Low serum C3, leukopenia, and thrombocytopenia: unusual features of Henoch-Schonlein purpura

Abstract
Henoch-Schonlein purpura (HSP) affects predominantly the skin, joints, gastrointestinal tract and kidney. Although the pathogenesis is probably of immune origin and complement activation is thought to play a role, laboratory findings including the serum level of the complement components are usually normal. We present a patient with a severe form of HSP nephritis who had unusual laboratory findings of a low level of C3, mild leukopenia and thrombocytopenia. These findings may further support the importance of complement activation in the pathogenesis of HSP.

Key words
Henoch-Schonlein purpura · C3 · Hypocomplementemia · Nephritis

Introduction
Henoch-Schonlein purpura (HSP) is a multi-system vasculitis affecting predominantly the skin, joints, gastrointestinal tract and kidneys. Other sites such as the central nervous system, lungs and scrotum may also be involved. Although complement activation, especially of the alternative pathway, is thought to play an important role in the pathogenesis of the disease [6, 26, 29], a low serum level of C3 is very unusual [6, 13, 15]. We present a child with HSP accompanied by a low serum level of C3 who developed nephritis and subsequently end-stage renal failure. He also presented with leukopenia and thrombocytopenia, unusual hematologic features for HSP.

Case report
A 10-year-old boy was admitted to Schneider Children’s Medical Center of Israel with leg pain and swollen ankles. His previous medical history was unremarkable except for mild asthma. One week before admission the patient complained of sore throat and fever of 38°C which subsided without treatment within 48 hours. He did not use any medication during the three months prior to this illness.

Positive findings on physical examination were mildly enlarged cervical lymph nodes, non-pitting pre-tibial and ankle edema, and fine non-palpable purpuric lesions over the calves and buttocks. Blood pressure was 110/60 mmHg. Laboratory tests showed an erythrocyte sedimentation rate of 7 mm/h, hemoglobin 13.9 g/dl, white blood cell count (WBC) 10,800/mm³ (7020 neutrophils, 2808 lymphocytes, 432 monocytes, 540 eosinophils), platelet count 200,000/mm³, creatinine 0.8 mg/dl, blood urea nitrogen (BUN) 23 mg/dl; liver enzymes were normal. Prothrombin time (PT) was 94%, partial thromboplastin time (PTT) 23 s, international normalized ratio (INR) 1.03, fibrinogen 426 mg/dl. Urine sediment showed seven red blood cells per high power field, mild proteinuria.
and no casts. Serum iron, transferrin, folic acid and vitamin B-12 were normal. The C3 component of the complement was 55 mg/dl, C4 27 mg/dl and CH50 96% (Table 1). Throat culture yielded streptococcus Beta hemolytic group A. Serum levels of thyroxine and thyroid-stimulating hormone (TSH) were normal; serology for hepatitis A, B, C viruses, human immunodeficiency virus (HIV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), and parvovirus B19, as well as repeated tests for antinuclear factor (ANF) and anti-dsDNA, anti-cardiolipin, anti-Ro, anti-La, anti-neutrophil cytoplasmic antibodies, cryoglobulin, cryofibrinogen, Coomb's and Ham tests were all negative.

On the fifth day of hospitalization transient leukopenia and thrombocytopenia with a WBC of 3600/mm³ (2088 neutrophils and 1224 lymphocytes) and a platelet count of 64,000/mm³ were noted; both conditions resolved spontaneously after a few days.

Abdominal pain and melena appeared one week after admission and were treated with oral prednisone 1 mg/kg daily and ranitidine 150 mg/day. Along with the gastrointestinal complaints renal function deteriorated: the creatinine level rose to 2.5 mg/dl and BUN to 211 mg/dl. In addition, hypertension (150/100 mmHg), anasarca, macroscopic hematuria and non-selective proteinuria ranging from 2 to 8 g/24 h developed. The patient was treated with furosemide, metolazone, hydrochlorothiazide, spironolactone, nifedipine, atenolol and penicillin VK. Hemodialysis was temporarily applied.

Kidney biopsy, performed 19 days after admission, showed diffuse proliferative glomerulonephritis with cellular crescents in two out of eight glomeruli (Fig. 1). The small number of glomeruli might have limited precise evaluation of the severity of the lesions. Excessive subepithelial and subendothelial wire loop-like deposits were detected by electron microscope (Fig. 2). Immunofluorescence demonstrated deposits of IgA, C3 and fibrinogen, located mainly in the periphery of the glomeruli; IgA was the most prominent deposit.

Rapidly progressive HSP nephritis was diagnosed. The patient was treated with methylprednisolone 1g/day for three days followed by oral prednisone 2 mg/kg daily and cyclophosphamide 2 mg/kg daily and dipyriramole 5 mg/kg daily, in accordance with a recently reported protocol [17]. Two weeks later pancytopenia was noted (WBC 3500/mm³ with 3080 neutrophils, 420 lymphocytes, Hb 6.7 mg/dl and platelets 35,000/mm³). The cyclophosphamide was stopped but the pancytopenia did not resolve during the following nine weeks. Bone marrow biopsy showed profound hypopcellularity (5%). The patient was treated with intravenous erythropoetin, 300 units/kg daily, with a good response and the blood count normalized. One month later the WBC count was 5600/mm³, Hb 14.2 g/dl and platelets 160,000/mm³.

Despite the treatment with plasmapheresis, intravenous immunoglobulins and repeated pulses of methylprednisolone the patient progressed to end-stage renal failure. He was treated by peritoneal dialysis for eight months and then successfully transplanted.

**Discussion**

Our patient presented with purpura, swollen ankles, abdominal pain, melena and combined nephritic and nephrotic features, accompanied by hypocomplementemia. The diagnosis of HSP was based on the typical clinical presentation of vasculitis involving the skin, gastrointestinal tract and kidneys, and dominance of IgA deposits in the kidney biopsy sample.

Complement activation is thought to play a role in tissue damage in HSP [26]. The complement system is activated mainly through the alternative pathway at both the glomerular and systemic levels [26, 29]. The