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Henoch-Schönlein purpura presenting with multiplex gastrointestinal manifestations and massive nephrotic syndrome in adulthood – a case report

Case Report

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Abstract: Henoch-Schönlein purpura (HSP) is a systemic small vessel vasculitis mainly affecting children. We report a case of a 49-year-old woman with severe gastrointestinal and renal involvement of HSP. Endoscopy revealed more characteristic findings in the terminal ileum than in the gastric antrum. Histological examinations of the biopsy samples from the ileum, antrum, skin and kidney confirmed the diagnosis of HSP. Parenteral corticosteroid therapy led to a rapid improvement of the gastrointestinal symptoms, but because of the excessive proteinuria intravenous cyclophosphamide therapy had to be introduced.

Keywords: *Henoch-Schönlein purpura • Nephrotic syndrome • Adulthood*

1. Introduction

Henoch-Schönlein purpura (HSP) is an idiopathic leukocytoclastic vasculitis affecting the small vessels of the skin, joints, gastrointestinal tract and kidneys. Palpable purpura, arthralgia, abdominal complaints and hematuria are the most characteristic symptoms of the disease. HSP is the most common vasculitis of childhood (annual incidence 14-18 per 100,000 children), and it occurs rarely in adults, but adults with HSP suffer from more severe disease as well as renal manifestations.

The American College of Rheumatology has established diagnostic criteria for HSP. These include age under 20 years at onset, palpable purpura, bowel angina (diffuse abdominal pain or bowel ischemia usually with bloody diarrhea), and biopsy showing evidence of granulocytes in the walls of arterioles and venules [1]. The diagnosis of HSP is made when at least two of these criteria are fulfilled.

2. Case report

A 49-year-old woman presented with a two-week history of colicky abdominal pain and bloody diarrhea. Her medical history was unremarkable, except for a varicotomy of the right lower limb in May 2007. There was no history of previous renal disease in the patient and in her family members. A few weeks prior to admission, she developed an upper respiratory tract infection, which was treated with cefuroxim acetyl. At the same time she noticed skin rashes over her left buttock and thigh. In

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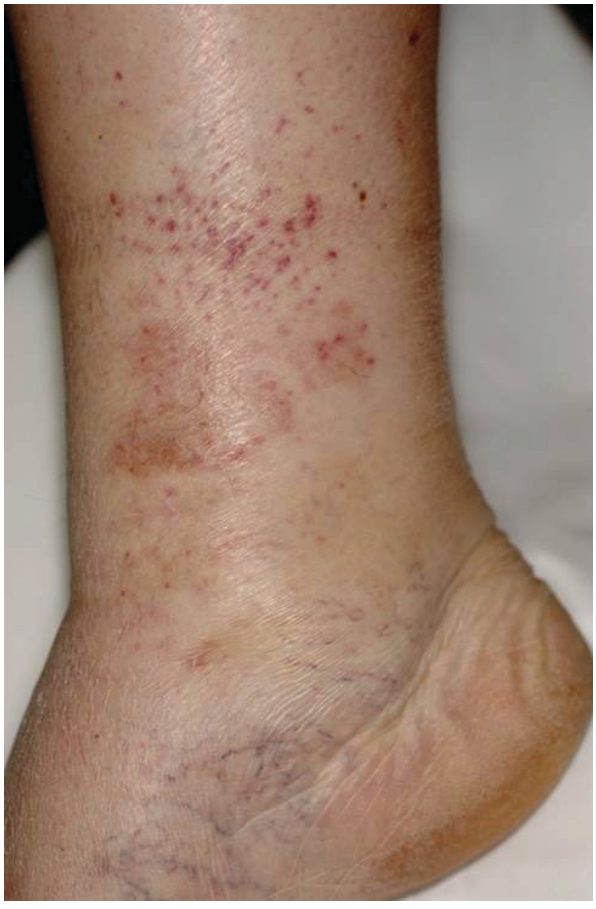
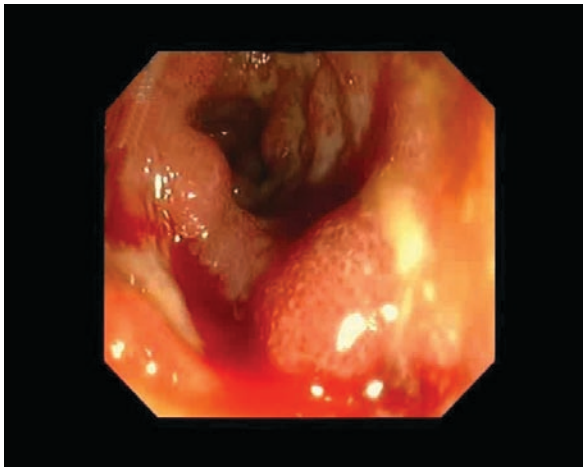
Figure 1. Swelling and purpuras on the lower extremity.



