Henoch-Schönlein Purpura Secondary to Subacute Bacterial Endocarditis

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GOAL

To recognize Henoch-Schönlein purpura (HSP) as a possible skin manifestation associated with subacute bacterial endocarditis (SBE)

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Describe the clinical features of HSP.
2. Understand the characteristics of bacterial endocarditis and its association with HSP.
3. Differentiate between HSP and other skin manifestations associated with SBE.

CME Test on page 280.

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Henoch-Schönlein purpura (HSP), a systemic, small-vessel vasculitic syndrome, is characterized by a nonthrombocytopenic purpuric rash, arthralgia, abdominal pain, and nephritis. These signs and symptoms may occur in any order, and not all are necessary for the diagnosis. Although most common in 4- to 7-year-olds, HSP is well documented in adults and is often preceded by a history of mucosal-based infections, especially of the upper respiratory tract. We report a case of HSP that occurred coincident with the onset of subacute bacterial endocarditis (SBE) in an otherwise healthy 41-year-old white woman. The patient presented with a purpuric rash and arthralgia and was found to have left-sided streptococcal SBE. She subsequently developed abdominal pain and immune complex glomerulonephritis. The bacterial endocarditis was treated with antibiotics and mitral valve replacement, followed by a spontaneous resolution of the associated signs and symptoms of HSP.

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Henoch-Schönlein purpura (HSP) is a systemic, small-vessel vasculitic syndrome characterized by a nonthrombocytopenic purpuric rash, arthralgia, abdominal pain, and nephritis. This symptom complex may resemble that of other multiorgan vasculitic syndromes, including mixed cryoglobulinemia, microscopic polyarteritis nodosa, systemic lupus erythematosus,

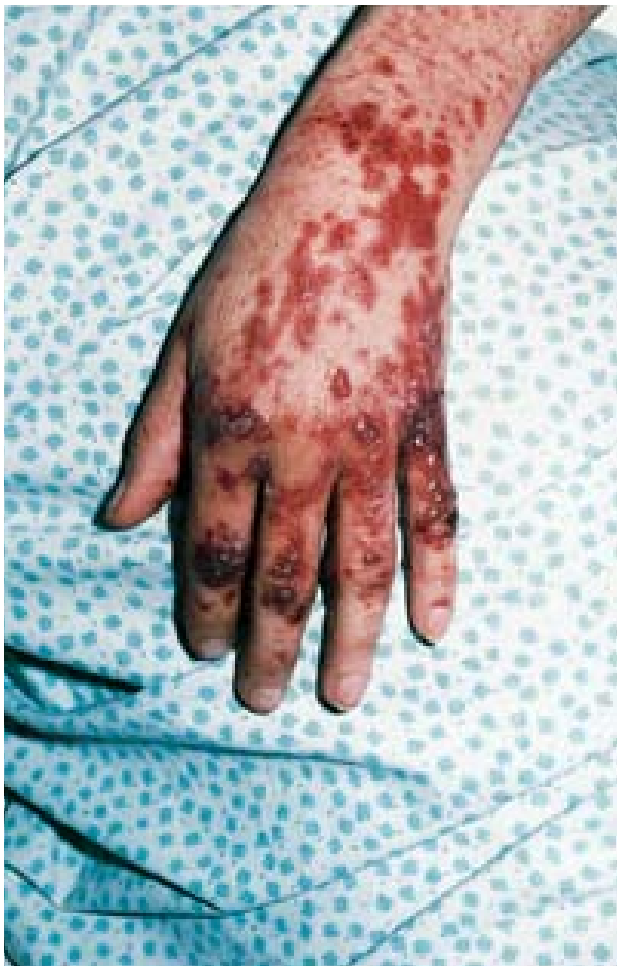

Figure 1. Hemorrhagic bullae and palpable purpura on left hand and forearm.

