

Henoch-Schönlein Purpura Associated With *Mycoplasma pneumoniae* Infection

To the Editor:

Henoch-Schönlein purpura (HSP) is a systemic vasculitic syndrome that is most common in children but also can occur in adults. Although group A β -hemolytic streptococci often have been implicated, other bacteria and viruses also may play a role.

We report a patient with HSP confirmed on histology and direct immunofluorescence (DIF), most probably due to *Mycoplasma pneumoniae*, and review the literature on cutaneous vasculitis caused by *M pneumoniae*.

Case Report

A 27-year-old man presented with a nonpruritic rash on his legs of 10 days' duration. It began as red spots around the ankles and later spread up the legs and dorsa of the feet. The spots around the ankles and on the dorsa of the feet became painful and some of them ulcerated. He reported a mild nonproductive cough, dry throat, and painful knee and ankle joints, but he denied any history of fever, abdominal pains, Raynaud phenomenon, or prior medication use including herbal medicines.

Physical examination revealed mild pharyngitis, palpable purpura on both legs, purpuric vesicles on the dorsa of the feet (Figure 1), and vasculitic ulcers on the left lateral malleolus. Chest auscultation and the rest of the findings from the physical examination were normal. Histology showed full-thickness necrosis with subepidermal clefting, nuclear dust, and red blood cells. Superficial dermal blood vessels showed fibrinoid necrosis, nuclear dust, and red blood cell extravasation. Occasional eosinophils were seen (Figure 2). Direct immunofluorescence showed granular deposits of IgA and C3 in a few dermal vessels (Figure 3). Other investigations included chest radiograph, complete blood cell count, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibody, anti-double-stranded DNA, rheumatoid factor, anti-Ro/anti-La antibodies, antineutrophil cytoplasmic antibodies, serum complement levels, renal and liver function tests, glucose, antibodies to streptolysin O, *M pneumoniae* particle agglutination titer, cold agglutinins, blood

culture, and urinalysis. Laboratory investigation revealed the following remarkable findings: erythrocyte sedimentation rate, 44 mm/h (reference range, 0–10 mm/h); *M pneumoniae* antibody titer, 1:640 (negative, <1:40); cold agglutinin titer, 1:256 (negative, <1:64); and swab culture yielding *Acinetobacter* species sensitive to ciprofloxacin, amoxicillin/clavulanate potassium, and ceftriaxone sodium.

The patient was treated with potassium permanganate compresses twice daily, mupirocin ointment 2% twice daily, intravenous (IV) ceftriaxone



Figure 1. The dorsum of the left foot had purpuric vesicles.

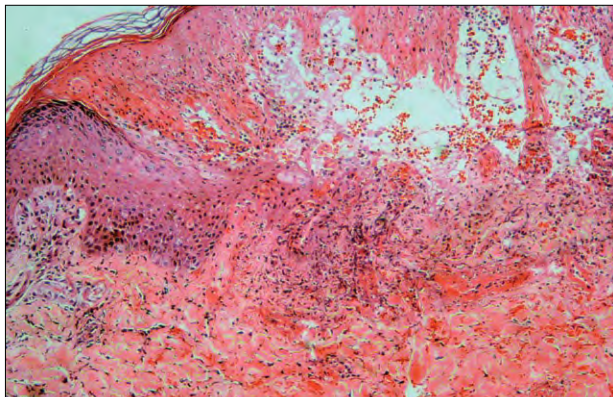


Figure 2. Histology demonstrated leukocytoclastic vasculitis with fibrinoid necrosis of superficial dermal blood vessels, infiltration of vessel walls by neutrophils, nuclear dust, and red blood cell extravasation (H&E, original magnification $\times 40$).

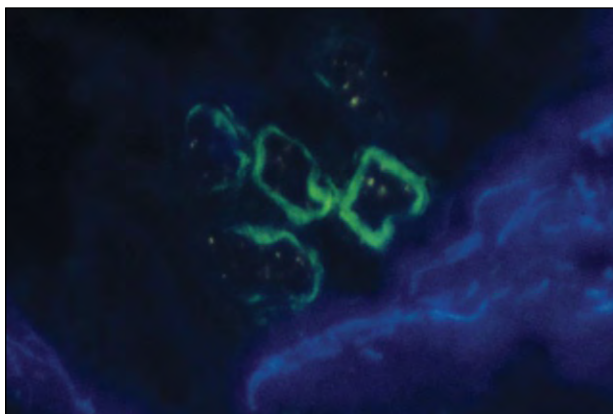


Figure 3. Direct immunofluorescence showed granular deposits of IgA in a few dermal vessels (original magnification $\times 40$).

sodium 1 g twice daily, and IV imipenem 500 mg/cilastatin sodium 500 mg twice daily. The IV antibiotics were changed 3 days later to oral ciprofloxacin hydrochloride 250 mg twice daily when blood culture results were negative and swab culture from the ulcers grew *Acinetobacter* species. Azithromycin dihydrate 250 mg twice daily was added on the fourth day when *M pneumoniae* antibodies returned positive. He improved after 1 week of azithromycin dihydrate and was discharged. He was clinically well with no signs of relapse when seen 1 month after admission, and convalescent sera for *M pneumoniae* antibody and cold agglutinins a month later were 1:160 and 1:64, respectively.