the fourth day of the antibiotic treatment, she had colicky abdominal pain, vomiting, and bloody diarrhea. Based on her gastrointestinal and dermatological complaints, systemic vasculitis was suspected. In the background of her deteriorating abdominal pain, a plain abdominal X-ray examination suggested the onset of ileus. Surgical intervention was avoided by conservative management (nasogastric suction, rectal tube, and intravenous fluid administration). Because of the constant, mainly periumbilical, cramping pain and bloody stool she was admitted to our clinic for further examinations. One day prior to her admission, she developed bilateral swelling of the lower extremities developed and a skin rash involving both the left and right buttocks, the lower extremities, and the hands (Figure 1).

Physical examination revealed swollen legs with pitting edema and numerous palpable purpuric lesions on the lower extremities, hands, and arms. Diffuse abdominal tenderness was noted with normal bowel sounds. Admission weight was 80 kg, axillary temperature 36.7°C, heart rate 76 min^{-1} and blood pressure 130/90 mmHg respectively. Laboratory findings showed anemia with a hemoglobin level of 101 g/L, hypoproteinaemia

Figure 2. Endoscopic findings of the terminal ileum with erosions and ulceration of the inflamed mucosa.



with total protein level of 40 g/L and albumin of 17 g/L, an elevated erythrocyte sedimentation rate of 44 mm/h, and C-reactive protein level of 53.8 mg/L. Total leukocyte count was 14.2 Giga/L and platelet count was 522 Giga/L. Elevated antistreptolysin O titer of 328 U/mL was also found. Microhematuria and significant proteinuria of 20-30 g/day total urine protein were also recently noted. Serological examinations did not reveal elevated anti-neutrophil cytoplasmic antibodies, anti-saccharomyces cerevisiae antibodies, and anti-double-stranded DNA antibody. Serum creatinine and urea levels were also within the normal limits, and the glomerular filtration rate was 56 ml/min according to the Modification of Diet in Renal Disease formula.

Skin biopsy of the purpuric lesion was consistent with leukocytoclastic vasculitis. Vascular immunoglobulin A (IgA) deposition was not detected.

Colonoscopy was performed about 40 cm up into the terminal ileum. The distal 10 cm of the terminal ileum and the whole colon were normal, but in the upper parts, mucosal edema and fibrin-covered ulceration were detected with confluent hyperemic lesions (Figure 2). Gastroscopy revealed macroscopically granulated, hyperemic mucosa in the gastric antrum with circumferential and superficial ulcers (Figure 3). Histological findings of the terminal ileum and gastric antrum were consistent with chronic inflammation in the lamina propria, leukocytoclastic vasculitis in the submucosal small vessels, the presence of dilated lymphatic vessels, and mild eosinophilic infiltration (Figure 4). Clinical, endoscopic, and histological findings confirmed the diagnosis of HSP.

