Henoch-Schönlein Purpura complicated with major gastro-intestinal hemorrhage

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Abstract

We report a case of Henoch-Schönlein Purpura in a 83-year old patient. The patient presented with a purpuric rash and arthralgia. During admission, he developed hematochezia and acute kidney injury. Because of protracted gastro-intestinal bleeding after initiating therapy with methylprednisolone and ileocaecal resection, azathioprine was started. Gastro-intestinal bleeding resolved, and renal function normalized. We present the clinical and pathological findings of Henoch-Schönlein Purpura, focusing on gastro-intestinal manifestations. (Acta gastroenterol. belg., **2014**, 77, **379-382**).

Key words : Henoch-Schönlein Purpura/IgA vasculitis, azathioprine, IgA, complication.

Abbreviations : HSP, Henoch-Schönlein Purpura ; IgA, immunoglobulin A ; eGFR, estimated Glomerular Filtration Rate ; CKD-EPI, Chronic Kidney Disease – Epidemiology Collaboration ; PT, Prothrombin Time ; aPTT, activated Partial Thromboplastin Time ; RBC, Red Blood Cell ; ANF, Anti-nuclear Factor ; ANCA, Anti-neutrophil Cytoplasmic Antibody ; CT, Computed Tomography ; URI, Urinary Tract Infection ; IgA V, IgA Vasculitis.

Introduction

Henoch-Schönlein Purpura (HSP) is a systemic vasculitis involving the small vessels, associated with immunoglobulin A (IgA) deposition in the small vessels of the skin, joints, kidney and gastro-intestinal tract. The disease generally is self-limited, but in severe cases, treatment with immunosuppressive therapy may be required. We present an adult patient with HSP complicated by important gastro-intestinal bleeding necessitating ileocaecal resection, treated with glucocorticoids and azathioprine.

Case report

A 83-year-old man was admitted 3 days after developing a purpuric rash and arthralgia. In the recent history, he suffered from a mild upper respiratory tract infection, with nasal congestion and coughing. He had a prior history of hypertension, non-insulin-dependent diabetes mellitus and cholecystectomy. His medical treatment consisted of telmisartan and metformin.

Clinical examination showed a palpable purpura, symmetrically distributed and most prominently on the lower extremities, but also on the hands (Fig. 1a). Furthermore, arthralgia of both knees was noted without pronounced swelling, tenderness, erythema or warmth. Biochemical evaluation demonstrated a mild anemia (hemoglobin 11.0 g/dL, normal range 14.0-18.0 g/dL), an elevated serum creatinine of 2.11 mg/dL (normal range 0.67-1.17 mg/dL), eGFR 28.1 mL/min/1.73 m^2 (CKD-EPI), and urea of 94 mg/dL (normal ≤ 50 mg/dL). Five months before admission, the serum creatinine was normal (0.99 mg/dL). There was no thrombocytopenia and normal PT and aPTT. Urine analysis showed dysmorphic microscopic hematuria (28 RBC/μL (normal ≤ 5 RBC/μL), 84% dysmorphic), no leucocyturia, and 1.69 g proteinuria/24 h. Further immunologic evaluation demonstrated negative testing for ANF and ANCA, normal serum complement levels (including total complement activity, C3, C3d and C4), normal serum levels of immunoglobulins, with a modest elevation of IgA cryoglobulins (2.27 mg/L, normal ≤ 2.00 mg/L). Renal ultrasonography showed normal size of the kidneys (bilateral 113 mm, cortex 14 mm and 15 mm) and absence of hydroureteronephrosis.

A skin biopsy of a purpuric lesion on the leg was performed and showed a perivascular inflammatory infiltrate with neutrophils and lymphocytes in the papillary dermis and reticular dermis. Immunohistochemistry showed complement deposition of C4d while staining for IgA, C3d and C1q were negative (Fig. 1b). During admission, the patient developed abdominal pain with hematochezia and acute kidney injury (AKIN stage 3).

The (classic) tetrad of palpable purpura, arthralgia, abdominal pain and renal disease suggested the diagnosis of HSP / IgA vasculitis.

Besides 6/28 obsolescent glomeruli, a diffuse mesangial hypercellularity accompanied by endocapillar inflammation was seen in the renal biopsy. There was a moderate degree of interstitial fibrosis with tubular atrophy but without crescent formation (Oxford classification : M1E1S0T1). On immunohistochemical examination, mesangial deposition of IgA and C4d was observed (Fig. 1c). Neither morphology neither immunohistochemistry was suggestive for cryoglobulinemia-associated glomerulonephritis.

