CASE REPORT

Henoch-Schönlein purpura

An atypical cause of abdominal pain in a 70-year-old man

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KEY WORDS

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ABSTRACT

Henoch-Schönlein purpura (HSP) is a leukocytoclastic small-vessel vasculitis involving small vessels with the deposition of immune complexes containing immunoglobulin A and neutrophil and eosinophilic infiltration. Clinical manifestations include 4 classic signs and symptoms: skin lesions, arthralgias, abdominal pain, and renal disease. HSP primarily affects children and is uncommon in adults. However, the clinical course of HSP is more severe and prognosis worse in the adult population, despite the fact that the incidence of this disease is 20-fold lower in adults than in children. We present a 70-year-old man with HSP who has been successfully treated.

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INTRODUCTION Henoch-Schönlein purpura (HSP) is a systemic vasculitis with deposition of immunoglobulin A (IgA) immune complexes and neutrophil and eosinophilic infiltration.[1] Inflammation mainly affects small vessels in the skin, joints, kidneys, and gastrointestinal tract (TABLE 1).[2] The etiology of HSP is unknown. Viral and bacterial infections, malignancies, vaccinations, some drugs, hypersensitivity to certain allergens, and cryoglobulinemia are believed to be potential risk factors. Genetic factors are also involved to some extent in the etiology of the disease (renin-angiotensin system gene polymorphisms, the presence of HLA-B35). However, the assessment of this genetic background in terms of predisposition to HSP and severity of the disease is varied.[3]

HSP is a predominant presentation of systemic vasculitis in children, and its prevalence peaks in 4–5-year-old children.[1] The course of the disease is usually mild, with full recovery within several weeks or months.[2] The disease recurs in about 40% of cases.[1] Although 20-fold less common[4], HSP is associated with more severe manifestations and prognosis in adults than in children[5]. The typical first symptoms, both in adults and children, are skin lesions including purpura, hemorrhagic vesicles, necrotic ulcers[1], mainly on the lower extremities and buttocks[2]. Skin necrosis rarely occurs in children (<5% of cases) and the probability of necrotic lesions increases with age.[5] The incidence of abdominal pain, nausea, vomiting, and joint symptoms is similar in children and adults. Diarrhea, gastrointestinal bleeding and renal involvement are significantly more prevalent in adults.[6] It has been demonstrated that the risk of chronic renal insufficiency is also higher in adults.[5] Based on a long-term follow-up of adults with HSP, it has been demonstrated that the risk of chronic renal insufficiency is increased by the following factors: presence of glomerular crescents, macrophage infiltration and tubulointerstitial lesions[2], early-onset renal failure, hypertension at presentation and during follow-up, proteinuria (>1 g/d) during follow-up, age <30 years and male sex[4]. Several investigators showed that the occurrence of proteinuria >1 g/d at the onset of disease is also an independent risk factor of chronic renal failure.[4]

In rare cases, HSP may coexist with monoclonal gammopathy (e.g. multiple myeloma)[7] or even precede its onset a few years[8].

CASE REPORT A 70-year-old male patient was admitted to the hospital with a history of severe diffuse abdominal pain lasting several weeks, progressive fatigue and weight loss (approximately 8 kg in the past year). Abdominal pain was

TABLE 1 Signs and symptoms of Henoch-Schönlein purpura

skin (90–100% of patients)	macular eruptions, urticaria, hemorrhagic vesicles, necrotic ulcers, lesions typically located on the lower extremities and buttocks
skeletal system (75% of patients)	arthralgia (mainly the lower extremities, typically knee and ankle joints), other symptoms of arthritis
gastrointestinal tract (60% of patients)	abdominal pain (usually diffuse, not related to meals), vomiting, diarrhea, gastrointestinal bleeding (overt or occult)
kidneys (45–85% of patients)	microscopic or macroscopic hematuria, proteinuria, hypertension, renal failure
lungs (<5% of patients)	hemoptysis
nervous system (<10% of patients)	headache, seizures

not related to meals, often occurred at night and was relieved by opioid analgesics administered on an ambulatory basis.

The patient had a number of concomitant diseases including hypertension, a history of myocardial infarction 4 years earlier, treated with primary coronary angioplasty with stent implantation to right coronary artery and coronary artery bypass graft surgery. During the postoperative period he was diagnosed with dissection of thoraco-abdominal aortic aneurysm, which probably represented a complication of the procedures performed. Because of extensive vascular lesions and high-risk aortic surgery, conservative treatment had been recommended. Furthermore, he had been diagnosed as having peptic ulcer 7 years earlier.

On admission the patient's general condition was moderate. He reported diffuse abdominal pain, and pain in the left hip area. Arterial blood pressure was 110/70 mmHg, heart rate regular – 68/min, body temperature was normal. Apart from a loud vascular murmur in the mid abdomen, abdominal examination was normal.

