Unexpected outcome (positive or negative) including adverse drug reactions

Henoch–Schönlein purpura: a clinical case with dramatic presentation

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Summary

A case study involving a 55-year-old Caucasian male with end-stage glomerulosclerosis is presented here. Kidney biopsies showed no deposits on immunofluorescent microscopy. Relapsing massive haemoptysis and suspected bronchovascular malformation required lung lobectomy which revealed malformative and tortuous small blood vessels, with no vasculitis. Blood antinuclear antibodies, antineutrophil cytoplasmic antibodies and antiglomerular basement membrane antibodies were undetectable. Seric immunoglobulins and complement levels were normal. Three months later, arthralgia and joint oedema first appeared. Skin biopsy revealed vasculitis immune-reactive to immunoglobulin A. Systemic corticotherapy was then started. Two weeks later, the patient presented with abdominal pain, melena and rectal bleeding (haematoquesia). Endoscopic study showed diffuse gastrointestinal haemorrhage. Angiographic study revealed diffuse lesions compatible with vasculitis and haemorrhage from multiple spots. Cyclophosphamide and then intravenous immunoglobulin were associated to treatment without response. Increasing blood loss occurred, with massive gastrointestinal haemorrhage and haemorrhagic ascitis. Death occurred due to uncontrolled diffuse bleeding. Necropsy findings showed generalised small vessels vasculitis compatible with Henoch–Schönlein purpura.

BACKGROUND

Henoch–Schönlein purpura (HSP) is a generalised small vessels vasculitic disease. Aetiology of HSP is not completely known, but immunoglobulin A (IgA) seems to play a central role in the pathogenesis of this disease.^{1–4} HSP has been extensively studied in children; thus, not much is known about its natural course in adults. Most cases occur under 10 years of age; however, it has been increasingly diagnosed in adults in whom clinical course may be more severe.^{1–5} It presents characteristically with a combination of purpuric rash, renal involvement, abdominal pain and arthritis.^{1–6} However, any of these symptoms may be absent, leading to confusion or delays in diagnosing the condition. It can be masquerade as many different conditions, depending on the symptoms. Pulmonary involvement is extremely rare and limited to few case reports and a few small case series.¹ Gastrointestinal involvement is common; nevertheless, severe presentation with diffuse massive haemorrhage with shock is also extremely rare.⁵

CASE PRESENTATION

The patient, a 55-year-old Caucasian male, presented with chronic renal failure of unknown origin on haemodialysis. He had a recent kidney biopsy showing end-stage glomerulosclerosis. A previous biopsy performed 4 years before revealed focal and segmental glomerulosclerosis. Both biopsies showed no glomerular deposits on immunofluorescent microscopy.

The patient had a history of relapsing massive haemoptysis, requiring admission to the Emergency Room (ER). A bronchovascular malformation on left-lung upper lobe was observed on angio-CT scan (figure 1), which was not confirmed on angiographic study (figure 2). Blood antinuclear

antibodies, antineutrophil cytoplasmic antibodies and antiglomerular basement membrane antibodies were undetectable. Seric immunoglobulins and complement levels were normal. After another episode of great volume haemoptysis, he was submitted to a left superior lung lobectomy. Histopathological exam revealed haemorrhagic infarct, malformative and tortuous small blood vessels, with no vasculitis or capillaritis.

Three months later, palpable purpura, arthralgia and joint oedema occurred.

INVESTIGATIONS

Skin biopsy revealed vasculitis immune-reactive to IgA (figure 3). Systemic corticotherapy was then started, followed by joint symptoms improvement.

Two weeks later he was admitted again, to the ER, this time with abdominal pain, melena and rectal bleeding (haematoquesia). Endoscopic study showed diffuse gastrointestinal haemorrhage. Celiac and mesenteric angiographic evaluation revealed diffuse arterial lesions compatible with vasculitis, and diffuse haemorrhage from multiple spots in communication with intestinal lumen (figure 4).

TREATMENT

Cyclophosphamide was then associated to systemic corticotherapy, with no response to treatment. Intravenous infusion of immunoglobulin was also carried out but without success.

