CLINICAL VIGNETTE

A Case of Atypical Henoch-Schonlein Purpura

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A 92-year-old male with a history of diabetes mellitus with neuropathy and proteinuria, congestive heart failure, hypertension, hyperlipidemia, and dementia presented for evaluation of a 3-week history of multiple worsening lower extremity ulcerous lesions accompanied by bilateral swelling. The lesions began as macules on his toes which transitioned to larger bullae and draining ulcers. The patient also reported joint pain involving his lower extremities and difficulty getting up due to the pain. He relied on his family for support with his ADLs and IADLs.

Review of systems was significant for a chronic cough as well as chest pain, palpitations, claudication, and peripheral edema. He denied fever, weight loss, rash, easy bruisability, and oral ulcers. He also denied genitourinary symptoms, recent travel, animal exposure, or medication changes.

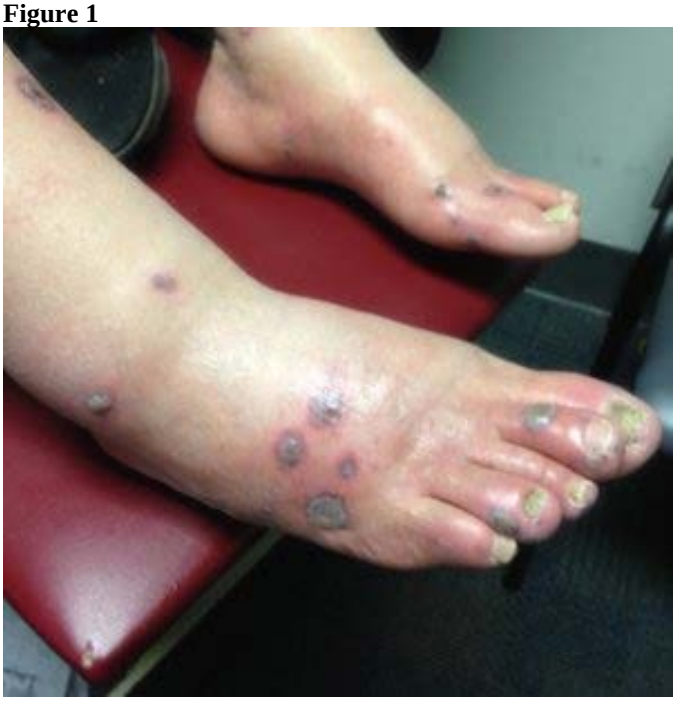
Family history was significant for diabetes, hyperlipidemia, and heart disease. The patient did not use tobacco, alcohol, recreational drugs and was currently not sexually active.

Initial presentation in the clinic revealed an alert, non-cooperative, elderly male sitting in a wheelchair. Vital signs were normal and cardiopulmonary and abdominal examinations were unremarkable. Lower extremities revealed multiple 5 mm to 3 cm discrete gun-metal gray tense bullae with violaceous and erythematous rims, some draining serosanguineous fluid and others which were ulcerated (Figure 1). His extremities showed 3+ edema bilaterally without cyanosis. Pulses were 2+ and symmetric. Neurologic examination showed full range of motion in his upper extremities and 4/5 lower extremity motion, limited by pain.

Initial laboratory evaluation included a urinalysis with 1+ blood (115 RBCs), 3+ proteinuria, and 3+ glucose. Due to concern for vasculitis with renal involvement, the patient was admitted to the hospital. Further evaluation yielded a creatinine of 1.1, and elevated urine protein:creatinine ratio of 6.47, erythrocyte sedimentation rate of 42, and C-reactive protein of 1.4. IgA was normal at 411 and 24-hour urine collection revealed 7g of proteinuria. Extensive rheumatologic and infectious disease labs (including hepatitis B/C, HIV, RPR, dsDNA, ANA, RF, ANCA, anti-GBM, SSA/SSB, Sm/RNP, TPO, C3/C4, SPEP/UPEP, anticardiolipin) were normal, though quantiferon gold test was positive. Chest radiography was within normal limits, and knee x-ray revealed osteoarthritis. Renal ultrasound revealed bilateral renal cysts with mural calcification in the left kidney, but no evidence of hydronephrosis and patent renal vessels.