Laboratory tests showed moderate normocytic anemia (hemoglobin concentration [Hb] 9.7 g/l, red blood cell count [RBC] 3.03×10^6 mm^3, hematocrit [Ht] 28.7%, mean corpuscular volume 93 fl), white blood cell count (WBC) – 5.9×10^3/mm^3, platelet count (PLT) 229×10^3/mm^3, serum ferrum 55 mg/dl (normal range: 37–181), transferrin 208 mg/dl (normal range: 200–360), ferritin 290 ng/ml (normal range: 15–275). The patient was also diagnosed with renal failure based on serum creatinine, 2.18 mg/dl, and creatinine clearance calculated by Cockroft-Gault formula, 24 ml/min. Sedimentation rate (SR) was 45 mm/h, and C-reactive protein (CRP) 14 mg/l (normal range: <3.0). Liver and pancreatic enzyme activities were normal. Urinalysis showed leukocyturia, microscopic hematuria, and proteinuria (570 mg protein in 24-h urine sample).

Differential diagnosis included bowel ischemia, peptic ulcer and renal artery dissection. Ultrasound examination showed no abnormalities of internal organs or abdominal lymph nodes, nor any signs of aortic aneurysm rupture. Computed tomography angiogram revealed no significant changes in the presentation of aortic dissection since the previous examination 2 years earlier (the diameter of ascending aorta was 60 mm, descending aorta was 35 mm in diameter). Aneurysm rupture and dissection of mesenteric, renal and iliac arteries were excluded. A 3 mm stenosis of the initial segment of the mesenteric artery (previously not described), extending from the aneurysm, was visualized. Arteriography with intravascular angioplasty of the stenosis was considered, but the procedure was abandoned due to normal blood flow in the mesenteric artery on Doppler ultrasound and the risk of renal dysfunction. In order to confirm or exclude suspected peptic ulcer, especially given persistent anemia, a radiogram of the upper gastrointestinal tract was performed and showed a lesion in the stomach fundus, which was difficult to interpret. Due to aortic aneurysm, gastroscopy was temporarily abandoned.

Abdominal pain persisted during hospitalization and there was a 2-day episode of vomiting and diarrhea. Despite empiric antibiotic treatment, followed by targeted antibiotic treatment (*Acinetobacter Baumanii* and *Enterococcus faecalis* susceptible to fosfomycin in urine culture), the patient reported dysuria and periodic gross hematuria. Furthermore, the joint symptoms aggravated. Apart from the left hip pain, the symptoms of arthritis in the ankle and left first metatarsophalangeal joints occurred.

The laboratory tests showed progressive anemia (Hb 8.0 g/dl) and increased inflammatory markers (SR 65 mm/h, CRP 58.9 mg/l [normal range: 0.0–10]). Serum uric acid was 7.6 mg/dl (normal range: 2.8–7.0). Latex agglutination test, Waaler-Rose test and autoantibody titer evaluation were negative. Porphyria was excluded based on negative urinary porphyrins. Fecal occult blood test was negative on three separate occasions.

During the following days purpuric lesions on the lower extremities and left forearm appeared (FIGURE 1). Plasma routine coagulation tests and PLT were normal. Based on the entire clinical manifestation, a provisional diagnosis of HSP was made. Histological examination of the skin specimen, which showed IgA deposits confirmed HSP (FIGURE 2). Treatment with 100 mg daily dapsone was started and abdominal pain, purpura and hematuria resolved after a few days. However, dapsone-induced severe methemoglobinemia resulted in drug discontinuation. Subsequently, oral prednisone at a dose of 1 mg/kg body weight daily was administered also with satisfactory results.

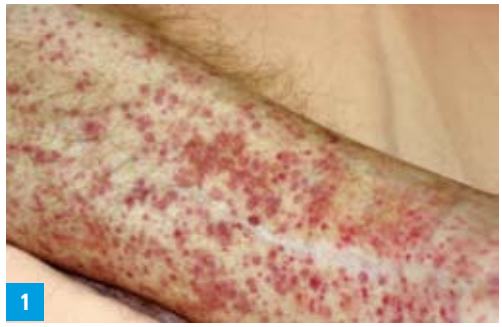

FIGURE 1 Skin lesions in a patient with Henoch-Scönlein purpura

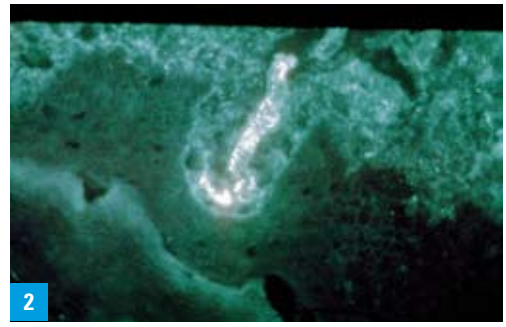

FIGURE 2 Immunopathology of the patient's skin biopsy specimen; fluorescent immunoglobulin A deposits

After 6 months, the patient was readmitted to the hospital for check-up. He reported no pain, hematuria or skin lesions. Laboratory tests showed Hb concentration 11 g/dl, RBC count $3.12 \times 10^6/mm^3$, Ht 31.5%, WBC count $9.5 \times 10^3/mm^3$, serum creatinine 1.45 mg/dl, SR 30 mm/h, CRP 1.5 mg/l. Urinalysis showed no proteinuria or microscopic hematuria. Repeat radiogram of the upper gastrointestinal tract showed smooth and mobile stomach walls with normal mucosa. Ultrasound examination of the urinary bladder showed no abnormalities. The treatment with prednisone was continued.