Parenteral corticosteroid therapy was initially administered, resulting in cessation of the abdominal pain and diarrhea and gradual resolution of the skin lesions.

Figure 3. Endoscopic findings of the gastric antrum with superficial ulcers and hyperamic mucosa.

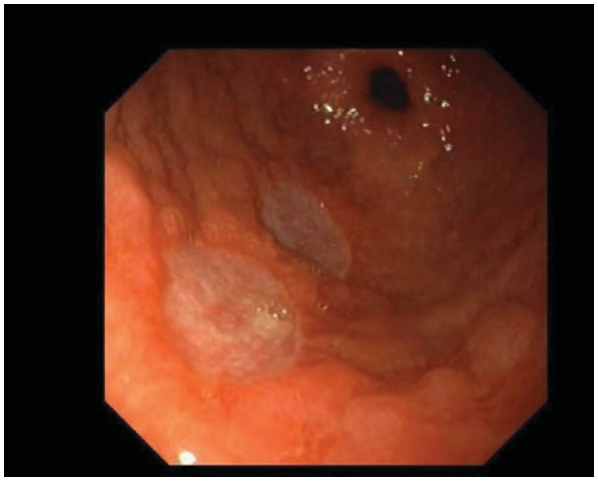


Figure 4. Histological findings of the terminal ileum with polymorphonuclear granulocyte infiltration of the small vessels.

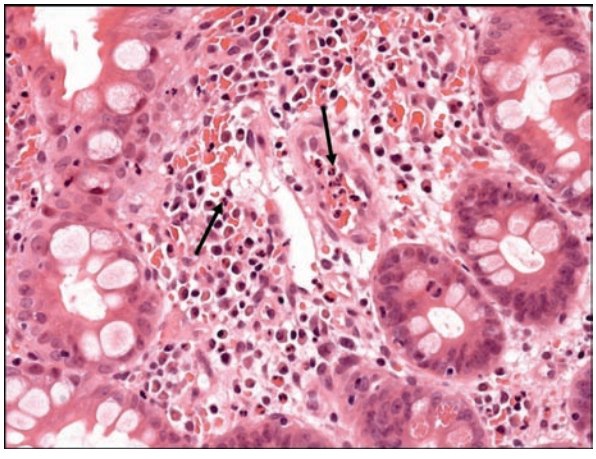
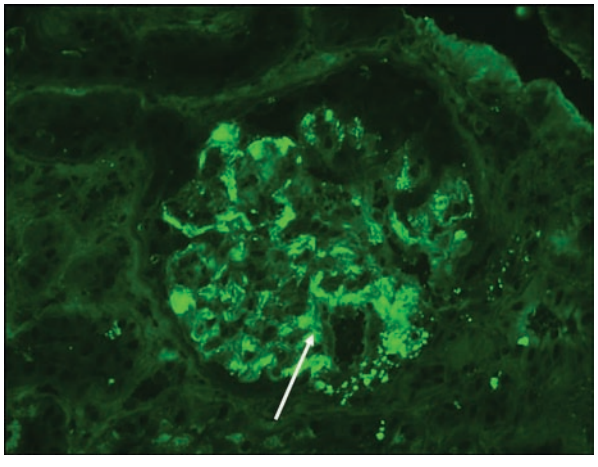


Figure 5. Immunofluorescence staining of the renal glomerulus with mesangial IgA deposition.



However, because after two pulses of methylprednisolone 500 mg there was no improvement in proteinuria, 400 mg of parenteral cyclophosphamide therapy was introduced, and a few days later, renal biopsy was performed. The patient had been receiving corticosteroid for one month at the time of the biopsy. The serum creatinine level measured at biopsy was 69 µmol/l. Histological samples of the kidney showed focal mesangial proliferative glomerulonephritis with mesangial IgA deposition (Figure 5). In serial sections, two small cellular glomerular crescents were found out of 13 glomeruli (15%). In the interstitium, minimal focal lymphoplasmocytic infiltrate was present in less than 5 % of the glomeruli. Few proximal tubules showed signs of regeneration related to acute tubular necrosis. No significant chronic tubulointerstitial damage was detected. In the medullary interstitium around a tubular castlike material, a small granulomatous inflammatory response was seen. Arterioles and arteries showed no pathological change.

