Case report

Pulmonary renal syndrome in an adult patient with Henoch-Shönlein purpura

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Astract

Henoch-Schönlein purpura (HSP) is a small vessel vasculitis characterized by purpuric skin rash, haematuria, abdominal pain, gastrointestinal bleeding and arthritis. Nephritis is more frequent and severe in adults than in children, with relatively more adults developing renal insufficiency. Another, fortunately rare, manifestation of HSP that increases mortality significantly, is diffuse alveolar haemorrhage. We report a rare case of an adult male patient with full-blown HSP that followed a respiratory tract infection. He successively, but not concurrently, developed all the clinical manifestations of HSP, i.e. arthritis, abdominal pain and bloody stools, a non-thrombocytopenic purpuric rash, and renal involvement; nephrotic range proteinuria first and haemodialysis-requiring nephritic syndrome later. Most interesting he developed life-threatening pulmonary haemorrhage fulfilling the criteria of the pulmonary-renal syndrome. An immunosuppressive regimen consisting of intravenous cyclophosphamide and corticosteroids was administered with success. In conclusion, HSP should be considered in the diagnosis of pulmonary-renal syndrome. In our opinion, the severity of the condition justifies the use of aggressive immunosuppressive treatment, like the one applied successfully to our patient. *Hippokratia 2006; 10 (4): 185-187*

Key words: *Henoch-Schönlein purpura, pulmonary renal syndrome, palmonury haemorrhage*

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Introduction

Henoch-Schönlein purpura (HSP) is a form of IgA mediated small vessel vasculitis characterized by purpuric skin rash without thrombocytopenia, haematuria, abdominal pain, gastrointestinal bleeding and arthritis[1]. The extent of renal involvement in HSP is the most important determinant of long-term prognosis. About 30% to 50% of patients with nephritis have persistent urinary abnormalities in long-term follow-up but only 1% of them will develop end-stage renal disease[2]. Although HSP affects children more often, it tends to be a more serious disease in adults. Nephritis is more frequent and severe in adults than in children, with relatively more adults developing renal insufficiency[3]. Another, fortunately rare, manifestation of HSP that increases mortality significantly, is diffuse alveolar haemorrhage[4].

This report presents a case of diffuse alveolar haemorrhage and severe renal involvement in an adult male with HSP. The patient responded well to treatment with corticosteroids and cyclophosphamide.

Case report

A 52-year-old male presented with a history of 3-day productive cough without fever to a general practitioner. A respiratory tract infection was diagnosed and after 10 days of oral macrolide administration the symptoms disappeared.

After a 10 days interval free of symptoms the patient presented to the local hospital with arthritis of the left wrist joint and right ankle joint. He was febrile (38.0˚C) his vital signs were normal and his blood pressure was 130/80 mmHg. Urine examination was unremarkable and all biochemical indices were normal. Haematology revealed an elevated white blood cell count (13200/μl) with neutrophilia (82.4%). Chest CT-scan showed subpleural reticular densities in the lower lobes of both lungs. Abdominal CT-scan was normal and his kidneys had normal size and shape. Blood, sputum and urine cultures, as well as, antinuclear antibodies and antineutrophil cytoplasmic antibodies, were all negative. The patient was treated with antibiotics without improvement. Progressively his clinical condition got worse; oedema of the lower extremities and pleural effusion with dyspnoea developed. Serum urea and creatinine continued to be normal, but he had low serum albumin (2.3 g/dl) and 24 hour urine revealed nephrotic

range proteinuria (4.6 g/24h) without haematuria. Two weeks after his presentation to the local hospital he began having abdominal pain, passed bloody stools and a non-thrombocytopenic purpuric rash on the extensor surface of his lower limbs was appeared.