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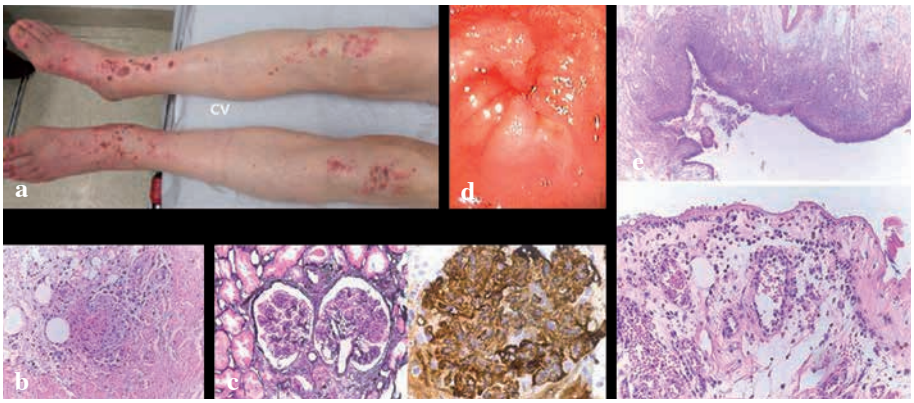

Fig. 1. — Clinical and pathological examinations
1a : Symmetrically distributed palpable purpura at time of presentation.
1b : Skin biopsy : perivascular inflammatory infiltrate with neutrophils and lymphocytes (HE stain, original magnification 200×).
1c : Renal biopsy : left panel : mesangial hypercellularity and endocapillar inflammation in the glomeruli (silver methenamine stain, original magnication 200×) ; right panel : mainly mesangial IgA positivity (anti-IgA stain, original magnification 400×).
1d : Endoscopic examination : multiple actively bleeding ileal ulcers.
1e : Ileal biopsy : upper panel : mucosal ulceration (HE stain, original magnification 25×) ; lower panel : serosal inflammation and vasculitis of the small vessels ans serosal capillaries (HE stain, original magnification 200×).

Therapy with methylprednisolone (500 mg/day during 3 days, and afterwards 0.8 mg/kg/day) was initiated. Prophylactic calcium and vitamin D treatment was administered, as well as proton pump inhibitors and antibiotics. A beneficial effect on renal function and proteinuria was observed, but hematochezia increased and the patient needed blood transfusions (Fig. 2). Gastroscopy did not show any abnormalities, while ileocoloscopy revealed multiple actively bleeding ileal ulcers (Fig. 1d). On CT scan of the abdomen, there was oedema of the terminal ileum, but no signs suggestive of intussusception or perforation. Coagulation was optimized with infusion of fresh frozen plasma, but nevertheless the need for blood transfusions remained high (Fig. 2). The presence of multiple and diffuse spread lesions precluded the option for endoscopic and angiographic treatment. Moreover, because of the precarious renal function, administration of more contrast was avoided. Because of protracted gastrointestinal bleeding, a laparotomy was performed. Because of peroperative signs of vasculitis with intestinal edema in the distal 70 cm of the small bowel, an ileocaecal resection with enterectomy (70 cm) was performed. Anatomopathologic examination of the ileum showed mucosal necrosis, serosal inflammation and vasculitis of the small vessels (Fig. 1e).

One week after surgery, there was melena in the ileostomy. Endoscopic investigation showed multiple bleeding ulcers. Pulse intravenous methylprednisolone (750 mg/day for 3 days) were administered but this did not result in an improvement of symptoms. Concomitantly, there was a deterioration of renal function (Fig. 2). Azathioprine was started 7 days after re- emergence of intestinal bleeding at a dose of 50 mg/day. After initiation of azathioprine, gastro-intestinal bleeding resolved, and renal function improved. There were several infectious complications, but patient eventually recovered and was discharged to a rehabilitation centre with a serum creatinine of 1.08 mg/dL and an eGFR of 63.1 mL/min/1.73 m^2.

There was no recurrence of gastro-intestinal blood loss or deterioration of renal function. However, several infectious complications (catheter related sepsis, UTI, pneumonia, osteomyelitis of the calcaneus) occurred and the patient died 3 months after discharge because of a pneumonia.