OUTCOME AND FOLLOW-UP

Increasing blood loss, massive gastrointestinal haemorrhage and haemorrhagic ascitis occurred. Patient died 2

weeks later on haemorrhagic shock. Necropsy findings showed generalised small vessels vasculitis immune-reactive to IgA, compatible with HSP (figure 4).

DISCUSSION

HSP is a systemic vasculitis involving arterioles, venules and capillaries, mainly affecting skin, joints, gastrointestinal tract and kidney, but sometimes it affects other organs too.

It was William Heberden, in 1806, who first described a case of a 5-year-old boy presenting all four clinical hallmarks of HSP (purpura, arthritis, gastrointestinal involvement and kidney inflammation). Johann Schönlein in 1837 and Edouard Henoch in 1874 reported additional cases and recognised that the disorder often followed upper-respiratory-tract infections and was not always self-limited, sometimes progressing to serious kidney involvement.

HSP is the most common form of vasculitis in children, with an annual incidence of 14 cases/100 000 persons.⁴ More than 90% of patients with HSP are younger than 10 years of age, and there is a peak incidence occurring in children 4 to 5 years old.^{2 3} In adults, median age at onset is 50 years.⁴

Specific pathogenesis of HSP remains unknown; however, it is generally considered an autoimmune process initiated by deposition of IgA containing immune complexes predominantly in dermal, gastrointestinal and glomerular capillaries. This immune complex-mediate reaction may

occur as response to infections caused by various viruses or bacteria, usually from the upper respiratory tract, or exposure to drugs or food allergens.^{3 4} HSP is generally a benign, self-limited, mild disease in children, with nearly complete recovery.

Presentation differs significantly with age as older patients exhibit much more severe manifestations.^{4 5}

Dermal lesions are the most distinctive, usually the earliest clinical feature and occur in almost all cases.³⁻⁵ They characteristically involve extensor surface of lower extremities in a symmetric manner. They originate as erythematous maculae, which develop into purpuric papules and may become confluent. In severe cases, they may become haemorrhagic, purpuric or necrotic. Skin biopsies of the lesions demonstrate leukocytoclastic vasculitis.

Joint involvement with arthralgia or arthritis is the second most common manifestation of HSP.³⁻⁵ It is often incapacitating but generally transient and leaves no permanent deformity. Ankles and knees are most frequently affected, but elbow, hands and feet may also be involved.

Gastrointestinal involvement occurs in approximately 2/3 of cases usually manifested by abdominal pain, diarrhoea and bloody stools.^{3-5 7} Abdominal pain is the second most frequent symptom.^{4 5} Bowel ischemia, perforation, fistula and massive gastrointestinal haemorrhage with shock are seen infrequently.^{4 5 7 8}

Renal involvement is a common, but inconstant, feature and has variable incidence.^{3 4} Patients develop haematuria,

Figure 1 Thorax angio-CT scan. Image suggestive of bronchovascular malformation on the left upper lobe.

Figure 2 Lung angiographic study. No images suggestive of arterio-venous malformation.

Figure 3 Histopathologic exam. Vasculitis immuno-reactive to immunoglobulin A. (A) Vasculitic lesions. (B) Fibrinoid necrosis, deep cutaneous blood vessels. (C and D) Fibrinoid necrosis, superficial cutaneous blood vessels. (E) Direct immunofluorescence testing immunoglobulin A positive.

Figure 4 Celiac and mesenteric angiographic evaluation. Diffuse arterial lesions and diffuse haemorrhage from multiple spots in communication with intestinal lumen. (A) Superior mesenteric angiogram: contrast extravasation in ascending colon. (B) Inferior mesenteric angiogram: contrast extravasation in descending colon. (C) Inferior mesenteric angiogram: contrast extravasation in sigmoid.

nephritis or nephrotic syndrome with renal failure. Chronic renal failure is the most important determinant of HSP outcome and its most serious sequela.^{4 5} Progressive deterioration of glomerular filtration rate may occur, and end-stage renal failure may ensue in a minority.^{3–5} There are no unique renal microscopic findings, but glomerular IgA deposits on immunofluorescent microscopy may be the only feature to distinguish HSP nephritis from other vasculitis.^{4 5} Complement levels are usually normal.

