Rare Association of Henoch-Schönlein Purpura with Recurrent Endocarditis

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ABSTRACT

We report a rare association of Henoch-Schönlein Purpura with recurrent endocarditis in a 36-year-old man presenting with rash and renal failure. Bacterial endocarditis can be complicated by renal failure of various etiologies. Biopsy may distinguish these and guide therapy as seen in this case. Here, timely diagnosis of Henoch-Schönlein Purpura in the setting of recurrent methacillin sensitive staphylococcus endocarditis led to steroid therapy and renal recovery. This is a rare reported case of Henoch-Schönlein Purpura during an episode of recurrent adult endocarditis that also highlights the complex interplay between genetic susceptibility and immune responses.

CASE REPORT

A 36-year-old man with a history of intravenous drug use initially presented with 3 weeks of fevers, chills, night sweats and malaise. He had a history of remote native tricuspid valve endocarditis with methacillin sensitive staphylococcus aureus (MSSA) 6 years earlier. Then, septic embolic complications required debridement of his tricuspid valve and several months of antibiotic therapy. He had recovered and was in good health until his current illness began sub-acutely with daily fevers greater than 101°F. At his first clinic evaluation, a white blood count of 22,000 prompted an injection of intramuscular ceftriaxone followed by oral cephalexin. No blood cultures were obtained. The next day he developed a diffuse, tender, purple raised rash on his arms and legs and then abdomen. Four days later, at a local emergency department, cephalexin was stopped, based on possible drug-induced vasculitis, and he was given a short course of dexamethasone. He had had no previous history of cephalosporin allergy, purpura, or leukocytoclastic vasculitis. A week later, with ongoing fevers and rash, he was admitted to the hospital. Then the patient reported diffuse arthralgias and abdominal pain without hematochezia. Steroids were stopped. A urinalysis showed hematuria and pyuria, and he was treated with levofloxacin for presumed urosepsis. Biopsy of a rash lesion was sent for pathology. On hospital day 2, blood cultures returned positive for MSSA. Antibiotic coverage included vancomycin, followed by daptomycin. Computed tomography of the chest showed multiple abscesses. A transesophageal echocardiogram showed a 1.6-cm vegetation on the lateral leaflet of the tricuspid valve and severe tricuspid regurgitation.

Upon rheumatology consult after transfer, the patient reported improving arthralgias, ongoing abdominal pain, and remaining rash on his extremities without evolution. His exam was notable for a pansystolic murmur heard best over the left lower sternal border, lack of synovitis, and numerous 1- to 3-mm, non-blanchable, dark-red macules and voilaceous papules. About 90% of his body surface area was involved, with the extremities being more severely affected, and sparing of the head, neck, palms, and soles. Laboratory data at the time are provided in Table 1.

Review of the prior skin pathology report described leukocytoclastic vasculitis with IgA deposition on immunofloures-cence. Nevertheless, given worsening renal function and potential therapeutic implications, a renal biopsy was obtained. This demonstrated focal, segmental proliferative glomerulonephritis with IgA and C3 staining and few subendothelial deposits (Figure 1). Staining was negative for immune complexes, and no thrombi or crescents were noted on light microscopy with H+E staining. The patient's clinical picture and biopsy results confirmed a diagnosis of Henoch-Schönlein Purpura (HSP) with renal involvement in the setting of recurrent native tricuspid valve endocarditis with MSSA.

DISCUSSION

We present a rare association of Henoch-Schönlein Purpura with endocarditis in an adult patient. As in this case, renal failure may accompany one-third of endocarditis cases, and

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pathology is often imperative, particularly in light of the broad differential diagnosis (Table 2).[1-3] Renal pathology was instrumental in this case to unify the skin pathology and renal disease, and reach a definitive HSP diagnosis. When HSP was confirmed, this case was particularly interesting in light of his prior MSSA endocarditis episode that did not precipitate vasculitis.

HSP is characterized by the triad of arthritis, purpura (Figure 2), and colicky gastrointestinal symptoms.[4] Histological evidence of granulocytes in the walls of small arterioles or venules plus IgA-dominant immune deposits confirms the diagnosis in appropriate clinical settings. HSP is primarily a disease of children that is typically self-limited, but 10% of cases occur in adults where features and outcomes may vary. In both children and adults, HSP often spontaneously resolves. More severe renal disease imposes significant morbidity and is often an indication for steroid treatment. When compared to children, adults with HSP have a lower frequency of abdominal pain and fever, a higher frequency of joint symptoms, and more frequent and severe renal involvement.[5] Adults are therefore more likely to require aggressive therapy, including steroids or cytotoxic agents. The prognosis for adult patients with HSP nephritis is also worse than in children. In a large cohort of 250 cases of HSP nephritis in adults, 11% reached end-stage renal failure and 13% had severe renal failure defined by creatinine clearance < 30 ml/min.[6] Full renal recovery was achieved in only 20%. Survival was only 74% at the end of follow-up after a median of 14.8 years.

