Letters to the Editor

Acute renal failure after intravenous immunoglobulin therapy

Sirs,

We present the case of a 66-year old man, treated for severe dermatomyositis with muscular, cutaneous and lung disease. The disease was diagnosed in 1999 because of muscular pain, muscular weakness, arthralgia and cutaneous eruption, associated with increased muscular enzymes (creatine kinase 2000 international units/l, IU/l, norm 30-230 IU/l). Electromyography showed myogenic signs. Muscle biopsy confirmed the diagnosis of dermatomyositis. Lung tomodensitometry showed fibrosis without abnormalities on the lung function tests, and cardiac and renal function were normal.

He was first treated with corticosteroids 1 mg/kg/day starting in 1999. On decrease of the corticosteroids in 2000, a relapse occurred leading to the introduction of several immunosuppressive drugs sequentially: azathioprine (2 mg/kg/day) then 3 pulses of cyclophosphamide in 2005, followed by methotrexate 20 mg/week. During 2006 and 2007, because of lung worsening and persistence of muscular signs, mycophenolate mofetil then rituximab were given without efficacy. Intravenous immunoglobulins (IV Ig) therapy was then prescribed in June 2007 (1, 2).

He had no other pathology and no other treatment than dermatomyositis treatment with corticosteroids (20 mg/day of prednisone) and azathioprine (150 mg/d). Renal function at the introduction of Ig IV was normal: serum creatinine level was 69 µmol/l (7.8 mg/l; Cockroft clearance 100 ml/min, norm >90ml/min) with no proteinuria, leucocyturia or haematuria.

The first cycle was performed in June 2007 at the dose of 1g/kg the first day and 1g/kg the second day with a saccharose-stabiliser product. Due to a manipulation error, the infusion rate was too fast (30 minutes/10 grams) for one of the bottles (*i.e.* 10 grams) on the first day. The patient did not report any immediate adverse events. However 48 hours later, he presented oligury and dyspnea: serum level creatinine was of 513 µmol/l (57 mg/l, Cockroft clearance 15 ml/min) and kaliemia was 7.9 mmol/l (norm 3.5-4.5 mmol/l). There was no obstruction of renal excretion on ultrasound and no urine infection.

The patient needed one hemodialysis therapy with normalisation of renal function with serum creatinine level of 80 µmol/l (8.8 mg/l), normal kaliemia and uremia. Thereafter there were no sequellae.

Acute renal failure is a known but rare adverse event (less than 1%) (3, 4) with IV Ig treatment and is more frequent in patients with other risk factors: age above 65 years, baseline renal insufficiency, hypertension, diabetes mellitus, hyperviscosity, inadequate hydration, or other nephrotoxic medications (3, 5-7). In the present case, the patient only presented the age risk factor. However the rate of infusion was too rapid which has also been described as a renal risk factor (5, 6) and we used a high-dose of sucrose stabilised-immunoglobulins. Acute renal failure often occurs after the first cycle (5), usually about 10 days after (6) and many patients need hemodialysis (between 40 to 75% of them) (6, 8). This acute renal failure is usually oliguric and reversible (6, 8). This adverse effect is more frequent with the use of sucrose stabiliser (90% of acute renal failure) (3, 5-8) and is dose-dependent (5).

Renal histological impairment consists in acute tubular necrosis and osmotic nephrosis (3, 5, 6, 8-10) with cytoplasmic vacuolisation in the epithelial cells of proximal tubules. There is no modification of the glomeruli and no interstitial inflammation, the immunofluorescence microscopy does not show any deposits.

In summary, IV Ig is a safe treatment but, to increase its safety, the infusion must be preceded by intravenous rehydration, with a slow infusion rate (at least one hour for 10 grams), without any other nephrotoxic products. The monitoring of urine output and renal function is necessary, particularly in patients with other risk factors of acute renal failure. If possible, it may also be preferable to use non-sucrose-stabiliser products (3, 5, 6, 8).

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Conflict of interest: Dr Dougados has participated in various symposia organised by BMS and has acted as a consultant in various advisory boards organised by BMS; the other co-authors have declared no competing interests.

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