Discussion

HSP, also called IgA vasculitis (IgAV), is a systemic vasculitis characterized by the tetrad of palpable purpura without thrombocytopenia and coagulopathy, arthralgia/arthritis, abdominal pain and renal disease (1). HSP usually affects children, while it is less common in adults. In adulthood, clinical manifestations are more severe, and renal involvement is more frequent (2,3). As in this case, the onset of IgAV is often associated with upper respiratory tract or gastro intestinal infection, immunizations or medications (4). According to the American College of Rheumatology, there are four main criteria for the diagnosis of HSP, including palpable purpura, an age of less than or equal to twenty years at onset of symptoms, acute abdominal pain and biopsy showing granulocytes in the walls of small arterioles and/ or venules. Two or more of these criteria had a sensitivity of 89.4% and specificity of 88.1% in separating adult patients with HSP from those with other causes of vasculitis (5).

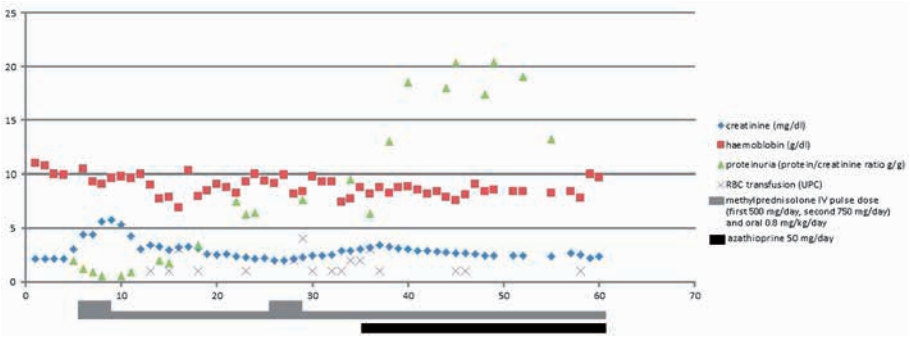

Fig. 2. — Biochemical evolution and treatment
Evolution of proteinuria, serum creatinine and hemoglobin, receiving treatment with methylprednisolone and azathioprine.

Gastrointestinal manifestations occur in 50-75% of patients and include colicky abdominal pain, vomiting, gastrointestinal hemorrhage, bowel ischemia and necrosis, bowel perforation and rarely hemorrhagic ascites, gall bladder involvement, acute pancreatitis, and protein loosing enteropathy. Intussusception, typically ileoileal, has been reported in children, and is rare in adults (6). Due to its predilection toward ischemic injury, the small intestine – especially the second portion of the duodenum and the terminal ileum- is the most frequently involved site in the gastrointestinal tract (7).

The pathogenic mechanism of organ involvement in HSP is thought to be due to the predominantly polymeric IgA1 immune complex deposition in the target-organ small vessel walls, that in turn activate complement factors, leading to neutrophil chemotaxis, which causes inflammation an necrosis of the vessel wall (resulting in focal fibrinoid necrosis), with occasional necrosis and red blood cell extravasations, histopathologically characterized as leucocytoclastic vasculitis (8).

In the present case, the initial presenting sign was the classic purpura, and patient was seen by a dermatologist, so skin biopsy was performed and showed a leucocytoclastic vasculitis. Since staining for IgA, that is pathognomic for HSP, was negative, diagnosis was not clear. The reason why staining for IgA was negative on skin biopsy might be the fact that immunohistochemical studies, essential to confirming the diagnosis of HSP, in our experience often requires biopsy of a second skin site. During admission, renal function deteriorated, and diagnosis was made by renal biopsy. HSP is characterized by endocapillary proliferation and IgA deposition in the mesangium on immunohistochemistry, identical to that in IgA nephropathy. However, in this case, the gastrointestinal bleeding was the most severe symptom and pathologic examination showed vasculitis of the small vessels.

The treatment for HSP is in first place supportive. In patients with crescentic HSP, high dose methylprednisolone (250-1000 mg /day for three days, followed by prednisolone 1 mg/kg/day for three months) may be beneficial (9). Since our patient did not improve after this treatment, we associated azathioprine, based on limited literature data suggesting a beneficial effect (10). Other regimens that have been evaluated are cyclosporine A (11), cyclophosphamide (12), plasmapheresis (13), immunoglobulins (14) and factor XIII concentrate (15).

In conclusion, association of therapy with azathioprine to the classic treatment with high dose methylprednisolone may have had a beneficial effect on renal function and on gastrointestinal bleeding in this case. However, because of the slow onset of effect of this medication, we can not know for certain that the quick recovery is related to the treatment with azathioprine. Nevertheless, the patient died because of the complications of his immunocompromised state.

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