Case Report

Acute renal failure associated with immunoglobulin administration

S. Michail1, L. Nakopoulou2, I. Stavrianopoulos1, D. Stamatiadis1, K. Avdikou1, G. Vaiopoulos3 and C. Stathakis1

1Department of Nephrology, Laikon General Hospital, Athens, 2Laboratory Department of Pathology and 3First Preparatory Clinic, Medical School, University of Athens, Greece

Key words: acute renal failure; immunoglobulin; vacuolization

Introduction

Intravenous administration of immunoglobulins is used for the treatment of primary immunodeficiency states, autoimmune disorders, primary and secondary glomerulonephritides, and for the prevention of infections, especially in immunosuppressed patients [1–9]. The available i.v. immunoglobulins (IVIGS) differ both as to the methods of preparation and the excipients, but are equivalent with regard to the therapeutic effectiveness and the undesirable effects. These are of an allergic nature, are encountered in 1–15% of the patients, and are usually expressed in the form of fever, chills, exanthems, headache, myalgias, hypertension, and thoracic pain [1–3]. Isolated cases of aseptic meningitis and thrombotic episodes have been also reported [4]. Cases of acute renal failure (ARF) after IVIGS reported in the literature are very few, and only in some of them have the underlying histological lesions been described [3–8,10–15].

Case report

Our case concerns an 18-year-old male patient with focal segmental glomerulosclerosis and nephrotic syndrome unresponsive to successive administration of methylprednisolone alone, a combination of methylprednisolone and cyclophosphamide, and a combination of methylprednisolone and cyclosporin. During his last recent hospitalization, on physical examination, his blood pressure was 140/85 mmHg and his pulse rhythmical with a 80/min rate. He presented oedema of lower extremities and waist and his daily urine output was 2500 ml. Laboratory data showed 12.1 g/dl haemoglobin, 36.4% haematocrit, 6500/μl white blood cells with normal differential count, 293 000/μl platelets, 1.6 mg/dl serum creatinine, 75 mg/dl blood urea, 98 mg/dl blood glucose, 75 ml/min/1.73 m² creatinine clearance, 140 mmol/l serum sodium, 4.2 mmol/l serum potassium, 9.6 mg/dl serum calcium, 18 IU/l serum AST, 12 IU/l serum ALT, 1.8 g/dl serum albumin, 620 mg/dl serum cholesterol and 32 g/24 h urine proteins. Serology for hepatitis surface antigen and hepatitis C antibody was negative. The patient was receiving per os 12 mg methylprednisolone every other day, 125 mg frusemide twice daily, 4 mg nicoumalone and 20 mg lisinopril daily. The patient was given 400 mg/kg body weight of IVIGS for 5 consecutive days. The daily dose of IVIGS was infused over 4 h.

From the second day of IVIGS administration a gradual reduction of daily urine output was observed simultaneously with an increase of blood urea and creatinine levels, which by the 5th day of treatment reached 150 mg/dl and 4.7 mg/dl respectively. On the 5th day of treatment the patient became oliguric with no allergic symptoms or evidence of haemodynamic derangements during the 5 days of IVIGS administration. On the 5th day the patient was submitted to renal biopsy. Light-microscopy showed swelling and vacuolization of the epithelial cells of the proximal tubules with preservation of the brush border (Figure 1). There also was swelling and vacuolization of the epithelial cells in most of the glomeruli and changes consistent with focal segmental glomerulosclerosis (Figure 2). Immunofluorescence was negative for immunoglobulins and complement components. Upon discontinuation of IVIGS a gradual increase of the urine output was observed, together with a decrease of blood urea and creatinine levels, which after 7 days were at the pre-IVIGS levels.

Discussion

ARF is an uncommon side-effect of IVIGS. Only 42 cases of ARF in adult patients have been reported [3–8,10–15]. Forty-eight percent of them were more than of 65 years of age and in 57% of them there was a pre-existing renal disease. In 36 patients ARF
hyperplasia which was, according to the reporting authors, due to chronic underlying renal disease [6]. The histological examination of the sixth case showed tubular atrophy and diffuse monocyte infiltration of the interstitium [12]. In no case was acute glomerular inflammation, immunoglobulin deposition in the glomeruli, or occlusion of the tubular lumina by immunoglobulins reported.

The appearance and the course of the ARF of our patient share common characteristics with that of most of the reported cases. Serum creatinine levels increased from the 2nd day of IVIGS administration and this was accompanied by a gradual decrease of the urine output, with serum creatinine reaching maximum levels of the 5th day when the patient remained oliguric. After discontinuation of IVIGS and within 7 days, serum creatinine and diuresis gradually returned to pretreatment levels.

The histological changes of the renal biopsy of our patient were similar to those of the other cases reported [3,5,6]. In particular we observed swelling and vacuolization of the epithelial cells of the proximal tubules with preservation of the brush border. The swelling and vacuolization of the epithelial cells of the glomeruli, found in the case of our patient, has been observed in only one other case [3]. Moreover, in accordance to the other reported cases, no acute glomerular inflammation or immunoglobulin deposition in the glomeruli or obstruction of the urinary tubules by immunoglobulins were observed.

The mechanism of ARF after IVIGS administration remains to be clarified. Experimental studies after parenteral administration of carbohydrates such as sucrose, manitol, glucose, sorbitol, and dextran have shown that the vacuoles are formed from rupture and fusion of lysosomes that contain the above substances [16–18]. From these findings the authors conclude that the carbohydrates are introduced into the tubular cells by pinocytosis and are incorporated in the lysosomes. Degradation of these substances is very slow and this leads to inflation and rupture of the lysosomes, which are finally fused together, resulting in vacuoles. The preparation administered to our patient contains sorbitol as a stabilizing substance.

In conclusion IVIGS can cause acute oliguric renal failure which is reversible after withdrawal of the drug and is histologically characterized by tubular vacuolization with preservation of the brush border. In our patient the vacuolization was found also in the epithelial cells of the glomeruli, a finding reported in only one other case.

References

ARF associated with immunoglobulin administration


17. Maunsbach AB, Madden SC, Latta H. Light and electron microscopic changes in proximal tubules of rats after administration of glucose, mannitol, sucrose or dextran. *Lab Invest* 1962; 11: 421–432


Received for publication: 3.2.97
Accepted: 13.2.97