Comment

Our patient presented with palpable purpura and small vessel leukocytoclastic vasculitis, thus satisfying

the American College of Rheumatology (ACR) criteria for the diagnosis of HSP. In addition, he had granular deposits of IgA and C3 in a few dermal vessels. Although not part of the ACR criteria, the presence of granular IgA deposits in the walls of the dermal blood vessels is highly characteristic of HSP.¹ The diagnosis of acute *M pneumoniae* infection is based on a 4-fold increase or decrease in antibody titer. In our patient, diagnosis was based on a 4-fold decrease in antibody titer from 1:640 to 1:160 a month later. He had a mild upper respiratory tract infection (URTI) and his chest radiograph was normal. *Mycoplasma pneumoniae* may cause URTI or atypical pneumonia, or it may be asymptomatic and can even resolve without antibiotic treatment. The isolation of *Acinetobacter* species suggests secondary infection of the vasculitic ulcers. All lesions healed after treatment with antibiotic therapy active against *M pneumoniae*, and there was no recurrence of his symptoms.

Mycoplasma pneumoniae is known for its propensity to cause cutaneous complications. Cutaneous lesions occur in as many as 25% of patients, ranging from erythema to more severe involvement such as Stevens-Johnson syndrome. We reviewed the literature on cutaneous vasculitis associated with *M pneumoniae* by conducting a PubMed search of articles indexed for MEDLINE using the terms *Mycoplasma*, *Henoch-Schönlein purpura*, and *vasculitis* and found 10 patients, including our patient, who satisfied the ACR criteria for diagnosis of HSP.²⁻¹⁰ The findings are summarized in the Table. Four patients with HSP were diagnosed on clinical grounds alone.^{2,3,8,10} The ACR criteria for HSP are not strict and include presence of any 2 of the 4 criteria for diagnosis: palpable purpura, age 20 years or younger at disease onset, bowel angina, granulocytes in the walls of arterioles or venules on biopsy.¹¹ Stricter criteria should at least include histology. If these criteria were applied, then only 6 patients, including our patient, would be considered to have HSP.^{4,7,9} Direct immunofluorescence probably was not available during the time of the earlier reports. Hence, DIF was performed in only 4 patients, including our patient.^{4,5,7} It was negative in one patient⁵; 1 patient showed IgA, IgM, and C3⁴; 1 patient showed IgM and C3⁷; and only our patient showed granular deposition of IgA and C3 that is characteristic of HSP. Current opinion highlights the deposition of IgA in vessel walls. The more recent European League Against Rheumatism and Pediatric Rheumatology Society classification includes palpable purpura as a mandatory criterion together with at least 1 of the following findings: diffuse abdominal pain, predominant IgA

Cutaneous Vasculitis Associated With *Mycoplasma pneumoniae* Infection

Reference	Noncutaneous Features	Histologic Findings	DIF Findings	Basis for Diagnosis of <i>M pneumoniae</i>
Liew and Kessel ²	Boy aged 8 years with pneumonia and hematuria	ND	ND	CFT
Stearé et al ³	Adolescent girl aged 17 years with URTI, abdominal pain, arthritis, melena, and hematuria	ND	ND	IgM antibody
Van Bever et al ⁴	Adolescent boy aged 13 years with adult respiratory distress syndrome and biochemical pancreatitis	Signs of vasculitis	IgA, IgM, C3	CFT
Perez et al ⁵	Woman aged 28 years with URTI and polyarthritis	Leukocytoclastic vasculitis	Negative	PA; IgM antibody
Perez and Montes ⁶	Man aged 75 years with pneumonia and encephalitis	Leukocytoclastic vasculitis	ND	Antibody titer (test method not specified); IgM antibody
Orlandini et al ⁷	Adolescent boy aged 16 years with fever	Leukocytoclastic vasculitis	IgM, C3	IgM antibody
Timitilli et al ⁸	Girl aged 5 years with pneumonia, migratory arthritis, and hematuria	ND	ND	PA
Greco et al ⁹	Boy aged 7 years with retinal vasculitis	Leukocytoclastic vasculitis	ND	PA; IgA, IgM, and IgG antibody
Kano et al ¹⁰	Girl aged 11 years with URTI	ND	ND	IgM antibody
Present case	Man aged 27 years with URTI and arthralgia	Leukocytoclastic vasculitis	IgA, C3	PA

Abbreviations: DIF, direct immunofluorescence; ND, not done; CFT, complement fixation test; URTI, upper respiratory tract infection; PA, particle agglutination titer.

deposition (confirmed on skin biopsy), acute arthritis in any joint, and renal involvement (as evidenced by the presence of blood and/or protein in the urine). The age criterion was removed.¹² If IgA deposition is central, then our case alone would qualify as HSP, with the remaining cases representing small vessel vasculitis of some other type.