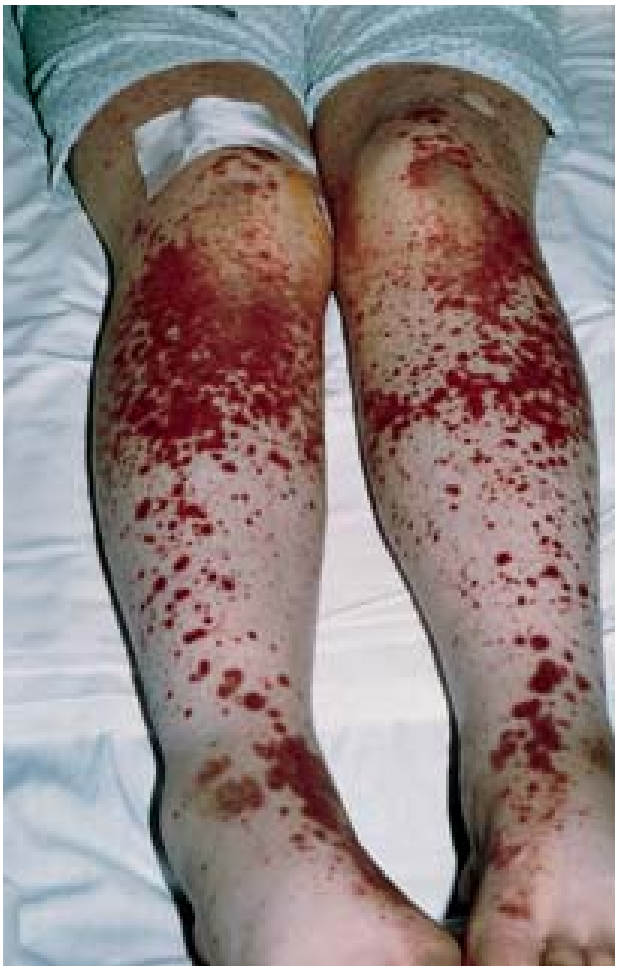

Figure 2. Extensive palpable purpura on lower extremities.

and chronic septic vasculitis. These syndromes characteristically involve the skin, kidney, and joints. Immunofluorescent testing is the primary method of distinguishing HSP from these syndromes. This testing method reveals prominent and dominant deposits of immunoglobulin A (IgA) within the cutaneous vasculature and renal glomeruli. The characteristic signs and symptoms of HSP may occur in any order, and not all are necessary for the diagnosis. However, the rash occurs at some point in the illness in 100% of cases and is the presenting complaint in 50% of cases. HSP rash classically consists of urticaria, palpable purpura, or erythematous maculopapules and characteristically involves the upper and lower extremities and the buttocks.[1] Although most common in 4- to 7-year-olds, HSP is well documented in adults. Seventy-five percent of patients have a presyndrome history of mucosal-based infections, especially of the upper respiratory tract, but numerous other inciting agents (eg, insect bites, food allgeries, pharmacologic drugs) have been reported.[1] In this article, we report a case of subacute bacterial endocarditis (SBE) leading to HSP in an adult. The pathogenic mechanism is immune complex deposition in the small vessels of the skin and mesangium; the complex consists of IgA and an antigen. The immunogenic stimulus is typically a mucosal-based nonviable microbial antigen.[1] Rarely, a nonmucosal-based infectious stimulus is implicated (when this happens, the basis for preferential induction of IgA is more elusive).

Case Report

A 41-year-old white woman presented with a history of mitral regurgitation dating back to childhood but was otherwise in relatively good health. Five days before admission, she developed a rash on her hands and ankles (Figure 1); this rash progressed from tiny papules to confluent areas of

