including Amway LOC High Suds and BDH Neutracon. Unfortunately, the former is no longer available but LOC Regular, which is a less concentrated formula, was used at a higher concentration than has been previously described to overcome this difference. It is suggested that although the method may be cheaper and is safer than the modified phenol ZN due to the absence of phenol, it should not be used for the modified ZN staining of *C cayetanensis*. The technique should not therefore be applied to the staining of cryptosporidia because incidental findings of *C cayetanensis* may be missed. Although the presence of oocysts of *C cayetanensis* could be detected in the preparations, the technique could not be used for screening purposes in a diagnostic laboratory because the possibility of error would be too great. Oocysts of *Cryptosporidia* spp. have been shown to stain well by others[6] and did so satisfactorily in this study. However, the intensity of staining was not as good as seen in the modified phenol ZN. The auramine–phenol technique is probably more widely used for the staining of cryptosporidia. *C cayetanensis* does not stain well by this technique and therefore a separate procedure should be followed for the laboratory diagnosis of this organism.

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Gelatinous degeneration presenting as a preleukaemic syndrome

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Abstract

Gelatinous degeneration of marrow is a rare histological disorder associated with chronic debilitating diseases, such as anorexia nervosa, AIDS and postchemotherapy aplasia. Solid tumours have been associated with this condition but it has been reported in only two patients with leukaemia. In these cases leukaemia and gelatinous degeneration were diagnosed simultaneously. In the case reported here, a 48 year old man, gelatinous degeneration was the only histological finding observed more than two years before the diagnosis of acute myelogenous leukaemia with monosomy 7. The significance of hyaluronic acid deposition remains uncertain. Two hypotheses have been put forward: (1) that gelatinous degeneration occurs during tissue repair; and (2) that gelatinous degeneration inhibits haemopoiesis by altering the microenvironment of the bone marrow. In the case reported here, the presence of monosomy 7 suggests that myelodysplasia was the underlying disorder which finally evolved into acute leukaemia.

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Keywords: gelatinous degeneration, acute myelogenous leukaemia, monosomy 7.

Gelatinous degeneration is generally diagnosed in bone marrow biopsy specimens by the presence of a focal or generalised extracellular deposition of a gelatinous material, identified as hyaluronic acid, in association with fat atrophy and marrow hypoplasia. This disorder has been referred as serous atrophy, mucoid degeneration and starvation marrow.[1] Gelatinous degeneration has been classically observed in association with chronic debilitating disorders, such as anorexia nervosa, starvation, malignancy, chronic infections, systemic lupus erythematosus, and myxoedema.[1–5] Recently, it has been widely reported in patients with AIDS and a variant form of the classical degeneration has been reported after the administration of chemotherapy.[6–8]

In the case reported herein, gelatinous degeneration was diagnosed in a previously healthy man, with no evidence of an underlying disorder. To our knowledge, this is the first reported case in which gelatinous degeneration preceded the diagnosis of acute myelogenous leukaemia (AML).

Case report

A 48 year old healthy, well nourished, white man was admitted to hospital in August 1992 because of fever and pancytopenia. He worked as a driver for a chemical company, smoked

cigars, did not drink, was not taking medication or illicit drugs, and was not at high risk of HIV infection. The patient had been well until 48 hours earlier, when he developed fever (39°C), malaise and dizziness. Physical examination revealed nothing remarkable except for mild skin pallor and small haematomas on his arms.

On admission, the patient had a haemoglobin concentration of 10.7 g/dl, a haematocrit of 32%, a mean corpuscular volume (MCV) of 98 fl, an erythrocyte sedimentation rate (ESR) of 119 mm/hour, a white cell count of 1.72×10^9/l (10% neutrophils, 72% lymphocytes, 18% monocytes), and a platelet count of 28×10^9/l. A peripheral blood smear was normal. Vitamin B_{12} and folic acid concentrations, and renal and liver function tests were normal, except for a γ-glutamyl transferase of 60 IU/l and a total bilirubin of 25.65 μmol/l. Results of other tests were as follows: haptoglobin, 5.46 g/l; serum iron, 3.22 μmol/l; transferrin, 23.64 μmol/l; ferritin, 476 μg/l; and saturation, 11 %. Coagulation tests were normal, except for a fibrinogen concentration of 6 g/l. Direct and indirect Coombs, Ham, and sucrose lysis tests were negative; haemosiderinuria was not detected. Serum protein electrophoresis showed a γ-globulin fraction of 20.3 g/l. Immunoglobulin levels were as follows: IgG, 20.50 g/l; IgA, 4.76 g/l; and IgM, 2.38 g/l. Monoclonal components were not detected in the serum or urine. The following tests were negative: autoimmunity screening; HBsAg; anti-HIV; anti-HCV; and the Mantoux test. Anti-HBs and anti-HBc were positive.