At that point, the patient was transferred to our hospital for further evaluation and treatment. His pulse rate was 100 beats/min, respiration rate 28/min, blood pressure 140/80 mmHg and auxiliary body temperature was 36.9˚C. His initial laboratory findings were Hct 30.4%, WBC 14600/μl, PLT 542000/μl, serum urea 12 mg/dl, creatinine 0.87 mg/dl, urate 4.48 mg/dl, total proteins 4.85 mg/dl, albumin 2.7 g/dl, cholesterol 102 mg/dl, triglycerides 138 mg/dl, SGOT 18IU/L, SGPT 12IU/L, ALP 47 IU/L, γ-GT 15 IU/L, LDH 171 IU/L, sodium 136 meq/l, potassium 4.3 meq/L, calcium 7.8 mg/dl, INR 1.2, aPTT 27.8 sec. Arterial blood pH was 7.47, PO_2 70.8 mmHg, PCO_2 23.5 mmHg and bicarbonate 17.3 meq/l. Urine examination revealed nephrotic range proteinuria of 4.8 g/24h without haematuria. Blood, sputum, urinary and stool cultures, as well as, serologic tests for streptococcus pneumoniae, legionella pneumonophila, mycoplasma pneumoniae, CMV, HBV, HCV and HIV were negative. Acid-fast bacilli on sputum smear were not detected and sputum cultures for Mycobacterium tuberculosis was obtained, which finally proved negative, as well. Antinuclear antibodies, antineutrophil cytoplasmic antibodies, antiglomerular basement membrane antibodies and cryoglobulins were all undetectable. Blood transfusion was initially necessary for preservation of an acceptable Hct level. Fortunately, bloody stools stopped within 10 days after his admission to our hospital, without any specific treatment. Chest radiographs showed large bilateral pleural effusion, which after chest puncture proved to be a transudate. Colonoscopy and upper endoscopy showed hyperaemia and small deep ulcers throughout the large intestine and in the duodenum. Histopathological examination from the lesions showed heavy inflammatory infiltration of the chorion mainly by neutrophils, which also penetrated the epithelium. Tissue from a skin lesion biopsy was compatible with leukocytoclastic vasculitis. The skin tissue specimen that was taken by the dermatologists was not proper for immunofluorescence. On the twentieth day in our hospital, nephrology consultation was asked. At that time, the patient's labs remained almost the same; serum urea and creatinine were normal and nephrotic range proteinuria without haematuria persisted. The possibility of HSP diagnosis was set and a renal biopsy was programmed for the next day. In the evening the patient developed acute respiratory distress. He had haemoptysis and arterial blood gas revealed severe respiratory acidosis. The chest radiograph showed bilaterally patchy alveolar infiltrates suggesting pulmonary haemorrhage. He required intubation with ventilatory support and he was transferred to the intensive care unit where he remained for 7 days. There, besides treatment with a combination of antibiotics; he also received 1gr methylprednisolone intravenously o.d. for 3 days followed by 12.5 mg of prednisolone i.v. b.i.d.

After extubation he was transferred to our department. Physical examination on arrival revealed oedema anasarca, a blood pressure level of 180/110 mm Hg, a regular pulse rate of 90/min, a respiratory rate of 26/min and a temperature of 37.3˚C. Arthritis and purpura were disappeared. Urine volume was decreased to 500ml/day. His laboratory tests were Hct 28.7%, WBC 5500/μl, PLT 276000/μl, serum urea 263 mg/dl, creatinine 3.61mg/dl, urate 10.22 mg/dl, total proteins 4.7 mg/dl, albumin 2.6 g/dl, SGOT 16 IU/L, SGPT 11 IU/L, ALP 46 IU/L, γ-GT 29 IU/L, LDH 4001 IU/L, sodium 139 meq/l, potassium 5.0 meq/L, calcium 7.3 mg/dl, phosphorus 6.59, INR 1.16, aPTT 28.2 sec. Serum IgG, IgM, IgA, rheumatoid factor, C3, C4 and CRP were normal. With the patient under a Venturi mask set at 50% O_2 the arterial blood gas examination showed pH 7.39, PO_2 91.0 mmHg, PCO_2 23.0 mmHg and bicarbonate 14.1 meq/l. Urine examination revealed proteinuria of 1.5 g/24h, haematuria >100 red blood cells per HPF and red cell casts. Creatinine clearance was 7 ml/min. Chest

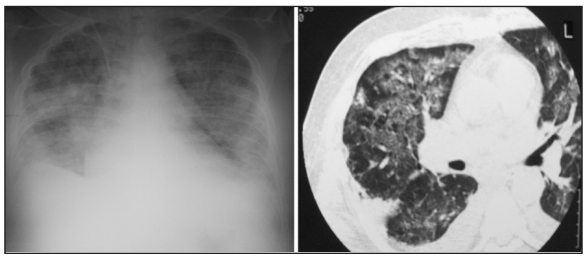

Figure 1. *Chest radiograph (in sitting position) showed bilaterally patchy alveolar infiltrates and chest CT-scan revealed bilateral pleural effusion, reticular densities and patchy ground-glass opacities suggesting pulmonary haemorrhage.*

