Hepatitis B virus markers in patients with acute hepatitis B

Case No	Months after onset	sAg	eAg	eAb	anti-HBc IgM
1	0	+	+	−	+
	3	−	−	+	+
2	0	+	+	−	+
	3	+	−	+	+
	11	−	−	+	−
3	0	+	+	−	+
	1	+	−	+	+
	5	−	−	+	−

sAg = hepatitis B surface antigen (Blood Products Laboratories, Elstree).
eAg, eAb, anti-HBc IgM = hepatitis B "e" antigen, "e" antibody, or IgM class core antibody (Wellcome Diagnostics, Dartford).

appearance of anti-HBc IgM antibody. Larger studies indeed confirm that "e" antigen to "e" antibody seroconversion occurs one to two months after the onset of symptoms, when acute HBV infection resolves[1]; the disappearance of anti-HBc IgM antibody (even when assayed in a 1/1000 serum dilution) occurs only three to four months after this event.[23] Assay of "e" antigen and "e" antibody responses therefore permits earlier confirmation of the diagnosis of acute HBV infection than does assay of anti-HBc IgM antibody responses. Assay of anti-HBc IgM antibody therefore has a major role in the diagnosis of acute hepatitis B only when hepatitis B surface antigen is absent from the serum.[1] In surface antigen positive cases the diagnosis is best made by detection of "e" antigen to "e" antibody seroconversion in serial serum specimens.

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Pulmonary aspergillosis in patients with leukaemia

We read with interest the paper by Boon *et al* concerning the serious problem of cerebral aspergillosis in liver transplant recipients.[1] Our recent experience in patients receiving chemotherapy for haematological malignancy indicates a similarly extensive problem in this patient group.

Since November 1987 we have treated 81 patients with intensive inpatient chemotherapy for acute leukaemia or lymphoma. Twenty eight subsequently underwent autologous or allogeneic bone marrow transplantation. All patients received prophylactic, oral, non-absorbable antifungal treatment but none received systemic antifungal agents prophylactically. All bone marrow transplant

recipients, but not those receiving standard chemotherapy, were nursed in sterile isolation. There were 15 episodes of aspergillus infection confirmed by culture during this period, predominantly due to *Aspergillus fumigatus*, indicating an infection rate of 19%. Fourteen patients had primary pulmonary infection and one an isolated cerebral infection; four patients with pulmonary infection also had aspergillus generally disseminated to other sites. All patients contracted aspergillus infection during chemotherapy for leukaemia or lymphoma; interestingly, no autologous or allogeneic bone marrow recipients were shown to be infected, indicating a protective effect of sterile isolation. Infection did not correlate with age or specific disease type. Aspergillus infection was diagnosed during life in 10 patients, six by bronchoalveolar lavage, three by histological examination of excised lung, and one by antigen titre. Aspergillus was present in the remaining five patients at necropsy. All but one patient were treated with intravenous antifungal treatment (amphotericin B 1 mg/kg daily) on the basis of clinically suspected fungal infection during life. Despite this, seven (47%) patients died of aspergillus infection. A seasonal variation in incidence of aspergillus infection is suggested by our data in that only one episode was diagnosed in the months May to September. Any temporal pattern, however, is more likely to be related to regular and extensive hospital building works which have been well documented as a source of outbreaks of aspergillus infection in bone marrow transplant recipients.[23]

Aspergillus infection is well known to be a problem in patients receiving chemotherapy for haematological malignancy, and our experience supports the points made by Boon *et al* regarding aspergillosis in immunocompromised patients. In view of the high mortality, despite treatment, it is accepted that an aggressive approach to treatment is required. The generally poor diagnostic yield from fibreoptic bronchoalveolar lavage[4] makes treatment on clinical suspicion alone necessary.

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Potential benefit of 1-α-cholecalciferol in hypomagnesaemia induced by cyclosporin

The association between cyclosporin neurotoxicity and hypomagnesaemia in al-

logeneic bone marrow recipients was reported in 1984.[1] Despite lowered serum magnesium concentrations, urinary excretion of magnesium remains inappropriately high, an effect assumed to be due to a defect in renal tubular reabsorption of magnesium as a result of taking cyclosporin. Treatment with oral or parenteral magnesium is usually successful, but large doses of oral magnesium salts are often poorly tolerated because of diarrhoea. Reduction of renal magnesium excretion using amiloride may be helpful, but the combination of this drug with cyclosporin may give rise to hyperkalaemia. In this report we describe a patient with persistent symptomatic hypomagnesaemia after treatment with cyclosporin A who was given 1-α-cholecalciferol with subsequent correction of the serum magnesium concentration.

Case report

A 44 year old woman with acute myelomonocytic (M4) leukaemia in second remission received an allogeneic bone marrow transplant and prophylaxis with cyclosporin A. Graft-versus-host disease ensued with typical skin manifestations and diarrhoea. High dose prednisolone was given and cyclosporin A continued. Paraesthesiae and muscle cramps developed, and both the serum magnesium and calcium were subnormal at 0·33 mmol/l and 1·3 mmol/l, respectively, the serum albumin concentration being 35 g/l. Chvostek's and Trousseau's signs were positive, and intravenous magnesium and calcium replacement was begun. Subsequently oral magnesium was given in the form of Maalox, but doses above 20 mmol/day worsened the diarrhoea. Despite several infusions of magnesium (25–50 mmol/day), the serum magnesium concentration repeatedly fell below the reference range and paraesthesiae recurred. Urinary magnesium excretion remained inappropriately high (figure), and amiloride, 5 mg twice a day, was given but had to be withdrawn because of hyperkalaemia. The serum concentration of 1,25 dihydroxycholecalciferol was subnormal at 10 pg/ml (reference range 18–66 pg/ml), and in an attempt to increase gastrointestinal absorption, and possibly renal tubular reabsorption of magnesium, 1-α-cholecalciferol 250 ng/day was begun. The serum mag-
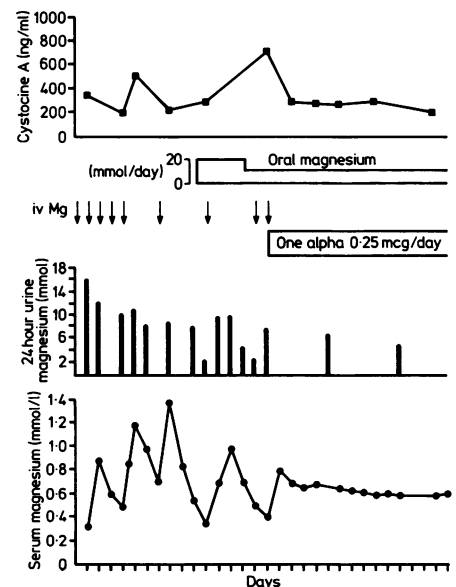
Hypomagnesaemia induced by cyclosporin: response to 1-α-cholecalciferol.