Bone marrow aspirates did not yield enough material for diagnosis, but mild displastic signs were detected in erythrocytic precursors. Examination of a bone marrow biopsy specimen disclosed an irregular cellular distribution with normal or hypercellular areas and others showing a significant reduction in haemopoietic cellularity, where there was an interstitial deposition of a homogeneous and eosinophilic ground material, associated with fat atrophy (fig 1). This material was digested by testicular hyaluronidase and stained with alcian blue (pH 2.5) and periodic acid Schiff. No fibrosis, granulomas or other abnormalities were found. No metaphases were obtained for cytogenetic studies.

Tumoral markers, thyroid function tests, chest *x* ray, abdominal computed tomography scan, and gastrointestinal studies were normal. The patient was diagnosed as having "idiophatic" gelatinous degeneration.

The patient responded to a course of steroids, administered between November 1992 and January 1993. At this time, the patient had a haemoglobin concentration of 13.2 g/dl, a neutrophil count of 1.1×10^9/l and a platelet count of 40×10^9/l . Bone marrow biopsy revealed a slight reduction in the amount of mucoid material present, but hypocellularity remained close to 15%. This response was maintained two months after steroid withdrawal. From April to June 1993, recombinant human graulocyte colony stimulating factor (Filgrastim; Neupogen, Amgen, Munich, Germany) was administered and a mild increase in the patient's neutrophil count was observed. In June 1993, a bone marrow biopsy specimen showed an increase in the amount of mucoid material present and dysplastic changes were observed in the three haemopoietic lines. Repeated tests for occult disease during this period were negative.

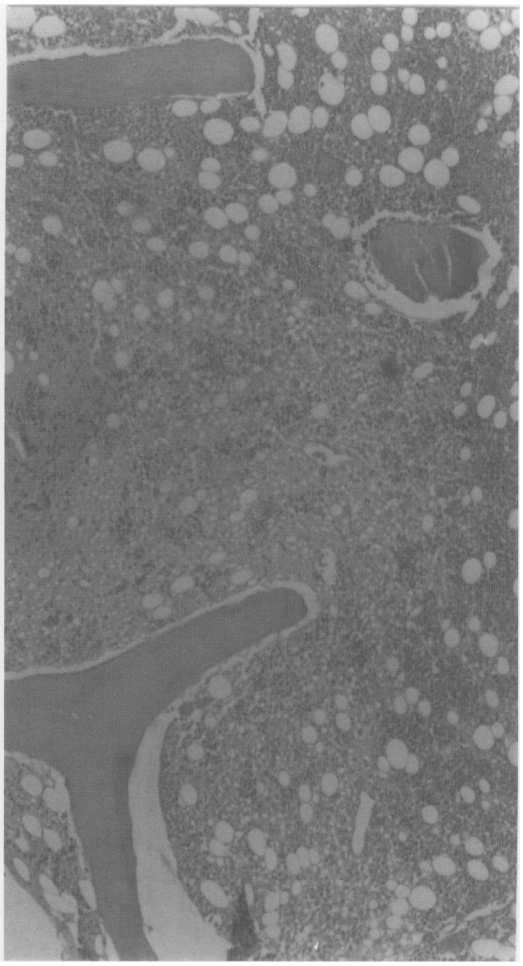

Figure 1 Bone marrow biopsy specimen showing an area with reduced haemopoietic cellularity, extensive interstitial deposition of mucoid material and fat atrophy (haematoxylin and eosin, ×40).

