Angiodysplasia and caecal diverticulosis

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B cell signet-ring cell lymphoma of bone marrow

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Abstract
A case of signet-ring cell lymphoma affecting the bone marrow and diagnosed by bone marrow trephine biopsy is reported. Normal marrow was replaced totally by cells with large central vacuoles, many of which displaced the nucleus to the periphery of the cell, imparting a signet-ring appearance. Initially, the favoured morphological diagnosis was metastatic signet-ring adenocarcinoma, but on immunocytochemistry the tumour cells were strongly positive for CD45 (leucocyte common antigen) and the B cell marker CD20 (L26). Electron microscopy revealed electron-lucent vacuoles with no discernable internal structure. The tumour was classified as a high grade centroblastic lymphoma using the upgraded Kiel classification. Immunocytochemistry showed the tumour to be of B cell lineage. The patient subsequently responded to chemotherapy. Here, we report a further case of signet-ring cell lymphoma affecting bone marrow and diagnosed by bone marrow trephine biopsy. Despite treatment with combination chemotherapy, the patient died during an episode of septicaemic shock within two months of presentation.

Case report
A 70 year old man was referred by his general practitioner for investigation of central abdominal pain, nausea, vomiting, night sweats, loss of appetite, and weight loss of approximately one stone.

Keywords: Bone marrow trephine biopsy, signet-ring cell lymphoma, electron microscopy.
phosphatase and gammaglutamyl transferase concentrations. Serum electrophoresis and serum calcium were normal and urinary Bence-Jones proteins were absent. A CT scan confirmed the presence of splenomegaly but there was no evidence of intra-abdominal or mediastinal lymphadenopathy. A peripheral blood film showed a leucoerythroblastic picture. Bone marrow aspiration was performed but this resulted in a dry tap. A bone marrow trephine biopsy specimen was obtained from the iliac crest.

Before the trephine biopsy report, the patient was placed on steroids with symptomatic improvement. Following the diagnosis of lymphoma, the patient was staged as IVB and treatment with cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) was instigated. This was followed by further modest symptomatic improvement and discharge. However, one week later the patient was readmitted with night sweats, weakness and malaise. He was given a second course of CHOP and again discharged. Repeat CT scan was not performed after the first and second courses of chemotherapy. There was still no evidence of peripheral lymphadenopathy. Red and white blood cell indices and platelet counts, measured on several occasions, were broadly similar to those on admission. He was re-admitted two weeks later with a clinical diagnosis of septicaemic shock. Despite intravenous broad spectrum antibiotics, he deteriorated and died on the day of admission. A necropsy was not performed.

Methods
The bone marrow trephine biopsy was received in 10% neutral buffered formalin and fixed overnight. Plastic embedding using Polarbed 812 resin was performed and 1 μm sections were cut. These were stained with haematoxylin and eosin, Giemsa, mucicarmine, and periodic acid Schiff (PAS) with and without prior diastase digestion.

Immunohistochemical staining was performed using the avidin-biotin peroxidase technique with antibodies against CD45 (leucocyte common antigen (LCA)), CD20 (L26), CD45R0 (UCHLI), CD3, IgG, IgM, κ and λ light chains, Cam 5.2, epithelial membrane antigen (EMA), and S-100.

The plastic embedded tissue was processed for transmission electron microscopy. Ultrathin sections from several representative areas were stained with uranyl acetate and lead citrate.

Pathological findings
The bone marrow was diffusely infiltrated by sheets of cells, the cytoplasm of which was occupied by large vacuoles, many of which compressed and displaced the nucleus to the periphery of the cell resulting in a signet-ring appearance (fig 1). Areas of necrosis were not identified. On high power examination, it could be discerned that in the few cells without nuclear compression and distortion, most of the nuclei were vesicular with one to three nucleoli.
Smaller numbers of small cleaved cells and small lymphocytes were also identified. A nodular pattern was not observed, the cellular infiltrate being diffuse with no predilection for paratrabeicular aggregation. The initial preferred morphological diagnosis had been metastatic signet-ring. However, this was revised following the results of histochemical and immunohistochemical analysis. Using the upgraded Kiel classification, the tumour was finally classified as a high grade centroblastic lymphoma.

The results of special stains were as follows. No intracytoplasmic mucins were identified with the mucicarmine or PAS diastase stains. Tumour cells were negative for Cam 5.2, EMA and S-100. All cell types identified (centroblasts, centrocytes, lymphocytes) showed strong positive staining with LCA and the B cell marker L26 and were negative with the T cell markers UCHL1 and CD3. No intracytoplasmic or surface staining could be identified with IgG or IgM, and k and l light chains showed no significant staining.