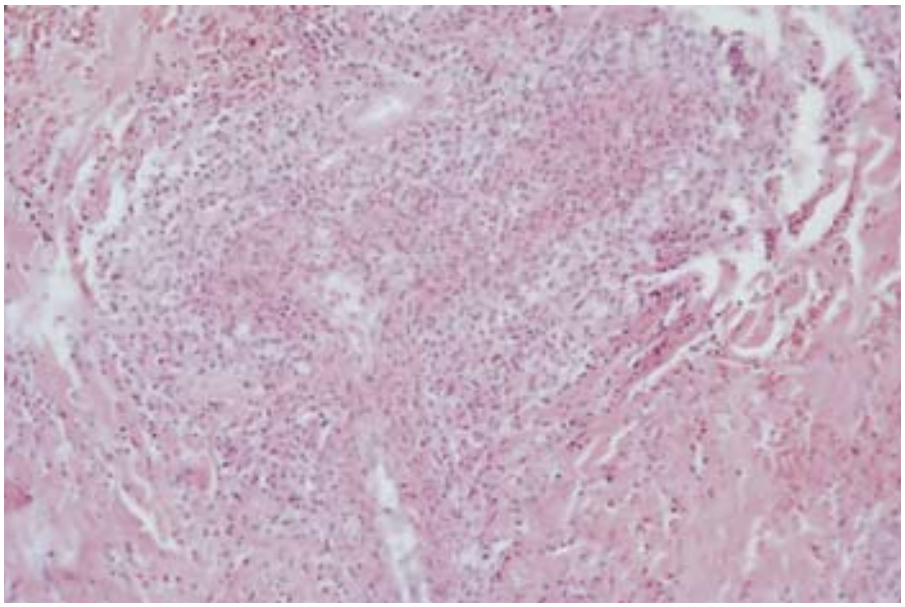

Figure 3. Superficial and deep perivascular infiltrate involving capillaries and venules (H&E, original magnification ×20).

striking palpable purpura that extended to involve large areas of the legs and arms (Figure 2). She also had joint pain in the wrists and proximal interphalangeal joints. The day of admission, she was evaluated in the emergency room. Results of laboratory tests were positive for antineutrophil cytoplasmic antibodies (ANCA). Test results also revealed that the patient had normocytic anemia (hemoglobin, 6.3; white blood cell count, 10.3, with normal differential; platelet count, 320). Erythrocyte sedimentation rate was 97, and coagulation screen and sequential multichannel autoanalyzer 7 were within normal limits. Blood cultures were positive for *Streptococcus sanguis*. An echocardiogram was performed, showing the presence of vegetations on the anterior and posterior areas of the mitral valve, and the patient was diagnosed with SBE (SBE is characterized by the presence of vegetations on the endocardium or in it, normally associated with a heart valve). Treatment was begun with 2-g intravenous ampicillin and gentamicin every 8 hours. Later during her hospital stay, the patient developed oligoarthritis, vague abdominal pain, and renal failure secondary to immune complex glomerulonephritis. She received methylprednisolone sodium succinate intravenously, docusate sodium, sucralfate, calcium carbonate, zolpidem tartrate, and oxycodone plus acetaminophen. Before hospitalization, she had not been taking any medications and had no allergies.

The patient underwent mitral valve replacement with a porcine valve because of her deteriorating condition and the fear of heart failure secondary to severe regurgitation. Following the valve replacement, the rash, abdominal pain, oligoarthritis, and glomerulonephritis resolved slowly, and she was discharged. The patient returned on a few occasions to the emergency room with chest pains but no recurrence of other symptoms.

Histology/Immunofluorescence—On day 5, results of a 4-mm punch biopsy from the leg showed a striking vascular reaction involving the venules and capillaries of both the superficial and deep dermis (Figure 3). Neutrophils infiltrated the vessel wall, and mural and luminal fibrin depositions were extensive. Extravascular neutrophilia was prominent, with neutrophils present along the dermal–epidermal junction and permeating the epidermis (Figure 4). These findings defined a case of severe leukocytoclastic vasculitis with prominent extravascular neutrophilia, which was, therefore, compatible with pustular vasculitis. Gomori methenamine-silver stains, periodic acid-Schiff stain, acid-fast bacillus stain, and gram stain were negative for fungal, mycobacterial, and bacterial elements.

Results of immunofluorescent studies performed on skin from the right leg showed striking granular deposits of IgA, with codominant deposition of fibrin, IgG, IgM, and C3 within the cutaneous vasculature as well as focal deposits of IgA and IgM along the dermal–epidermal junction.

Comment

We presented a case of HSP secondary to SBE. The infecting organism in our patient was *S sanguis*,