A recent transthoracic echocardiogram showed no evidence of valvular vegetation. A lower extremity duplex study showed posterior tibial and peroneal artery occlusions which were deemed to be chronic requiring no intervention.

Figure 1

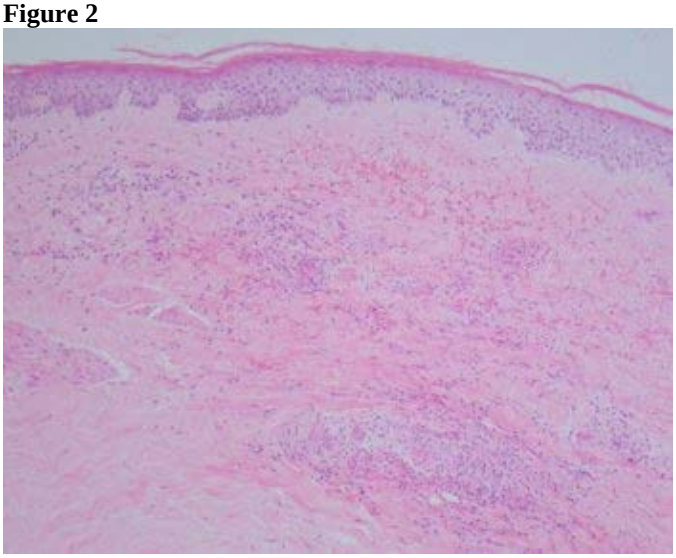


Skin tissue cultures were negative for both bacterial and fungal organisms. Two punch biopsies along the left shin and right foot revealed leukocytoclastic type vasculitis and 1+, granular deposition of IgA in dermal blood vessels (Figure 2). The shin biopsy was negative for PAS, gram, and AFB stains and showed no evidence of malignancy.

Based on the patient's clinical presentation, exam findings, laboratory results, and, biopy results, he was diagnosed with Henoch-Schonlein Purpura (HSP). Treatment was started with parenteral methylprednisolone for three days, followed by oral prednisone. After discharge he developed HSP lesions, severe anasarca which did not improve with IV diuretics, and worsening renal function. He was treated with repeat course of steroids as well as rituximab to reduce steroid dosage. CT scan of his chest, abdomen, and pelvis did not show evidence of

lymphadenopathy or neoplasm. Due to his multiple comorbidities, worsening HSP, and renal decline despite rituximab, the patient was made comfort-care and died a few months after his initial presentation.

Figure 2



Epidemiology

HSP is a common primarily childhood immune complex systemic vasculitis affecting small vessels. Ninety percent of cases occur between the ages of 3 and 15 years.[1, 2] HSP is uncommon in adults, with incidence of 0.1-1.2 per million in adults over 20 years old and unknown prevalence.[1,3] The disorder is more common in males, with a male/female ratio of 1.5.[4,5] Though the disorder is often self-limiting in children, it is more complicated in adults commonly with renal symptoms and a high incidence of renal insufficiency.[4,6]

Pathogenesis

HSP is a systemic vasculitis characterized by deposition of immunoglobulin A (IgA) immune complexes and neutrophil and eosinophilic infiltration mainly in small blood vessels of the skin, joints, kidneys, and gastrointestinal tract.[7] While the exact etiology is unknown, infections, malignancies, vaccinations, drugs, allergens, and cryoglobulinemia are thought to be potential risk factors.[7]

Clinical Manifestations

The classic tetrad of HSP includes non-thrombocytopenic palpable purpura, arthralgias, abdominal pain, and renal involvement. Cutaneous involvement of IgA vasculitis consists of symmetric palpable purpura predominantly in pressure areas, especially around the ankles.[5] In one-third of adults, the purpura may be necrotic or hemorrhagic.[5] Arthralgias are frequent, occurring in about two-thirds of cases, mainly involving the knees or ankles.[5] Gastrointestinal involvement also occurs in about two-thirds of cases, with colicky abdominal pain as the most common complaint.[5] Finally, renal involvement has prevalence ranging from 45 to 85%.[3] Microscopic hematuria is the most sensitive and earliest symptom, and may be associated with urine protein excretion sometimes in the nephrotic range.[5]

