Resolution of Sinus Bradycardia, Complete Heart Block and Left Ventricular Dysfunction with Rituximab Therapy in Henoch-Schönlein Purpura

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Introduction

- Henoch-Schönlein purpura (HSP) is a leukocytoclastic vasculitis of small vessels, known as IgA vasculitis.
- 90% of cases occur in the pediatric age group. HSP is self-limited in majority of the cases. It is characterized by palpable purpura (without thrombocytopenia and coagulopathy), arthralgias/artheitis, abdominal pain and renal disease.
- It is associated with glomerulonephritis, immunoglobulin deposition of immunoglobulin A1 (IgA1) like monospecific nephropathy. HSP behaves similarly to mesangiocapillary IgA nephropathy.
- Cardiac involvement is extremely rare, seen with severe HSP.
- Advanced age at the time of diagnosis, decreased kidney function, high patient renal insufficiency, severe active vasculitis lesions/necrosis are associated with poorer outcome.
- Primary pathogenetic mechanism in HSP is unclear. Immunosuppressive therapy regimens may include steroids and alkylating agents such as cyclophosphamide.
- Reportedly mortality in patients with HSP, heart block, and LV systolic dysfunction who have been treated with immunosuppression (prednisone, azathioprine, and cyclophosphamide) exceeds 40% (5/12 reported cases). Many survivors have residual LV systolic dysfunction (37 reported cases) Lutz et al

Case

- We present a case of a 61-year-old man with HSP that is remarkable due to cardiac involvement and resolution of left ventricular systolic dysfunction and bradyarrhythmias with immunosuppression with rituximab and steroid therapy.
- Past medical history notable for idiopathic thrombocytopenia purpura (ITP), asthma, bipolar disorder and diabetes. Patient initially presented on an outside hospital with a purpuric rash.
- He was diagnosed with HSP based on renal and skin biopsy.
- His skin showed diffuse confluent, erythematous lesions with petechiae which were mixed with areas of focal lesions that were localized to the lower extremities, along with the lower abdomen, thighs, and back. His back showed some sloughing of the skin. No palpable and plateletless lesions were appreciated.
- The renal biopsy showed a severe background of nodular diabetic glomerulosclerosis and diffuse proliferative glomerulonephritis with exudative features, IgA diomey deposits. Skin biopsy showed IgA deposits. Abdominal CT revealed wall thickening of the duodenum & proximal jejunum with dilatation and an EGD revealed duodenitis, jejunal and ileum ulcerative esophagitis. Colonoscopy with terminal ileum biopsy showed mild active ileitis.
- Serologies were negative. UA confirmed proteinuria (3 gm/d). Microscopy showed dysmorphic erythrocytes.
- He developed new onset sinus tachycardia with initial ventricular fraction of 35%. He was not able to enable downward conformational myocardial biopsy for HSP. HSP was confirmed immunohistologically due to progressive renal dysfunction.
- He developed symptomatic bradycardia requiring transvenous pacing. Myocardial HSP involvement with severe acute LV systolic dysfunction and essential node dysfunction (SAN) was presumed given extracardiac HSP histological diagnosis.
- Treatment with tapering corticosteroids and weekly rituximab, a chimeric monoclonal antibody against the B cell protein CD20, was initiated for a total of four doses and resulted in resolution of SAN and conduction system disease in 2 weeks. His temporary pacing wire was discontinued 2 weeks after initiation of rituximab therapy.
- LV systolic function improved to 49% over a period of 3 weeks. Hemodynamic evaluation revealed normal pressures other than mild pulmonary hypertension and did not require further diuretics.
- Patient’s thrombocytopenia slowly improved with rituximab therapy without any complications.

Figure 1. 12 lead ECG prior to rituximab treatment

Figure 2. Telemetry strips prior to rituximab treatment

Discussion

- HSP related mortality in patients with heart block, and LV systolic dysfunction who have been treated with immunosuppression (prednisone, azathioprine, and cyclophosphamide) exceeds 40% (5/12 reported cases). Many survivors have residual LV systolic dysfunction (37 reported cases) as reported by Lutz et al.
- There have been only a few previously reported cases where HSP involving cardiac vessels has led to clinical abnormalities. These patients had marked vascular inflammation, which resulted in myocardial necrosis and death. Deaths occurred despite the early use of immunosuppression with high-dose corticosteroids, cyclophosphamide and azathioprine (Polizzotto et al).
- Post-mortem examination from previously reported cases revealed extensive vasculitis and necrosis of the right atrium and left ventricle. Also, deposition of IgA and C3 in intramyocardial vessel walls was found without any cardiac symptoms and these deposits resolved following treatment with immunosuppressive agents stressing subtotal cardiac involvement in a patient with HSP (Polizzotto et al).
- We present a unique case of HSP with cardiac involvement with resolution of the sinus bradyarrhythmias, conduction system abnormally and LV systolic dysfunction with rituximab and steroid therapy.

Conclusion

- Henoch-Schönlein purpura is a small vessel vasculitis and affects the SA node, conduction system and myocardial systolic function.
- Early recognition of cardiac involvement in HSP and prompt treatment with rituximab with steroids may prevent severe consequences like LV systolic dysfunction, bradyarrhythmias, conduction system abnormalities and potentially death.

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Rituximab

- A chimeric murine/human anti-CD20 monoclonal antibody targeting auto-antibody producing lymphocytes
- Typically dosed at 375 mg/m2 weekly for 4 weeks, although optimal dosing has not been defined.
- Side effects can be serious but fortunately are very rare. Glucocorticoid administration with the first infusion can minimize acute reactions. Studies in HSP patients in adult suggest that combination therapy with high dose methotrexate and rituximab may improve response rates as compared with monotherapy with either agent.

References


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