Acute renal failure during interfon treatment

Drs I H Faisal, N Murrey, P Chu, and G M Bell (Royal Liverpool University Hospitals, Liverpool L7 8XP) write: Interferon alfa-2b is used as maintenance treatment in patients with multiple myeloma. Although renal toxicity is rare, mild proteinuria may be found in about 10% of patients, suggesting that the case of a patient who developed acute renal failure during treatment with recombinant interferon alfa-2b.

A 49 year old woman was admitted with a week's history of nausea, vomiting, and declining urinary output. Two years previously an IgG κ multiple myeloma had been diagnosed. Ten months before admission maintenance treatment with recombinant interferon alfa-2b (intron A) 3 MU was started subcutaneously three weekly. She took additionally only ferrous sulphate and vitamin B complex.

On admission she was pale and apryxial, with a blood pressure of 120/70 mm Hg, a sinus tachycardia of 114 beats/min, and a central venous pressure of 1 mm H2O. Cardiovascular, respiratory, and abdominal examination showed nothing abnormal. Investigations showed: serum sodium 134 mmol/l (normal 136-148), potassium 4.2 mmol/l (3.8-5.0), blood urea 26.8 mmol/l (2.5-6.6), and serum creatinine 1020 μmol/l (62-124). Hypertension, headache, and no cough with a peripheral blood count of 11×10⁹/l, platelet count 405×10⁹, and erythrocyte sedimentation rate 130 mm in first h, and plasma viscosity was raised (1.77%Pas). Urine dipstick gave normal results. Serum IgG was raised at 35 g/l (5-14), with a monoclonal IgG κ paraprotein. Repeated infection screens were negative. Urine examination revealed considerable protein (+ + ) but no blood or myoglobin. Renal biopsy suggested severe tubular cell damage, but no tubular casts or myeloma and no amyloid deposits or urate crystals were seen.

Interferon was discontinued and the patient managed conservatively with dopamine and fluid restriction. Urine output gradually improved and she underwent a polytransfusion with resolution of her renal failure.

Mild proteinuria, the nephrotic syndrome, and interstitial nephritis have been reported in association with interferon alfa. Acute tubular necrosis in this patient was possibly a toxic effect of interferon alfa-2b, which had been an apparent cause. The renal biopsy excluded uric acid crystals or myeloma casts causing tubular obstruction, and there was no history of drug overdose, ingestion of chemical, or evidence of drug rashes or eosinophilia. Renal dysfunction is known to increase the toxicity of interferon and adequate hydration is always necessary during treatment. Although the renal failure developed 10 months after the start of interferon treatment, mild dehydration secondary to varicose veins might have triggered the nephrotoxic reaction.

Interferon is used to treat haematological malignancies,1,2 and such adverse reactions as acute renal failure have been reported. Regular urine analysis, monitoring of fluid balance, and renal function are therefore advisable. Discontinuation should be urgently considered at early signs of renal impairment.


Hypersensitivity vasculitis related to monoclonal

Drs R Susano, A Garcia, A Altadill, and J Fierrez (Hospital Central de Asturias, 33006-Oviedo, Spain) write: Only certain allergic reactions, mainly bleeding due to depressed coagulation factors and microvascular thrombosis leading to necrosis, have so far been regarded as related to monoclonal related reactions.4-6 We report a case of vasculitis, not previously presented in the classic literature6 or to the Spanish drug surveillance programme.

A 74 year old white woman with bilateral silicone veins was admitted with deep venous thrombosis, pulmonary embolism, and arrhythmia. Levels of antithrombin III and protein C were normal, and she was negative for antiphospholipid antibodies. There was no indication of any neoplastic disorder. Heparin was prescribed and the patient was discharged after 16 weeks taking aspirin 75 mg/day, aminodarone, and amiodarone. Three weeks later she was readmitted with six day old palpable purpura in both legs with no other clinical features. The prothrombin time was 18 seconds (control 12 seconds) and the partial thromboplastin time 35 seconds. The following investigations all gave normal findings: differential blood count, erythrocyte sedimentation rate, blood biochemistry, measurement of plasma protein complement, antistreptolysin O, urinary sediment, cryoglobulins, and latex and antinuclear antibodies. All drugs were stopped. A skin biopsy displayed features of leucocytoclastic vasculitis. She was given prophylactic heparin and steadily improved over 15 days. The skin lesions reappeared, however, a few hours after a single dose of nicotinamide 4 mg, and the patient was finally discharged taking just subcutaneous heparin. One year later she remained free of symptoms.

While the re-exposure suggests that nicotinamide caused the vasculitis, there remains a possibility that amiodarone—capable both of immune based alterations and involvement in the metabolism of these drugs, even months after its withdrawal—might have acted as a co-factor by an unknown mechanism.


A new skin lesion associated with intravenous streptokinase

Drs J E Smithson, C T C Kennedy, and S Hughes (Southend Hospital, Bristol BS10 5NB) write: We describe three patients with discrete purpuric papules following intravenous streptokinase dissimilar to skin necrosis previously described.9 All three received aspirin 150-300 mg daily by mouth, intravenous streptokinase (1-5 MU), and subsequently heparin infusion for 24 hours.

Case 1—After admission for a 66 year old smoker with confirmed anterior myocardial infarction developed five small non-blanching purple papules on the dorsum of the right hand. No other rash was present and the lesions resolved spontaneously over several days. On admission the patient was taking timolol eye drops (0.25%), and he received one oral dose of atenolol 50 mg before the rash appeared.

Case 2—A 46 year old man with inactive ulcerative colitis and a confirmed antineutrophilic elastase developed fever (39°C) and a painless dark blue-black papule on the dorsum of his left hand 24 hours after admission. The fever and skin lesion both resolved over 48 hours, and there was no microscopic haematuria and subsequent lipid profile was normal. The patient was taking no medica-

Case 3—A 75 year old woman with a confirmed inferior myocardial infarction was discharged after 24 hours with the dorsum of the right ring finger 24 hours after admission. Sections of the lesion stained with haematoxylin and eosin showed a subepidermal collection of lymphocytes, macrophages, and eosinophils and fibrin. Beneath these were superficial dermal venules showing endothelial cell swelling. Epithelial downgrowths at the periphery separated the collection of neutrophils and fibrin from the dermis. Complement and platelet aggregation studies were normal. On admission the patient was taking doxepin 50 mg at night, and she received one intravenous dose of dexamethasone (5 mg) and metoclopramide (10 mg) shortly after admission.

In all three cases the platelet count was normal and activated partial thromboplastin time was in the therapeutic range in the two men. In the third case activated partial thromboplastin time was raised but there was no evidence of spontaneous bleeding.

Although the histology is consistent with vasculitis, the distribution would be unusual for vasculitis of the embol. Such lesions have not been described with aspirin, heparin or β blockers. These lesions do not appear to be clinically important and resolve spontaneously without scarring.