After repeated cyclophoshamide and corticosteroid pulse therapy, symptoms of the renal manifestation also started to show an improvement. The patient was discharged from the clinic with oral corticosteroid (64 mg methylprednisolone) and diuretic therapy. An angiotensin-converting-enzyme inhibitor was also given at 4 mg/day for renoprotection. Intravenous cyclophosphamide with corticosteroid pulse therapy was repeated three times after the patient was discharged at the same doses, resulting in a significant improvement five months after the onset of the disease. Oral methylprednisolone 64 mg/day was tapered by 8 mg until the next corticosteroid pulse therapy. Kidney function tests were within the normal ranges (creatinine, 65 µmol/l; urea, 7.2 mmol/l), and the level of proteinuria decreased to 3 g/day at the last follow-up.

3. Discussion

Henoch-Schönlein purpura is the most common cutaneous small-vessel vasculitis in children and is characterized by IgA and C3 deposition in the small vessels, although diagnosis can also be made in the absence of dermal IgA deposition [2]. Different vasculitic conditions such as microscopic polyarthritis, Wegener's granulomatosis, and systemic lupus erythematosus should be considered during the differential diagnostic procedure in the presence of palpable purpura with abdominal pain, renal symptoms, or arthritis/arthralgia. Abdominal symptoms occur in 50% to 85% of the patients affected by the disease, mainly with colicky pain that can mimic an acute abdomen. In some cases

(14%), abdominal symptoms precede the development of a skin rash [3]. Renal and lower gastrointestinal involvement at the onset of the disease occur with a higher incidence in adults. Severe colorectal bleeding, occult blood loss, vomiting, and diarrhea are also common symptoms of gastrointestinal involvement in HSP [4]. Involvement of the terminal ileum has been reported only in a few cases, predominantly in males [5]; however, simultaneous ileal and gastric manifestation has not been previously reported.

Renal involvement occurs in about 33% of children and 63% of adults with HSP. Segmental focal glomerulonephritis associated with IgA deposits in the mesangium is the most characteristic renal histological finding in the disease [6]. Prognosis of the disease is mainly determined by the appearance and severity of renal manifestations. The risk of developing end-stage renal failure is about 1% to 7% in patients with HSP nephritis [7]. On the basis of previous reports, it remains unclear whether severe abdominal pain, persistent purpura, or corticosteroid treatment is associated with the development of HSP nephritis. Multivariate analysis performed by de Almeida et al. found severe abdominal pain to be the only independent variable predicting to HSP nephritis, while their univariate analysis indicated that all of these are associated with renal improvement [8]. In our case, renal manifestation occurred before corticosteroid initiation, and it was accompanied by severe abdominal pain and gastrointestinal bleeding. Multivariate analysis performed by Coppo et al. found a higher age, female sex, and increasing mean proteinuria during follow-up to contribute to predicting the risk for progression of HSP nephritis [9].

Our patient fulfilled three of the criteria for the diagnosis of Henoch-Schönlein purpura, except for her age. Her severe abdominal symptoms necessitated surgical observation, but after corticosteroid pulse therapy, she recovered completely. Endoscopy proved to be very helpful in the precise diagnosis of the disease, as it revealed manifestations in both in the upper and lower GI tract. Interestingly, the endoscopic images were significantly different in the stomach and in the terminal ileum, despite similar microscopic findings.

Renal involvement is more frequent and more severe in adults than in children, and it requires aggressive treatment. Intravenous cyclophoshamide therapy seems to be effective in the treatment of the HSP nephritis, but long-term follow-up is needed to prevent disease recurrence and the development of progressive renal failure.

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