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Letters to the Editor

Simultaneous presentation of chronic granulocytic leukaemia and multiple myeloma

The association of multiple myeloma (MM) and acute myelomonocytic leukaemia (AMML) either following long term treatment with alkylating agents[1] or occurring simultaneously without previous chemotherapy[2] is well documented, as is the association between MM and the myeloproliferative disorders[3] (polycythaemia rubra vera and myelofibrosis).

The occurrence of CGL in two patients with chronic lymphocytic leukaemia (CLL), one treated with total body irradiation and one untreated has also been reported.[4]

However, the simultaneous presentation of MM and CGL has, as far as we are aware, not yet been documented.

CASE REPORT

A 58-year-old caucasian man presented in April 1978 with a two month history of lower lumbar back pain, and a six month history of increasing lassitude.

On examination he was obese, but his spleen tip was just palpable on deep inspiration. A later liver and spleen scan revealed considerable splenic enlargement, but no hepatomegaly. His full blood count revealed haemoglobin 10·2 g/dl, WBC 140×10^9/l with a differential count of myelocytes 35%, metamyelocytes 29%, mature neutrophils 20%, promyelocytes 2%, lymphocytes 7%, eosinophils 4%, and basophils 3%. The platelet count was 309×10^9/l.

Chronic granulocytic leukaemia was suspected and a bone marrow aspiration was performed. The bone marrow was hypercellular with marked myeloid hyperplasia. However, scattered amongst the myeloid cells were numerous plasma cells. The diagnosis of CGL was substantiated by the finding of the Philadelphia chromosome 46 XY t (9; 22) (q 34; q 11). The leucocyte alkaline phosphatase (LAP) score was 0 (NR = 20-90).

The diagnosis of MM was substantiated by the presence of a paraprotein IgGk at a concentration of 26 g/l. There was an accompanying immune paresis. Bence-Jones protein was present in the urine. Skeletal survey revealed marked osteoporosis with wedge collapse of L2 and L3 and 4 thoracic vertebral bodies.

The patient was managed initially with irradiation to L2 and L3 with total pain relief. Subsequently he had 15 courses of melphalan (10 mg/day for 4 days) and prednisolone (40 mg/day for 4 days) at monthly intervals. The paraprotein concentration has remained static. The WBC fell dramatically following the spinal irradiation (total 3300 r) to 7×10^9/l, but gradually rose to $>100 \times 10^9$/l over the next four months. His CGL has subsequently been controlled with intermittent courses of hydroxyurea and more recently busulphan and thioguanine.

DISCUSSION

The chance occurrence of two distinct haematological malignancies is unlikely. A common aetiological agent, affecting two cell lines, is a possible explanation or the emergence of an abnormal clone of cells secondary to the immunological defect caused by the multiple myeloma.

However, the most attractive theory is for the existence of a totipotential myelolymphoid stem cell.[5] A malignant proliferation of this common stem cell could lead to the simultaneous occurrence of a lymphoid B cell tumour—MM and a tumour of the haemopoietic pluripotential stem cell—CGL. The existence of this totipotential stem cell is suggested by the now well documented occurrence of the lymphoblastic crisis in CGL. The proof, in our case, would be the finding of the Philadelphia chromosome in the malignant plasma cells, but divisions of plasma cells are very difficult to obtain even under the very best conditions without crowding out by other cell divisions. Alternatively, the presence of a marker X-linked isoenzyme in a female heterozygote where the malignant haemopoietic cells and plasma cells contain a single isoenzyme but other tissues exhibit both isoenzymes, might confirm the origin.

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Methods of early detection of systemic or local vascular disease

There is critical need for useful methods for the early clinical detection of systemic (or local) vascular disease. The rectal biopsy technique described by Tribe *et al*[1] provides convincing objective evidence of vasculitis and parallels my experience[2 3] in the study of nasal biopsies in systemic or local vascular diseases. The presence of vascular changes in nasal biopsies should alert the pathologist and surgeon and contribute to the early and correct diagnosis of the diseases forming the midfacial granuloma syndrome.[4 5] Vasculitis provides the pathogenetic basis for linking under the same heading, idiopathic pleomorphic midfacial granuloma (Stewart's type) and giant cell Wegener's granuloma and granulomatosis. It is interesting to note in this context that the material examined by Tribe *et al*[1] has included rheumatoid vasculitis, polyarteritis nodosa and what the authors called "overlap syndromes" indicating the terminological difficulties when describing some of these often rare diseases.

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Double embedding in agar/paraffin wax as an aid to orientation of mucosal biopsies

Orientation of intestinal mucosal biopsies so that histological sections can be cut perpendicularly to the epithelial surface is of paramount importance to their histological examination and reporting.[1] Many biopsies of both small and large intestine yield little or no useful diagnostic information because correct orientation has not been achieved.

Orientation of strips of mucosa in the laboratory is greatly facilitated if they are allowed to adhere, flat, to a piece of frosted glass[2] or thin card.[3] However, although such a procedure can be easily implemented in gastroenterological units, many intestinal biopsies, particularly rectal biopsies, are taken in diverse, non-specialised clinics and often reach the laboratory irregularly curled-up in formol saline and are a significant potential cause of wasted laboratory and clinical time and effort.

To increase the precision of orientation of all biopsies, regardless of their state on reaching the laboratory, we decided to use a method of embedding the tissue in the fixed but unprocessed state using a technique based on embedding in agar before processing into paraffin wax.[4-6]

The formalin-fixed biopsy fragments are embedded in molten 1% aqueous agar at 45°C, under dissecting microscopic control. The agar solution has several remarkable useful properties; although its melting point is 98°C, gelling does not occur until the temperature falls to 42°C. Solidification is fairly slow and correct orientation of a biopsy, even if curled, is easily achieved by gentle manipulation with a mounted needle during cooling. Moreover, the agar is colourless and transparent in both liquid and gel forms so that the process of orientation can be viewed through a dissecting microscope. Even photography of the dissecting microscopic appearance is possible at this stage. The embedding in agar can be conveniently performed in standard moulds, such as those used for preparing paraffin wax blocks—for example, Tissue Tek.

The block of solidified agar, with its embedded biopsy is trimmed with a scalpel or razor blade so that it presents a flat surface perpendicular to the epithelial surface and it is then processed through alcohols and chloroform to paraffin wax in the usual way. The agar does not shrink appreciably during processing and is impregnated by wax just as if it were tissue. Paraffin sections are cut in the usual way. No technical difficulties have been experienced; the agar cuts just as if it were wax. On staining, the agar takes up a minimal amount of eosin and can just be seen as a very faint background stain but does not interfere with the histological appearances. Quantification and photomicrography are unimpeded.

This technique has been used in our laboratories now for three years. Although it is unnecessary for well presented, mounted biopsies or for tiny oesophageal and gastric biopsies it has proved invaluable for rendering small, unmounted, curled and apparently "unorientatable" biopsies reportable.

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Culture of Chlamydia

There is currently much interest in the role and importance of Chlamydia as pathogens both in adults and neonates. Isolation is still a complicated procedure and we have devised a simplified method