high-volume CVVH (blood flow 300 ml/min, ultrafiltration 5 l/h) for 16 h (Figure 1), lactic acidosis improved, the haemodynamic situation of the patient stabilized and he was discharged from the ICU.

In conclusion, metformin intoxication should be considered in the differential diagnosis for patients with lactic acidosis in the absence of obvious tissue hypoxia [5]. Only early treatment, even in a suspicious case of metformin intoxication, is able to reduce the high mortality rates in these patients. This case report demonstrates the usefulness of the combination of intermittent haemodialysis with high-volume CVVH using two vascular access sites in the treatment of a patient with severe metformin-induced lactic acidosis and extremely high serum metformin concentrations.

Conflict of interest statement. None declared.

1Medizinische Klinik IV Ulf Panzer1
2Medizinische Klinik I Stefan Kluge2
Universitatsklinikum Hamburg Georg Kreymann2
Eppendorf Gunter Wolf1

Germany
Email: panzer@uke.uni-hamburg.de

The authors wish to be known that, in their opinion, the first two authors contributed equally to this work.


DOI: 10.1093/ndt/gfh337

Neutropenia associated with the use of low-dose methotrexate in a peritoneal dialysis patient

Sir,
We describe a case of neutropenia associated with the use of low-dose methotrexate in a patient undergoing continuous ambulatory peritoneal dialysis, who subsequently developed invasive pulmonary aspergillosis.

Case. A 64-year-old man was admitted with fever 23 days after starting methotrexate for the treatment of psoriasis, receiving a cumulative dose of 35 mg. Mouth ulceration developed at day 13 and the full blood count was normal at days 5 and 13. He had end-stage renal failure treated with continuous ambulatory peritoneal dialysis. On admission, examination revealed only oropharyngeal ulceration. The patient had a haemoglobin level of 11.9 g/dl, white cell count of 0.3 × 10⁹/l, zero neutrophils and a normal platelet count. Imipenem, teicoplanin, fluconazole, lenograstim and folinic acid were started as per local neutropenic protocol. A chest radiograph showed no signs of infection and blood cultures were subsequently sterile. The patient’s condition improved, with neutropenia resolving within 10 days, leading to discontinuation of antibiotics and lenograstim.

The patient developed dyspnoea and fever 15 days later with a neutrophilic leukocytosis of 49 × 10⁹/l. The chest radiograph (Figure 1) showed infiltrates at the bottom right and throughout the left field, with suggestion of a cavity formation in the left upper zone. Sputum cultures yielded Aspergillus versicolor. Computerized tomography of the thorax (Figure 2) showed consolidation in both upper lobes and the lower lobe, with adjacent thick walled dilated bronchi, consistent with bronchopulmonary aspergillosis. Treatment was commenced with amphotericin, but despite respiratory support the patient died 3 weeks later.

Discussion. The kidney is the main route of excretion of methotrexate and the British National Formulary recommends reducing the dose for mild renal impairment and avoiding in moderate–severe impairment [1]. The renal drug handbook advises it is contraindicated in peritoneal dialysis and haemodialysis [2].

In a pharmacokinetic study of one patient undergoing peritoneal dialysis, a 15 mg intravenous dose had a 120 h elimination half-life, compared with 8 h in normal renal function [2]. This patient developed an unspecified drop in leucocyte and platelet count between days 3 and 7.

Fig. 1. Chest radiograph taken at onset of dyspnoea, and fever 15 days after resolution of neutropenia.
In a study examining outcomes of patients with rheumatoid arthritis and normal renal function, methotrexate was associated with an incidence of neutropenia of one in 58.4 patient-years. In this group of patients, in contrast with this report, when neutropenia occurred, it did so at a median time of 16.9 months [3].

Le Mense et al. [4] showed the duration between commencing methotrexate and the development of an opportunistic infection was between 11 weeks and 17 years (median: 10 months). Only one other case of invasive pulmonary aspergillosis associated with low-dose methotrexate has been reported, although, in contrast with this case, it occurred in a patient with rheumatoid arthritis after 8 years of treatment in the absence of neutropenia [5]. It has been described that invasive aspergillosis can have a prodromal period of fever with no radiological signs, as in this case, that may last 3–11 days [6].

Caution should be exercised with the use of methotrexate in patients with end-stage renal failure, as even the immunosuppression of ‘low-dose’ methotrexate can lead to opportunistic infection early in the course of treatment.

Conflict of interest statement. None declared.

Department of Nephrology Morriston Hospital Swansea UK
Email: NDT@xmed.org


DOI: 10.1093/ndt/gfh357