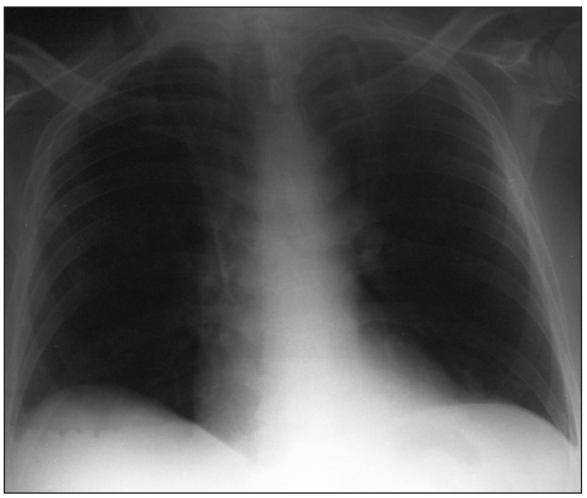

Figure 2. *Normal chest radiograph (in sitting position) after a two-month immunosuppressive treatment.*

radiograph showed bilaterally patchy alveolar infiltrates and high resolution chest CT-scan revealed bilateral reticular densities and patchy ground-glass opacities suggesting pulmonary haemorrhage (Figure 1). The patient started haemodialysis and he was treated with immunosuppressive therapy consisting of cyclophosphamide at a dose of 500 mg every 15 days and prednisolone at a dose of 75 mg daily intravenously. Renal biopsy was performed, and showed mesangial cell proliferation and expansion of mesangial matrix. Immunofluorescence revealed diffuse granular mesangial deposition of IgA and C3 but not of C1q, C4, IgG or IgM. The speculated diagnosis of HSP was confirmed. Under the above immunosuppressive regimen, the patient's clinical condition gradually improved. He became independent of dialysis and O_2 administration. After a two months treatment in our department, he was discharged from the hospital with serum urea 72mg/dl, creatinine 1.3mg/dl, and a normal chest radiograph (Figure 2). Proteinuria (1 gr/day) and haematuria (50 red blood cells per HPF) persisted. He continued the immunosuppressive treatment with oral methylprednisolone at a dose of 36mg per day and intravenous cyclophosphamide 1gr monthly. Today, two months after discharge, he is doing well and visits our department monthly in order to complete a six month immunosuppressive therapy.

Discussion

We report a case of an adult male patient with full-blown HSP that followed a respiratory tract infection. He successively, but not concurrently, developed all the clinical manifestations of HSP, i.e. arthritis, abdominal pain and bloody stools, a non-thrombocytopenic purpuric rash, and renal involvement; nephrotic range proteinuria first and haemodialysis-requiring nephritic syndrome later. Most interesting he developed life-threatening pulmonary haemorrhage fulfilling the criteria of the pulmonary-renal syndrome. An immunosuppressive regimen consisting of intravenous cyclophosphamide and corticosteroids was administered with success.

As it is already noted, HSP is more frequent in childhood, but in adults it tends to be a more serious disease. Nephritis is more frequent and severe in adults than in children, with relatively more adults developing renal insufficiency[3]. Crescent formations in more than 50% of the glomeruli or an acute onset of nephrotic range proteinuria are independently indicative of poor prognosis[5]. In a review of cases, Miura et al[6] showed that in middle aged patients (ages from 40 to 59 years) with HSP, the incidence of nephrotic range proteinuria was 13.1% and progress to chronic renal failure occurred in 16.4% of patients. Mortality rate in middle aged patients was 8.2%, lower than the mortality rate in older patients (25.9%), but much higher than the mortality rate in children (1-3%). It should be noted that the literature reviewed in this study concerns a period from 1948 to 1992. So, dialysis facilities were not available in all cases. However the high mortality rates indicate the severity of HSP in adults.

Pulmonary haemorrhage is a life-threatening, but fortunately very rare complication of HSP. Many textbooks of Internal Medicine or Nephrology do not even mention this complication. In two case series, one focusing on 38 patients with severe forms of HSP nephritis[7] and the other describing 250 adults with HSP[8], pulmonary involvement was absent. On the other hand, Cream at al[9], reported pulmonary involvement in 4 (5%) of 77 adult patients with HSP. In a retrospective study, Nadrous et al[4] examined the records of 124 patients with HSP; 56 patients being older than 18 years, and identified two patients 20 and 76 years old with pulmonary haemorrhage, i.e. 1.6% of all cases or 3.8% of adult patients with HSP. In the same study, the authors, reviewing the literature from 1967 to 2004, reported only 27 cases with HSP and pulmonary haemorrhage. Although HSP affects children more often, 17 of the above patients were older than 15 years (63%). Death was the outcome in 9 cases (33.3%) and 6 of the 18 survivors (33.3%) required mechanical ventilation. Most of the above patients received an immunosuppressive regimen with corticosteroids alone or in combination with cyclophosphamide.

In conclusion, along with more frequent causes, like pauci-immune vasculitides, HSP should be considered in the diagnosis of pulmonary-renal syndrome especially in adult patients. Because of the rarity of cases, no definite conclusion regarding therapy is available. In our opinion, the severity of the condition justifies the use of aggressive immunosuppressive treatment, like the one applied successfully to our patient.

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