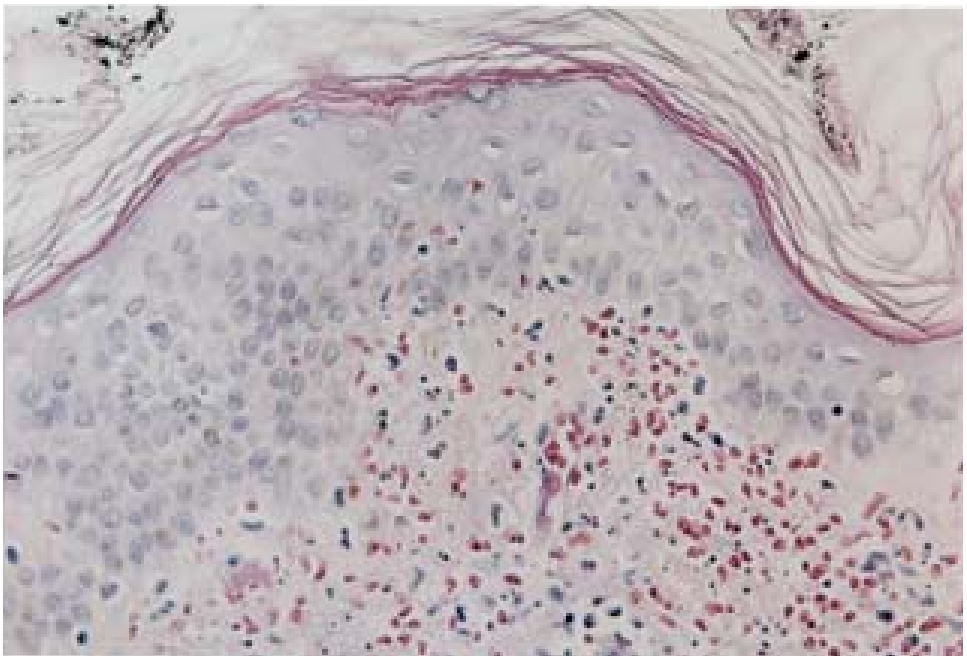

Figure 4. Prominent extravascular neutrophilia with neutrophils along the dermal–epidermal junction and permeating the epidermis (H&E, original magnification ×40).

the most common viridans streptococcus involved in endocarditis. This organism accounts for approximately 60% of cases of native-valve endocarditis.[2] As in our patient, the entry point in an initiating episode of infection with *Streptococcus viridans* usually is not apparent.

Circulating immune complexes (CICs) are present in infective endocarditis, and their measurement may be used to monitor a patient's clinical progress. CICs may consist of Ig and C1q along with components of the organism.[3] Another CIC source in this case is polyclonal Ig directed against components of the organism complexed with an Ig with rheumatoid factor activity. IgA and IgM rheumatoid factor activity correlates most strongly with subacute or chronic infective endocarditis.[4] Presence of CICs is thought to lead to glomerular and skin lesions. As HSP occurs with autoantigens (eg, IgA rheumatoid factor, IgA ANCA), it is possible that a symptom complex defining HSP could develop in a patient with endocarditis.[5]

Skin lesions often occur with bacterial endocarditis. However, with acute disease and organisms of low pathogenicity (eg, *S viridans*), skin lesions generally manifest as small, hemorrhagic areas of a slightly nodular character, occurring on the palms and soles. Called *Janeway lesions*, such lesions indicate septic embolic vasculitis.[2]

Another skin manifestation commonly occurring with bacterial endocarditis is thrombotic thrombocytopenic purpura–like (TTP-like) syndrome.[6,7] These cases of bacterial endocarditis often present with petechiae, particularly on the palate and upper extremities, and with renal dysfunction that is reversible with treatment of the bacteremia.[6,7] However, it is unlikely that the case presented involves a variant of TTP-like syndrome, for several reasons. First are the clinical differences, including the nature of purpura (ie, palpable vs nonpalpable purpura). Second, pathologically, results of renal biopsy immunofluorescence show a granular "lumpy-bumpy" pattern of basement membrane deposition of IgG and C3 in TTP-like syndrome, whereas results of our patient's biopsy showed predominant IgA deposition. Third, our patient had IgA ANCA positivity, which occurs in a large number (79%) of adults with HSP but not in patients with other systemic vasculitides, or with TTP.[8] Fourth, our patient's histomorphology was pustular vasculitis, which typically indicates either active infection or an id reaction to hematogenous-disseminated nonviable microbial pathogen. Fifth, the platelet count was normal.

To our knowledge, we have presented the second known case of HSP complicating bacterial endocarditis. In the first case,[9] although bacterial endocarditis was presumed to be the most likely cause of HSP, administration of cloxacillin sodium before development of symptoms made the trigger less obvious, as penicillins are linked to the devel-

opment of HSP. With our patient, the relationship between HSP and bacterial endocarditis is stronger, as the symptoms of HSP developed before administration of antibiotics.

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