The underlying pathogenesis of HSP remains unknown. Streptococcal infections, staphylococcal infections, vaccinations, medications, and even insect bites all have been implicated as possible triggers, although some cases lack a clear precipitating event.[5] In cases with an identifiable trigger, upper respiratory infections and medications, including beta-lactam or cephalosporin antibiotics, are the most frequent culprits. One study of 6 cases with staphylococcus-associated HSP nephritis demonstrated a unique profile of T-cell receptor activation and cytokine production that normalized following clearance of infection.[7] The outcome of these 6 patients was poor, including 2 deaths and 2 patients requiring maintenance hemodialysis.

To date, only 2 cases of adult endocarditis-associated HSP have been described in the English literature, and no cases involved recurrent endocarditis. The first case report described a 21-year-old man with a history of IV drug use and right-sided staphylococcal endocarditis who developed skin and renal-biopsy-proven HSP.[8] When the endocarditis was initially diagnosed, prior to the onset of HSP, he received cloxacillin and netilmicin, so it was impossible to know whether the drug or the infection was the precipitating event. Like our patient, he had multiple pulmonary cavitary embolic lesions and large bilateral effusions. At discharge, that patient had mild proteinuria, but did not require steroids, though he was lost to follow-up. The second report described a 41-year-old woman with left-sided streptococcus sanguis subacute bacterial endocarditis who presented with a purpuric rash prior to the diagnosis of endocarditis.[9] The rash was biopsy-proven to be consistent with HSP. She was started on ampicillin and gentamicin, and eventually underwent mitral valve replacement. Due to renal fail-

Table 1. Laboratory Data on Inpatient Transfer

Test	Patient Value	Normal Range
WBC (K/uL)	4.9	3.8-10.5
Hemoglobin (g/dL)	8.7	13.6-17.2
Hematocrit (%)	28	40-52
Platelet (K/uL)	160	160-370
Creatinine (mg/dL)	2.0	0.6-1.3
Albumin (g/dL)	1.7	3.3-4.7
CRP (mg/dL)	4	0-1
ESR (mm/Hr)	94	0-15
Urinalysis	6-10 RBC	0-2
	2-5 WBC	0-2
Protein/creatinine ratio	1.6	0
C3 (mg/dL)	139	90-180
C4 (mg/dL)	17	10-40
IgA (mg/dL)	586	50-450
c-ANCA, p-ANCA	Negative	Negative
Cryoglobulin	Negative	Negative
ANA	Negative	Negative
HIV 1 and 2 antibody	Negative	Negative
Hepatitis B surface antigen	Negative	Negative
Hepatitis C antibody	Negative	Negative

WBC = white blood count; CRP = C-Reactive Protein; ESR = erythrocyte sedimentation rate; C3 = complement component 3; C4 = complement component 4; ANCA = anti-neutrophilic cytoplasmic antibody; ANA = anti-neutrophilic antibody.

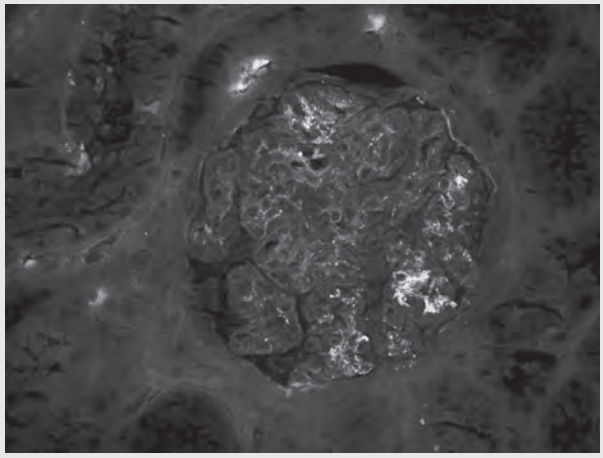

Figure 1. Immunoflourescence of the patient's renal biopsy showing a glomerulus with diffuse and segmental IgA staining.

Table 2. Causes of Kidney Disease in Infective Endocarditis

Immune Complex Mediated Glomerulonephritis	
	Post streptococcal
	Other post infectious
	Cryoglobulinemia
Drug-induced	
	Acute interstitial nephritis (eg, penicillin)
	Acute tubular necrosis (eg, aminoglycosides)
Embolic disease	
	Renal infarction
	Renal abscess
Primary Vasculitis	
	Henoch-Schönlein Purpura
	ANCA Vasculitis (anti-neutrophilic cytoplasmic antibody)

ure, she received methylprednisolone, although a kidney biopsy was not performed. Renal recovery status was not reported.

Our patient went on to develop more severe renal failure, with a peak creatinine of 5.3 mg/dL. He required a short course of hemodialysis and a prolonged steroid taper, but subsequently regained his renal function. He received a prolonged course of antibiotics, and his tricuspid valve was ultimately replaced successfully.

CONCLUSION

Henoch-Schönlein Purpura is a vasculitis that is frequently triggered by upper respiratory infections, though less commonly specifically linked to endocarditis. In contrast to the classic pediatric presentation, HSP in adults is characterized by more severe renal disease that often requires renal replacement and steroid therapies. Our case was unique given that the patient did not develop HSP during his first episode of MSSA endocarditis, but developed biopsy-proven HSP during his subsequent episode years later. This case highlights the complex interplay between genetic susceptibility and infection-specific immune triggering in HSP.

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Figure 2. Classic ankle distribution voilaceous palpable rash seen in Henoch-Schönlein Purpura.

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