In December 1994, blast cells were detected on peripheral blood smears and a bone marrow aspirate revealed immature cells with a myeloid appearance, vacuolated cytoplasm and visible nucleoli, comprising 28% of the total cell population. Peroxidase, non-specific esterase and periodic acid Schiff stains were negative. Immunological markers in peripheral blood showed expansion of immature myeloid precursors with expression of CD34, CD33, CD56, and CD13. Cytogenetic studies showed monosomy 7 in all metaphases studied. Examination of a bone marrow biopsy specimen revealed proliferation of immature myeloid cells with reticulin fibrosis; mucoid material was not detected (fig 2). Two cycles of daunorubicin and cytarabine were administered without response. The patient died in May 1995.

Discussion

To our knowledge, gelatinous transformation of the bone marrow has been described in only two patients with acute leukaemia. However, in

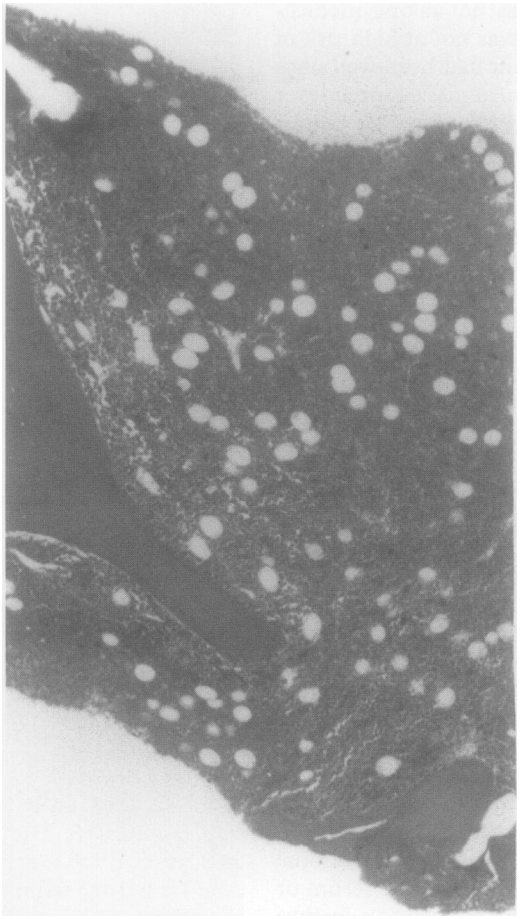

Figure 2 Bone marrow biopsy specimen showing a hypercellular marrow without gelatinous transformation taken around the time the patient developed AML. Bone marrow iron stores are increased (haematoxylin and eosin, ×40).

these cases, gelatinous transformation and leukaemia were diagnosed simultaneously.[1 9] In our patient gelatinous transformation was present for 28 months prior to the diagnosis of AML.

The pathogenic mechanism of gelatinous degeneration is still a matter of debate. Hyaluronic acid, a ubiquitous component of the extracellular matrix, plays an important role in repairing damaged tissue. This role could explain its presence in the marrow of patients with chronic debilitating diseases, such as anorexia nervosa and postchemotherapyaplasia, the disorders most commonly associated with gelatinous transformation. Our patient, however, did not have any of these conditions.

We speculate that deposition of hyaluronic acid resulted from a metabolic imbalance generated by altered bone marrow function. The presence of monosomy 7 might indicate that myelodysplasia was the underlying haematological disease in our patient, which finally developed into AML.[10] In fact, although the bone marrow aspirates were too scanty for an accurate haematological diagnosis, myelodysplastic changes could be detected at the later stages of the patient's clinical course.

Anaemia or moderate pancytopenia are the most common findings described in patients with gelatinous transformation. In that regard, Seaman *et al*[1] suggested that hyaluronic acid is a putative inhibitor of haemopoiesis which acts by altering the microenvironment of the bone marrow. Indeed, deposition of hyaluronic acid in the bone marrow of our patient may have lead to the development of AML, although we believe that this is unlikely.

In patients with anorexia nervosa the gelatinous material may disappear when their nutritional status improves. It also disappears in patients with postchemotherapy aplasia, when haemopoietic recovery takes place.[2 8] These observations support a role for hyaluronic acid in tissue repair. Interestingly, in our patient the gelatinous ground material disappeared when he developed leukaemia.

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