DISCUSSION In the present case, the four main symptoms of the disease appeared in a confusing order, thus hampering the diagnostic evaluation. For a couple of weeks, the first and only clinical manifestation was abdominal pain. It might have been caused by concomitant conditions (aortic dissection, peptic ulcers); however, this was not confirmed by the tests performed. Urinary symptoms were thought to be related to urinary tract infection refractory to treatment. Arthralgia was mostly associated with osteoarthritis or gout, based on typical location (left first metatarsophalangeal and ankle joints).

Following the occurrence of purpuric lesions, typically located on the extensor surface of the lower extremities, it was finally possible to establish a connection between the symptoms. The diagnosis of HSP was confirmed by immunopathology of skin biopsy specimen, which showed IgA deposits. Due to the patient's age and coexistent conditions, kidney biopsy was not performed.

A possible underlying cause was urinary tract infection. Also, the adverse effect of drugs, particularly angiotensin-converting enzyme inhibitors and non-steroidal anti-inflammatory drugs, cannot be excluded.

Dapsone is the drug of choice for leprosy and is also used in the treatment of cutaneous diseases with neutrophil infiltration and vasculitis.[9] Dapsone use for HSP have been mostly reported in children.[10,11] In all patients receiving dapsone skin lesions, abdominal pain and joint symptoms resolved.[9,11] However, after discontinuation of treatment some patients experienced recurrence of macular lesions, which might suggest that dapsone did not completely abolish skin lesions, but only improved them. No beneficial effect of the drug on kidney function was observed, which might limit its use.[10] Other challenges to be faced involve numerous side effects of dapsone (TABLE 2). Apart from close clinical observation, evaluation of complete blood count and smear, serum methemoglobin, SR, CRP and liver enzymes during the therapy is necessary.[12]

In the present case, treatment with 100 mg daily dapsone was administered, and abdominal pain, macular lesions and arthritis resolved in a couple of days. Furthermore, hematuria resolved and the laboratory tests showed decreased serum creatinine levels.

However, after a week of therapy, there were several adverse effects including significant fatigue impairing patient's activity, dyspnea and cyanosis as a result of increased methemoglobin, and biochemical markers of liver damage. Methemoglobinemia is one of the most common side effects of dapsone.[12] The normal level of methemoglobin in healthy adults is 0.2– 0.6%; during dapsone therapy it should not exceed 3%. A marked increase in methemoglobin levels in our patient (up to 10%) resulted in the discontinuation of dapsone treatment.

TABLE 2 Adverse effects induced by dapsone

systemic	headache, fatigue, nausea
hematologic	hemolytic anemia, methemoglobinemia
neurologic	peripheral neuropathy
dermatologic	Stevens-Johnson syndrome, necrotizing dermitis
hepatic	cholestasis, hepatitis
renal	nephritis
pulmonary	pneumonia
thyroid	hypothyreosis

Corticosteroids have been used in the management of HSP for over 50 years[6], despite a lack of prospective randomized clinical trials evaluating their effectiveness[5]. In case reports and series of cases, there are often contradictory views about corticosteroid efficacy in treating HSP.[6,10] The reported patient was treated with prednisone 1 mg/kg body weight daily, and we did not observe a recurrence of the disease either directly after therapy modification, or during a 6-month follow-up. It should be emphasized that despite numerous risk factors, the patient did not develop chronic renal failure.

In recent years the beneficial effect of intravenous immunoglobulins (IVIG) in cases of HSP resistant to corticosteroid treatment has been demonstrated.[13] It can be an effective alternative to corticosteroids for patients with severe gastrointestinal involvement (gastritis, gastrointestinal bleeding).[14] Because of possible nephrotoxicity of IVIG, special attention should be paid while treating elderly patients or patients with concomitant renal failure.[13] We hope that the present case will be helpful in differential diagnosis of abdominal pain.

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Plamica Henocha i Schönleina

Nietypowa przyczyna bólów brzucha u 70-letniego mężczyzny

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SŁOWA KLUCZOWE

dorośli, leczenie, objawy, plamica Henocha i Schönleina

STRESZCZENIE

Plamica Henocha i Schönleina (*Henoch-Schönlein purpura* – HSP) jest leukocytoklastycznym zapaleniem małych naczyń, w przebiegu którego dochodzi do odkładania się kompleksów immunologicznych zawierających immunoglobuliny A oraz nacieku granulocytów obojętno- i kwasochłonnych. Cztery główne objawy kliniczne choroby to: zmiany skórne, ból stawów, bóle brzucha i zapalenie nerek. HSP występuje przede wszystkim u dzieci; rzadko jest spotykana u dorosłych. Mimo dwudziestokrotnie mniejszej zapadalności u dorosłych niż u dzieci, objawy kliniczne HSP są cięższe, a rokowanie gorsze w populacji osób dorosłych. W artykule omówiono przypadek skutecznego leczenia 70-letniego chorego z HSP.

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