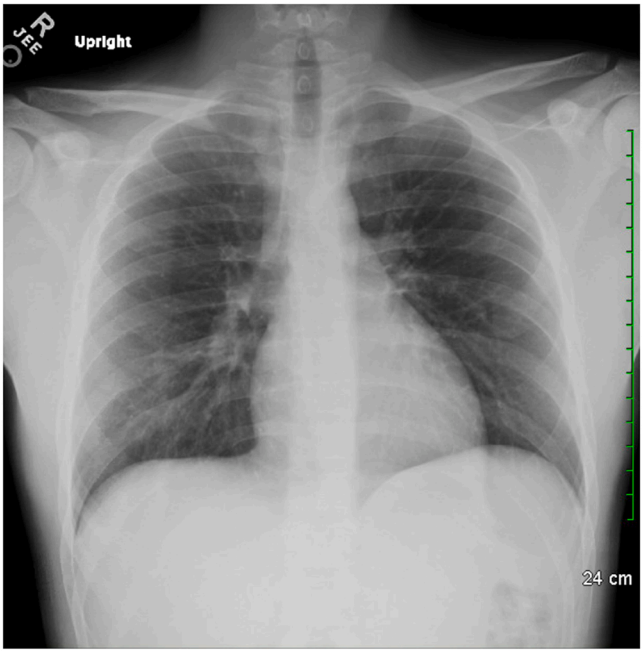

Fig. 4. Chest x-ray. Subtle opacities in the right middle lobe.

C. pneumoniae, which triggered the IgAV. Given the natural course of *C. pneumoniae* infection, the cough was likely a late symptom of the overall infectious course.

IgAV is a diagnosis based on clinical manifestations. A skin or renal biopsy can help confirm the diagnosis, particularly in adults as they are less likely to be affected by IgAV compared to children [15]. In addition, a skin biopsy is helpful in excluding alternative diagnoses in those presenting with unusual skin findings, such as an extensive rash with diffuse lesions [16]. Though no laboratory test is diagnostic for IgAV, workup is necessary to investigate the extent of organ involvement and eliminate the presence of other diseases. The recommended initial workup includes a complete blood count, erythrocyte sedimentation rate, coagulation studies, basic metabolic panel, anti-streptolysin O titer and anti-deoxyribonuclease B, and urinalysis [17]. If the diagnosis remains unclear, further workup can be done with an antinuclear antibody, double stranded-DNA, anti-neutrophilic cytoplasmic autoantibody, complement C3 and C4, and immunoglobulins [17]. Erythrocyte sedimentation rate and C-reactive protein may be normal or elevated [17]. However, these nonspecific markers of inflammation have limited utility as they do not allow distinction between vasculitis disease activity and a concomitant infection, which is a common occurrence. Complement is typically normal in patients with IgAV, though transient hypocomplementemia is more likely to be observed in those with evidence of a recent streptococcal infection [18].

As it is a self-limiting disease, most patients with IgAV can be treated with supportive measures and adequate analgesia [16]. In infection-related vasculitis, identification of the organism and timely institution of appropriate antimicrobial therapy is a critical part of treatment [19]. Case reports of *Mycoplasma pneumoniae*-induced IgAV in children showed complete resolution of symptoms, including rash and pneumonia, after treatment with clarithromycin [5,20]. But, in the single case of IgAV in the adult patient with *C. pneumonia*, treatment with antibiotics lead to an improvement in pneumonia but not the rash or hematuria and proteinuria. This prompted further treatment with oral prednisolone, which resolved the rash and urinary abnormalities [12]. Because our patient was given both empiric antibiotics and corticosteroids upon presentation, we do not know if he would have improved on antibiotics alone.

Corticosteroids have been shown to decrease pain and may be considered in IgAV in patients with severe abdominal and/or joint pain [16]. Still, the role of corticosteroids in treating cases of IgAV with renal involvement has been controversial as it is unclear if it prevents the disease from progressing to end-stage renal disease [4]. Current guidelines recommend reserving corticosteroids for those with moderate to severe kidney involvement [4]. In our case, the patient presented with mild facial and periorbital edema, which could have been an early manifestation of renal involvement. At the same time, however, his labs showed a normal serum creatinine and an absence of hematuria and proteinuria. Since steroids were given early in the patient's disease course, it is unknown if they helped prevent overt renal damage or if their administration was unnecessary. Nonetheless, further research is warranted to investigate the appropriate use of corticosteroids in adults with IgAV [4].

Conclusion

Our report illustrates that *Chlamydophila pneumoniae*, a bacterial pathogen that causes atypical pneumonia, was the trigger for IgA vasculitis in an adult patient. In infection-induced vasculitis, early identification and treatment with appropriate antimicrobial therapy is a crucial aspect of management.

Ethical approval

N/A.

Informed consent

Verbal informed consent was obtained from the patient's relative for the publication of this case report and accompanying images.

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CRediT authorship contribution statement

Seung Ah Kang: Writing – original draft preparation. **Suha Abu Khalaf**: Supervision, Conceptualization, Writing – review & editing. **Taylor Nelson**: Supervision, Writing – review & editing.

Declarations of Competing Interest

None.

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