Mycoplasma pneumoniae infections are endemic and common throughout the world. However, our investigation was only able to reveal 10 patients, including our patient, of HSP (based on ACR criteria) associated with *M pneumoniae*. Of these reported cases, only our patient had HSP confirmed on histology and DIF, which suggests that cutaneous vasculitis, especially HSP, is either an uncommon cutaneous complication of *M pneumoniae* infection or is underdiagnosed. Although atypical pneumonia represents the most common severe manifestation of *M pneumoniae* infection, many more patients develop a mild URTI or may even be asymptomatic. It also is known that persons infected with *M pneumoniae* may experience extrapulmonary complications at variable times after onset of or even in the absence of respiratory illness. Furthermore, *M pneumoniae* antibodies increase slowly in the course of the illness, reaching peak titers 5 weeks after the onset of clinical symptoms, and the diagnosis would most likely be missed if convalescent sera were not tested. These factors may help explain why *M pneumoniae* is only infrequently implicated as a cause of cutaneous vasculitis. A more rapid diagnostic test for *M pneumoniae* infection is required and the highly sensitive and specific *M pneumoniae* polymerase chain reaction (PCR) analysis is a welcomed development. Hopefully this test will become more standardized and widely available soon. Demonstration of *M pneumoniae* in the skin using PCR could have confirmed a causal relationship in our patient, but this test was not available to us.

In summary, our patient most probably had acute *M pneumoniae* infection and HSP supported by histology and IgA deposits in the dermal vessels on DIF. Tests for *M pneumoniae* should be included in the etiologic screening of cutaneous vasculitis, including HSP, even when respiratory symptoms are absent or mild.

Sincerely,
Christopher SH Lim, MBBS
Siew-Lin Lim, MBBS

Acknowledgment—We are indebted to Kah-Beng Lim, MBBS, MRCP, for allowing us to publish his case.

Dr. C.S.H. Lim is from the Department of Urology, St. George Hospital, Kogarah, New South Wales, Australia. Dr. S-L Lim is from K B Lim Skin Clinic Pte Ltd, Gleneagles Hospital and Medical Centre, Singapore.

The authors report no conflict of interest.

REFERENCES

1. Van Hale HM, Gibson LE, Schroeter AL. Henoch-Schönlein vasculitis: direct immunofluorescence study of uninvolved skin. *J Am Acad Dermatol.* 1986;15(4, pt 1):665-670.
2. Liew SW, Kessel I. Letter: mycoplasmal pneumonia preceding Henoch-Schönlein purpura. *Arch Dis Child.* 1974;49:912-913.
3. Steare SE, Wiselka MJ, Kurninczuk JJ, et al. *Mycoplasma pneumoniae* infection associated with Henoch-Schönlein purpura. *J Infect.* 1988;16:305-307.
4. Van Bever HP, Van Doorn JW, Demey HE. Adult respiratory distress syndrome associated with *Mycoplasma pneumoniae* infection. *Eur J Pediatr.* 1992;151:227-228.
5. Perez C, Mendoza H, Hernandez R, et al. Leukocytoclastic vasculitis and polyarthritis associated with *Mycoplasma pneumoniae* infection. *Clin Infect Dis.* 1997;25:154-155.
6. Perez C, Montes M. Cutaneous leukocytoclastic vasculitis and encephalitis associated with *Mycoplasma pneumoniae* infection. *Arch Intern Med.* 2002;162:352-354.
7. Orlandini V, Dega H, Dubertret L. Cutaneous vasculitis revealing a *Mycoplasma pneumoniae* infection [in French]. *Presse Med.* 2004;33(19, pt 2):1365-1366.
8. Timitilli A, Di Rocco M, Nattero G, et al. Unusual manifestations of infections due to *Mycoplasma pneumoniae* in children. *Infez Med.* 2004;12:113-117.
9. Greco F, Sorge A, Salvo V, et al. Cutaneous vasculitis associated with *Mycoplasma pneumoniae* infection: case report and literature review. *Clin Pediatr (Phila).* 2007;46:451-453.
10. Kano Y, Mitsuyama Y, Hirahara K, et al. *Mycoplasma pneumoniae* infection-induced erythema nodosum, anaphylactoid purpura, and acute urticaria in 3 people in a single family. *J Am Acad Dermatol.* 2007;57(suppl 2):S33-S35.
11. Mills JA, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of Henoch-Schönlein purpura. *Arthritis Rheum.* 1990;33:1114-1121.
12. Ozen S, Ruperto N, Dillon MJ, et al. EULAR/PReS endorsed consensus criteria for the classification of childhood vasculitides [published online ahead of print December 1, 2005]. *Ann Rheum Dis.* 2006;65:936-941.