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A fatal case of severe gastrointestinal and renal involvement in Henoch–Schönlein purpura

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ABSTRACT

Henoch–Schönlein purpura (HSP) is an immune-complex mediated vasculitis affecting small vessels with dominant IgA deposits. It is seen mostly in children, with a self-limiting disease, but can present with more severe clinical features in older patients, such as gastrointestinal (GI) involvement, with a propensity for rapid progression. In this report, we describe our experience with a male HSP patient who presented with pneumonia, palpable purpuric rash, severe GI involvement with hemodynamic compromise and acute kidney injury. Even though we escalated therapy over time given the lack of response with each previous strategy, with corticosteroids and cyclophosphamide, he developed massive lower gastrointestinal hemorrhage that was not responsive to any supportive measure and died as a result of hemorrhagic shock. There was no established protocol that guided this treatment due to lack of rigorous data, which emphasizes the need for more studies on adult HSP in order to establish the optimal management for HSP patients with severe gastrointestinal manifestations.

Implication for health policy/practice/research/medical education:

HSP is a small vessel vasculitis which rarely presents in adults. As a consequence, there is a paucity of clinical studies and no treatment guidelines exist. Additional research is vital to define management strategies for HSP in adults. We describe a rare presentation of HSP in an adult male with a fatal outcome.

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1. Background

Henoch–Schönlein purpura (HSP) is an immune-complex mediated small vessels vasculitis with dominant immunoglobulin A (IgA) deposits (1). It usually presents with the classic symptoms of purpura, arthritis/arthralgia, abdominal pain and renal disease (2). It is mostly seen in children, with an estimated annual incidence of 15 cases/100 000 (3,4). In contrast, it rarely presents in adulthood, with an estimated annual incidence of 1.3 cases/100 000 (4,5). As such, the natural history of the disease is less understood in adults. While self-limited in children (3,4), adult patients exhibit more serious clinical features (4,5). Although the cause of this condition remains unknown, it is clear that IgA system plays a

central role in its pathophysiology (6). IgA1 levels are commonly elevated in the serum of patients, resulting from an increased production and a defective clearance. Recent studies have shown aberrant glycosylation of IgA1 to be a key feature of this condition (4). Management in adults is also challenging, as few studies assessed the efficacy of different therapeutic options.

2. Case Report

We present a case of a 67-year-old Caucasian male with past medical history of hypertension, dyslipidemia and stable essential thrombocytosis with a JAK2 mutation treated with hydroxycarbamide. He was initially admitted for pneumonia, treated empirically and discharged. Three

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days later he was readmitted with palpable purpuric rash with pustular lesions and partially necrotic tissue scattered over the distal portion of the lower extremities (Figure 1).

The laboratory tests revealed an acute kidney injury (serum creatinine [sCr] level of 3.26 mg/dL) and hematuria (proteinuria of 50 mg/dL on dipstick and 417 red blood cells [RBCs] per high power field on automated urinalysis).

He underwent workup for possible vasculitis and glomerulonephritis, including antinuclear antibody, perinuclear anti-neutrophil cytoplasmic antibodies, cytoplasmic anti neutrophil cytoplasmic antibodies, anti-glomerular basement membrane serologies, complement levels, cryoglobulins, human immunodeficiency virus and hepatitis panel serologies, IgA levels, and serum protein electrophoresis, all of which were unremarkable. His hemoglobin, which was 8.1 g/dL on presentation, trended down to 7.1 g/dL over 2 days, with normal haptoglobin values (2.3 g/L), lactate dehydrogenase (200 U/L) and platelet count ($556 \times 10^9/L$). Additional laboratory findings showed proteinuria 3.4 g/24 h, serum albumin of 2.7 mg/dL, erythrocyte sedimentation rate 103mm/h and elevated C-reactive protein 12.1 mg/dL.

Three days later he developed diffuse abdominal pain and diarrhea and a computed tomography of the abdomen and pelvis was performed that showed marked continual thickening of the wall from the duodenum to the jejunum (Figure 2A) and from the ileum to the cecum (Figure 2B). The disease was dominant in the ileum, which also showed stenosis and inflammation. Colonoscopy revealed an irreducible bowel loop beyond the transverse colon. With a strong suspicion of HSP, he was started on intravenous methylprednisolone at 1 g/d for three consecutive days, followed by oral prednisolone 60 mg daily. He was also treated with antibiotics - ceftriaxone and metronidazole.

A renal biopsy was performed and the findings confirmed our hypothesis. Of the 10 glomeruli viewed on light microscopy, all of them showed diffuse endocapillary hypercellularity with intracapillary neutrophils (Figure



Figure 1. Palpable purpuric rash on lower extremities.

3A) and one presented with a global cellular crescent (Figure 3B). Immunofluorescence staining on a paraffin embedded tissue section showed strong mesangial and peripheral capillary wall staining for IgA (Figure 3C), C3 (Figure 3D), kappa and lambda light chains. The abdominal symptoms faded over time and the renal function gradually improved which is why we decided to treat with corticosteroids alone.

Shortly after he was readmitted due to hematochezia and acute anemia with an abrupt drop in hemoglobin to 5.3 g/dL. Upper gastrointestinal (GI) endoscopy was normal, but colonoscopy showed blood throughout the entire bowel and again an irreducible bowel loop beyond the transverse colon. Capsule endoscopy showed erosions and ulcers throughout the ileum and duodenum. His worsening GI involvement (recurrent episodes of hematochezia, with hemodynamic compromise) and renal function (sCr reached a peak of 1.5 mg/dL with proteinuria of 4.3 g/24 h) prompted an escalation of the immunosuppressive regimen. Thus, IV cyclophosphamide 750 mg once monthly was initiated. The patient showed a full recovery and was discharged after one month and a half.