Subclinical interstitial lung disease and impaired gas exchange has been reported. Clinical pulmonary involvement, particularly haemorrhage, is a rare occurrence. It has primarily been reported in adults and adolescents, but seldom in children younger than 10, and is associated with significant rates of morbidity and mortality.^{1 3 5 9} According to Nadrous *et al*, until 2004 there were 28 cases of HSP with clinical pulmonary involvement referred in the literature.¹ Of these patients 75% were older than 10 years.¹ In these 28 cases analysed, 26 manifested as diffuse alveolar haemorrhage (DAH).¹ The onset of DAH is abrupt and of short duration; 9 patients have died, and 8 of them from respiratory failure due to DAH.¹

Other unusual features and rare complications that have been reported include oesophageal stenosis, haemorrhagic pancreatitis, protein-losing enteropathy, pleural haemorrhage, thrombocytosis, neurological complications, including encephalopathy, seizures, intracerebral haemorrhage, cerebral vasculitis and behavioural changes; scrotal swelling and testicular necrosis; and renal haemorrhage, haemorrhagic ascitis and haemorrhagic cystitis.

Diagnosis of HSP depends on history and clinical findings. It usually comprises a classic combination of non-thrombocytopenic purpuric rash, arthralgia or arthritis, renal involvement and abdominal pain often with mild gastrointestinal haemorrhage. However, any of these may be seen in other vasculitic conditions. Diagnosis is not difficult if this classic scenario is present. Nevertheless, when one or more symptoms are absent or symptoms are not typical, differential diagnosis may become difficult. There is no specific laboratory test for diagnosis. Skin biopsy shows a leukocytoclastic vasculitis, sometimes with necrosis of small blood vessels and immunostaining may reveal deposition of IgA in the walls of involved blood vessels. Renal biopsy findings are diverse and may vary from proliferative

glomerulonephritis to glomerulosclerosis. Immunofluorescence usually reveals mesangial IgA deposition. Meanwhile HSP may be misdiagnosed, most commonly because of the failure to perform direct immunofluorescence and the consequent failure to detect IgA.

There is no specific treatment for HSP, and there is no clear evidence that treatment may change natural history of disease.²⁻⁴ In children overall prognosis is excellent; thus, no treatment or supportive care is needed for most patients.³⁻⁵ When necessary, symptomatic treatment with non-steroid anti-inflammatory drugs can relieve joint and soft-tissue discomfort. Treatment for aggressive HSP is controversial, as throughout the medical literature there are no clinical trials or meta-analysis that can guide treatment. Some authors consider corticosteroids as the mainstay of treatment.¹⁻³⁻⁵ Aggressive supportive management and steroid therapy may be adequate in the majority of severe cases.¹⁻³⁻⁵ In high-risk or acutely ill patients, combination of corticosteroid with cyclophosphamide or azathioprine may achieve better results.¹⁻³⁻⁵ Plasmapheresis has been used in some adults with vasculitis and rapidly progressive nephritis. High-dose intravenous immunoglobulin has also been used successfully in adults with renal involvement.⁵⁻¹⁰ Some reports of corticosteroid-resistant cases suggest that severe intestinal HSP may respond preferentially to intravenous immunoglobulin therapy, suggesting that in these cases it provides an effective alternative to corticosteroids.⁸ Gut vasculitis with significant blood loss, bowel ischemia or perforation may require surgical intervention.

Learning points

- ▶ HSP is uncommon in adults and generally associated with severe courses.
- ▶ Even after putting in all the required efforts, diagnosis may remain inconclusive, which delays the beginning of treatment.
- ▶ Some cases may show poor response to treatment, and even disease progression, despite aggressive therapy.
- ▶ Exceptional, fatal, cases have been reported in adults, mainly due to massive and diffuse haemorrhagic events refractory to treatment.

Competing interests None.

Patient consent Obtained.

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