Necrotising lymphadenitis without granulocytic infiltration: case from Western Samoa

Kikuchi's disease (necrotising lymphadenitis) was first reported by Kikuchi and Fujimoto et al in Japan in 1972. It is characterised by cervical lymphadenitis in young patients, and may simulate malignancy both clinically and histopathologically. Patients present with tender cervical or submandibular lymphadenopathy for a couple of weeks. There are generally no other abnormal physical signs and laboratory findings. The principal microscopical features are effacement of the lymph node architecture, coagulative necrosis to a varying degree, and infiltration of histiocytic cells without polymorphs; coagulative necrosis with an absence of polymorphs is the most striking histopathological finding of this disease. Since 1972 cases outside Japan have also been reported in North America, the Far East, and the United Kingdom. This report concerns a case of Kikuchi's disease encountered in the island of Western Samoa believed to be the first such case report in that country. A 25 year old Samoan (Polynesian) woman presented with left cervical and axillary lymphadenopathy which she had had for a few months. She first developed left tender cervical lymphadenopathy and later painful swelling in the left axillary. Routine radiological and laboratory investigations showed no other important findings. A Paul-Bunnell test was negative. Finally, the cervical node was biopsied with the presumptive diagnosis of tuberculosis.

Macroscopically the node was 2 cm in diameter, hard in consistency, with a grey-whitish cut surface. Microscopically the node showed essentially similar features to those mentioned above: complete loss of the nodal architecture with varying degrees of necrosis, nuclear debris, and phagocytic histiocytic cells (figure). There was no neutrophil polymorph infiltrate. Acid fast stain was negative, as was bacteriological culture for tuberculosis. After consultation with the Department of Anatomical Pathology of the Sydney Royal Prince Alfred Hospital, Australia (Dr S McCarthy) the appearances were thought to be those of Kikuchi's disease. The disease is thought to be benign; the aetiology is unknown, although a viral aetiology has been suggested.

Lymph node biopsy specimens showing necrotic foci and histiocytic cells with phagocytic debris (haematoxylin and eosin).

Fibrinogen standards

In our laboratory fibrinogen concentrations are determined by the method of Clauss using a semiautomated technique (Fibrom System BB1, Becton Dickinson). The precision of our method is high (coefficient of variation of replicate samples < 4%). Recently, however, we have noticed a discrepancy between results obtained when using different commercially available fibrinogen standards.

At present there is no international standard available for fibrinogen which would permit assessment of these standards (GK Cook, National Institute for Biological Standards and Control). We therefore prepared fibrinogen standards from six commercial sources and prepared a standard curve from each of these (figure). A variety of methods are used to assign fibrinogen values to these standards, such as "clot weight," Kedjahl protein determination, and Clauss methods.

There was close agreement between standards with one exception. The fibrinogen values determined using this standard produced higher values which could be clinically misleading.

There is a strong case for the production of an international standard for fibrinogen and perhaps guidance on which method to use when assigning values to commercial standards. Meanwhile we would recommend that when producing a standard curve for fibrinogen using the Clauss technique, that at least two (preferably three) commercial standards be used: this will enable standards with discrepant values to be identified.

ANTI-HBc IgM assays and diagnosis of acute hepatitis B

Although a high titre of IgM class antibody to hepatitis B core antigen (anti-HBc IgM) is considered to be diagnostic of recent acute hepatitis B virus (HBV) infection, such an antibody response occurs not only during episodes of acute HBV infection but also in 5% of patients with chronic HBV infection. As anti-HBc IgM antibody titres decline after infection, the disappearance of reactivity in serial serum specimens tested for high titres of this antibody could perhaps be diagnostic of acute infection. Detection of "e" antigen to "e" antibody seroconversion is an alternative method of diagnosis in this situation. Personal observations and published data show that the disappearance of high titres of anti-HBc IgM antibody is of lesser value than the detection of "e" antigen to "e" antibody seroconversion as a diagnostic marker for acute HBV infection.

A study of hepatitis B surface antigen, hepatitis B "e" antigen and "e" antibody, and high titre (titre of ≥ 1/400) anti-HBc IgM antibody responses by commercial immunoassays in serial sera collected from three patients with acute hepatitis B (table) suggested that seroconversion from "e" antigen to "e" antibody positivity preceded the dis...
Hepatitis B virus markers in patients with acute hepatitis B

<table>
<thead>
<tr>
<th>Months after onset</th>
<th>Case</th>
<th>anti-HBc</th>
<th>eAg</th>
<th>eAb</th>
<th>IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>1</td>
<td>0</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

AG = 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-HBe 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; the disappearance of anti-HBe IgM antibody (even when tested in a 1/1000 serum dilution) occurs only three to four months after this event. Assay of "e" antigen and "e" antibody responses therefore permits earlier confirmation of the diagnosis of acute HBV infection than does assay of anti-HBe IgM antibody responses. Assay of anti-HBe 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. In surface antigen positive cases the diagnosis is best made by detection of "e" antigen to "e" antibody seroconversion in serial serum specimens.

DJ MORRIS
North Manchester Regional Virus Laboratory, Booth Hall Children's Hospital, Charlestown Road, Manchester M9 2AA

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. 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 aspergillosis 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 aspergillosis generally disseminated to other sites. All patients contracted aspergillosis 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. Aspergillosis infection was diagnosed during life in 10 patients, six by bronchoalveolar lavage, three by histological examination of excised lung, and one by antigen titre. Aspergillosis 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), three patients had surgically suspected fungal infection during life. Despite this, seven (47%) patients died of aspergillosis infection. A seasonal variation in incidence of aspergillosis 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 aspergillosis infection in bone marrow transplant recipients.

Aspergillosis 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 fibroptic bronchoalveolar lavage makes treatment on clinical suspicion alone necessary.

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. 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 aspergillosis 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 aspergillosis generally disseminated to other sites. All patients contracted aspergillosis 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. Aspergillosis infection was diagnosed during life in 10 patients, six by bronchoalveolar lavage, three by histological examination of excised lung, and one by antigen titre. Aspergillosis 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), three patients had surgically suspected fungal infection during life. Despite this, seven (47%) patients died of aspergillosis infection. A seasonal variation in incidence of aspergillosis 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 aspergillosis infection in bone marrow transplant recipients.

Aspergillosis 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 fibroptic bronchoalveolar lavage makes treatment on clinical suspicion alone necessary.

SM KELSEY
AC NEWLAND
Department of Haematology, The London Hospital, Whitechapel and London Hospital Medical College, London E1 1BB

H DORAN
Department of Mortal Anatomy


Potential benefit of 1α,25-dihydroxycholecalciferol in hypomagnesaemia induced by cyclosporin

The association between cyclosporin neurotoxicity and hypomagnesaemia in allogeneic bone marrow recipients was reported in 1984. 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 1α,25-dihydroxycholecalciferol 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 and interferon-α. She developed typical skin manifestations and diarrhoea. Despite several infusions of magnesium (25–50 mmol/day), the serum magnesium concentration, which were initially normal at 0.33 mmol/l and 1.3 mmol/l, respectively, the serum albumin concentration being 35 g/l. Chvoostek’s and Trousseau’s signs were present, and intravenous magnesium and calcium replacement was begun. Subsequently oral magnesium was given in the form of Malox, 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, 1α,25-dihydroxycholecalciferol 250 mg/day was begun. The serum magn-