Paradoxical and Persistent Renal Impairment in Henoch-Schönlein Purpura after High-Dose Immunoglobulin Therapy

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Dear Sir,

Intravenous high-dose immunoglobulin (IVHDI) has proved to be effective in the treatment of several immune-mediated diseases, including systemic vasculitis [1, 2]. In this sense, Rostoker et al. [3, 4] have reported that both low- and high-dose immunoglobulin therapy may be effective in treating either moderate or severe nephritis in Henoch-Schönlein purpura (HSP) and IgA nephropathy (IGAN). However, concern about renal deterioration has been raised in cases of systemic vasculitis and systemic lupus erythematosus following IVHDI [5-7]. We report a patient diagnosed as having HSP who paradoxically presented an acute and persistent renal impairment after IVHDI.

A 24-year-old man presented to our hospital with a history of abdominal pain and purpura involving the lower extremities and trunk. He was asymptomatic until 10 days before admission, when he abruptly developed palpable rapidly increasing purpura and edema in his lower extremities. At the emergency room he had colicky abdominal pain and arthralgias in his ankles and knees. The rest of the patient's history was unremarkable. On examination his temperature was 36 °C, blood pressure 140/80 mm Hg and pulse 80/min. Cardiopulmonary examination was normal. The abdomen was soft with tenderness. Edema and palpable purpura were present in the lower third of the inferior extremities. There were also scattered purpuric lesions in the buttocks. On admission full blood count, coagulation tests, blood chemistry profile and urinalysis were normal. The Westergren erythrocyte sedimentation rate was 22 mm/h. Test for hepatitis B and C, human immunodeficiency virus serology, antinuclear antibodies, cryo-globulins, immunoglobulins (including IgA, IgG and IgM), rheumatoid factor, serum C3 and C4, and ANCA were negative or normal. Chest and abdomen X-ray films, electrocardiogram and echocardiogram were also normal. A skin biopsy showed a leukocytoclastic vasculitis with IgA immune deposits affecting capillaries and venules. Thirty-six hours after admission, nausea, vomiting and an increase in diffuse abdominal pain as well as melena along with new skin lesions were observed. Endoscopic examination showed petechial mucosal lesions in the duodenum. Treatment with 40 mg of intravenous methylprednisolone every 6 h was started. A rapid improvement of the abdominal pain was observed within the first 5 days after the onset of

the therapy. However, in spite of the treatment with corticosteroids, a new flare of cutaneous purpuric lesions associated with proteinuria (5.1 g/24h) without an impairment of renal function (serum creatinine: 1.17 mg/dl, 89.2 μ mol/l; serum urea: 30 mg/ dl, 4.98 mmol/l) was observed 5 days later. Because of that, therapy with IVHDI (1 g/kg/ day for 2 successive days) was administered. Paradoxically, a progressive deterioration in renal function tests was observed during the next 4 days – the maximum values recorded were as follows: serum creatinine 3.0 mg/dl (229 μ mol/l) and urea 181 mg/dl (30 mmol/ l). For this reason, treatment with a single bolus of intravenous cyclophosphamide (0.75 g/m²) was administered. However, only partial recovery of renal function was observed about 13 days after the IVHDI therapy (creatinine: 2.2 mg/dl, 169 μ mol/l; urea: 107 mg/dl, 17.8 mmol/l). As expected, renal biopsy yielded focal proliferative glomerulonephritis with mesangial IgA and C3 deposits. New monthly boluses of 0.75 g/m² of cyclophosphamide were given during the following months. Three months after the onset of the disease, no significant decrease in the proteinuria (4.8 g/24 h) was recorded and plasma values of creatinine and urea were 1.78 mg/dl (136 μ mol/l) and 67 mg/dl (11.1 mmol/l), respectively.

Our patient was diagnosed as having HSP according to the criteria proposed by the American College of Rheumatology in 1990 and those proposed by Michel et al. [8]. In children, HSP is considered a benign and self-limited disorder. However, the majority of reports discussing HSP in adulthood have found a significant increase in the incidence of gastrointestinal and renal disfunction as well as a poor prognosis [8, 9]. Based on the good therapeutic results described by some authors and considering the relatively low incidence of complications following therapy with immunoglobulins for IGAN and HSP [3, 4], IVHDI treatment was considered in our patient. Paradoxically, a rapid deterioration in renal function following immunoglobulin therapy was observed. Such an acute increase in plasma creatinine has been previously described by Schifferli et al. [5]. However, in their cases the impaired renal function reverted to pretreatment val-

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ues after 10 days. In this sense, Rostoker et al. [10] considered that occurrence of acute renal failure after IVHDI seems to be rare, moderate, transient and reversible. By contrast, in our patient, only partial recovery in renal function occurred 2 weeks after IVHDI treatment.

However, in our case, it is possible that renal involvement in the context of HSP prior to the IVHDI therapy may have accounted for the incomplete normalization in the renal function once that IVHDI treatment was discontinued. Also, we are uncertain of the potential role that treatment with intravenous cyclophosphamide might have played in the reduction of the plasma creatinine values. Experience of IVHDI in HSP is limited to a very few patients [4]. Therefore, we consider that IVHDI therapy in HSP should be at least closely monitored. Also, a long-term prospective study with a larger number of cases might shed light on this controversy.

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