One month later he was once again readmitted with spondylodiscitis. Soon after he presented with several episodes of massive lower GI hemorrhage and abdominal pain with hemodynamic compromise with nadir hemoglobin of 3.3 g/dL. He received four units of RBC concentrate and fresh frozen plasma with a good response (7.8 g/dL). Even though methylprednisolone pulses 1 g daily for 3 days were initiated, he presented once again with massive lower GI hemorrhage, abdominal pain, hypotension and tachycardia irresponsive to any supportive measure. The patient went into shock and died, despite aggressive RBC transfusion.

3. Discussion

HSP is the most common vasculitis in children, where a clinical diagnosis is usually sufficient, has a predictable course and is usually self-limiting (4). However, in adults, HSP tends to have an atypical and aggressive presentation, and a biopsy is usually required to confirm the diagnosis

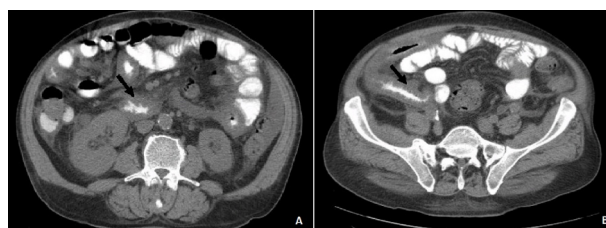


Figure 2. Computed tomography scan with IV contrast. Diffuse thickening of duodenum (A) and ileum (B) can be observed (arrow).

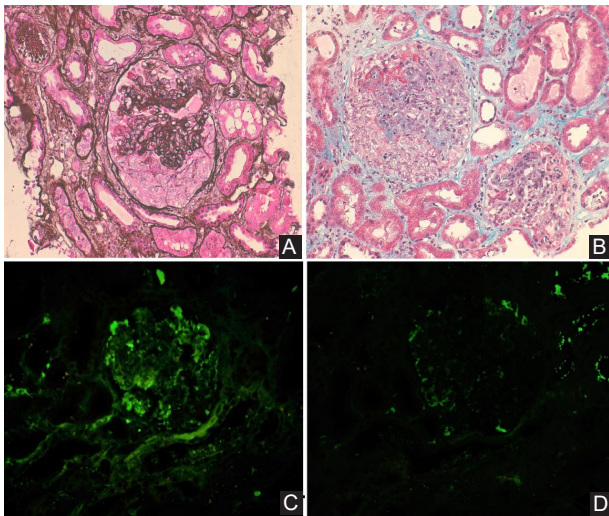


Figure 3. Kidney biopsy. (A) Endocapillary hypercellularity (Methenamine silver, $\times 200$), (B) global cellular crescent with fibrinoid necrosis (Masson's trichrome, $\times 200$), (C) mesangial and peripheral capillary wall staining for immunoglobulin A and (D) C3.

(4,5). In fact, adults have a higher risk of significant renal involvement including progression to end stage renal disease (7,8). The most common renal manifestation in children is microscopic hematuria, while adults more frequently present gross hematuria with nephritic and nephrotic features (4,9). GI manifestations are frequent, ranging from commonly seen abdominal pain, nausea, vomiting, to more severe and rare involvement with GI hemorrhage, bowel ischemia and perforation (10,11). The small intestine is the most frequently involved part in the GI tract, most likely because of its predilection to ischemic injury (12), while the second portion of the duodenum, as well as the stomach, terminal ileum and colon, are often affected (10,12). In children, HSP usually responds to steroids. Optimal management in adults, including HSP nephritis, remains controversial. Randomized control trials in this area are scarce and often inconclusive (13). Due to a more aggressive clinical course, immunosuppressive treatment is administered more often in adults despite the lack of evidence, with successful results in children often extrapolated to adults. Small studies have not been able to prove benefit of adding cyclophosphamide to steroid treatment (4). Similarly, a small case series identified patients with severe HSP nephritis who were treated with steroids in combination with plasma exchange with mixed outcomes (7). Knowledge about treatment of severe GI manifestations comes mainly from case reports and series in children, in which immunosuppression and plasma exchange have been used in the event of steroid failure (8).

Overall, our patient showed abdominal pain, purpuric rash, imaging showing severe GI involvement and renal

injury, sharing features with other adult patients reported in the literature. However, severe bowel involvement with recurrent hematochezia that ultimately lead to the fatal outcome in such a short period of time makes our patient a rare case. With such scarce evidence on what constitutes the ideal management strategy of adults, we escalated therapy over time given the lack of response with each previous strategy. Even though he was first discharged from the nephrology ward almost fully recovered from the initial symptoms and without any signs of GI bleeding, he was quickly readmitted and died shortly after despite aggressive RBC transfusion.

4. Conclusions

Additional research is vital to define management strategies for HSP in adults. While various combinations of steroids, immunosuppressive agents and plasma exchange have been used with mixed results in small series, randomized control trials are required to prove its benefit.

Authors' contribution

All authors wrote the manuscript equally.

Conflicts of interest

Authors declare no conflict of interests.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors. Because the patient passed away, informed consent was obtained from a family member.

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