Diagnosis

There are various classifications of IgA vasculitis often adapted for children, with the most recent revision in the 2012 of the Chapel Hill International Consensus Conference. They defined vasculitis as one with IgA1-dominant immune deposits affecting small vessels, and often involving the skin, GI tract, joints, and kidney with glomerulonephritis indistinguishable from IgA nephropathy.[5] Laboratory findings generally include increased ESR, elevated circulating immune complexes and IgA, elevated complement, and hematuria.[8] The main histopathologic features on skin biopsy are leukocytoclastic vasculitis on hematoxylin and eosin staining and vascular IgA and complement 3 deposits on direct immunofluorescence.[8]

Treatment

Treatment of HSP is usually supportive as the disease is often benign. Some report use of corticosteroid and immunosuppressive drugs, in cases of severe organ involvement. Both colchicine and dapsone have been shown to be effective for the cutaneous purpura of HSP.[5] Dapsone may also alleviate abdominal pain and arthritis.[5] Corticosteroids have been shown to be effective for abdominal pain and arthralgias. The role of corticosteroids in renal involvement is controversial. Some studies in children show a lack of effect but other studies in adults show efficacy of corticosteroid pulses in *IgA nephropathy*.[5] Other, studies evaluating cyclosporine A in combination with corticosteroids for patients with IgA nephritis have been favorable and rituximab has also been shown to be effective in case reports for renal remission.[5] Finally, the use of intravenous immunoglobulin as well as plasmapheresis may be helpful in treating patients with renal involvement.[4,5] There are no guidelines for renal biopsy, but it may be considered with acute renal failure, nephrotic syndrome, or persistent proteinuria.[5]

Prognosis

HSP is more common in children than adults, with more severe disease occurring in adults.[5] In particular, GI and renal involvement cause morbidity and mortality in adults.[5] Short-term prognosis of HSP is determined by the gastrointestinal manifestations which can include vasculitic colitis, whereas long-term prognosis is dependent on the presence and severity of renal involvement.[3] The percentage of glomeruli showing crescents is the most important prognostic finding.[1] Adult follow-up studies show up to one-third developing end stage renal failure.[3]

Discussion

The prevalence of HSP in adults is better recognized, but still underappreciated in adults, especially the elderly. Our patient initially presented with lower extremity purpura, chronic arthralgias, and both hematuria and proteinuria on urinalysis. While his lower extremity purpura in pressure areas are characteristic of HSP, our patient had vascular insufficiency which may also present with blistering lesions. Furthermore, his significant proteinuria could have been due to diabetic complications as he had considerable proteinuria prior to presentation. However, his new onset hematuria raised suspicion for an acute glomerulonephritic process with a differential including not

only vasculitidies, but also lupus, anti-GBM disease, membranoproliferative glomerulonephritis, or mixed cryoglobulinemia.

Our patient's renal involvement was not surprising, as the literature shows that it occurs in about 63% of adults with rheumatoid purpura.[9] Factors associated with long term end-stage renal disease include poor baseline renal function, baseline proteinuria, and interstitial fibrosis, sclerotic glomeruli and fibrinoid necrosis on renal biopsy. Our patient did not undergo a renal biopsy due to his multiple comorbidities.[5] His risk for future renal involvement was high because of his significant proteinuria as well as hematuria.[10] One retrospective study of adults found patients with hematuria at disease onset or renal involvement during the course of the disease more commonly developed renal sequelae.[10] For adults with HSP, the rate of progression to chronic renal failure is about 30%.

HSP may be triggered by infection or malignancy. Our patient had no symptoms of recent infection, but fit the demographic for malignancy-associated HSP. One study reported patients with HSP-associated malignancies, were overwhelmingly males with a mean age of 60. They presented primarily with solid tumors, of which non-small cell lung cancer was most prevalent.[8]

Because of our patient's severe disease, corticosteroids were appropriately initiated and eventually started on rituximab, which has been shown to be effective in renal disease. Our patient ultimately progressed to severe renal failure and significant uncontrolled anasarca.

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