Ultrastructural examination showed the preservation of cellular detail to be less than perfect. However, the principal cell type showed nuclei with sparse chromatin and one or more prominent nucleoli. Lesser numbers of cells with nuclear indentations or grooves were also observed. Most of the cells contained large intracytoplasmic vacuoles, some of which indent and compartmentalised the nucleus imparting a signet-ring appearance (fig 2). These vacuoles were electron-lucent with no discernable structure. Occasional vacuoles were bound to the membrane. In addition to these vacuoles the cell cytoplasm contained a moderate amount of rough endoplasmic reticulum and sparse numbers of other organelles. There was no evidence of epithelial differentiation such as intercellular adhesion specialisations or microvillous processes. There was no evidence of melanocytic differentiation; melanosomes and premelanosomes were not identified.

Discussion

The first cases of signet-ring cell lymphoma were reported by Kim et al in 1978 when they described seven non-Hodgkin's lymphomas arising within lymph nodes. These lymphomas were characterised by a follicular growth pattern and an abundance of cells containing clear vacuolated cytoplasm resulting in a signet-ring morphology. The authors attributed this signet-ring appearance to the accumulation of intracytoplasmic immunoglobulin and offered both immunohistochemical and ultrastructural support for this. Immunohistochemically, they were able to demonstrate intracytoplasmic IgG in three cases, all of which contained cells with clear, vacuolated cytoplasm. Intracytoplasmic IgM was demonstrated in a further three cases, whose tumours were composed of cells with abundant eosinophilic cytoplasm, imparting a Russell body-like appearance.

Since the original description by Kim et al, approximately 40 cases of signet-ring cell lymphoma have been reported in the literature, the majority involving lymph nodes. Bone marrow involvement appears to be rare, not having been documented prior to the description by Talbot et al. The majority of cases of signet-ring cell lymphoma have been of B cell lineage and derived from follicular centre cells. Most authors believe that intracytoplasmic accumulation of immunoglobulin and have concluded that the signet-ring appearance is caused by the abnormal production or secretion, or both, of immunoglobulin products. However, several reports of T signet-ring cell lymphoma have appeared in the literature, mostly exhibiting cutaneous involvement. These cases demonstrate that the presence of signet-ring cells within a lymphoma should not be considered proof of B cell origin.

Electron microscopy of several T signet-ring cell lymphomas has revealed giant cytoplasmic vacuoles identical with those reported in B cell types. Clearly, in these T cell lymphomas the signet-ring morphology cannot be explained on the basis of intracytoplasmic immunoglobulin accumulation. It has been postulated that the vacuolated appearance may be a result of abnormal internalisation of surface T antigens or the sequestration of T antigen containing, Golgi derived, vesicles. Such aberrant membrane recycling may be the common denominator of signet-ring formation in both B and T signet-ring cell lymphomas. The absence of demonstrable intracytoplasmic immunoglobulin by immunohistochemical techniques in the present case, as well as in several previously reported B signet-ring cell lymphomas could be explained on this basis. A possible alternative explanation for the failure to demonstrate intracytoplasmic immunoglobulin accumulation in the present case is our routine use of a plastic embedding technique to preserve cellular morphology in bone marrow trephine biopsy specimens. With such plastic embedding techniques, antigen preservation may be impaired and negative immunostaining can be difficult to interpret. Strong positive immunostaining of tumour cells, however, was obtained in the present case with CD45 and CD20 antibodies.

The presence of signet-ring cells within a lymphoma does not seem to influence the clinical outcome, the classification and behaviour of these lymphomas being dependent on nuclear morphology. As in the present case, the nuclear features may be best appreciated in those cells which do not have the signet-ring appearance and therefore do not sustain nuclear compression and distortion.

As in the present case, signet-ring cell lymphomas may present in a variety of extranodal sites without evidence of lymphadenopathy, these lesions having been described in a variety of organs including skin, stomach, thyroid gland, and salivary gland. The presence of large numbers of cells with a signet-ring appearance may suggest a diagnosis other than lymphoma. Signet-ring cells are seen in a variety of tumours including adenocarcinoma, malignant melanoma and liposarcoma. Unless pathologists are aware of the existence of this morphological variant of lymphoma, an-
Degenerative changes in myometrium simulating diffuse leiomyomatosis after treatment with gonadotrophin releasing hormone analogue

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Abstract
Degenerative changes are encountered relatively frequently in uterine leiomyomas. Morphologic changes within leiomyomas, particularly necrosis and alterations in cellularity, have been described following treatment with gonadotrophin releasing hormone analogue, but the effects of this form of treatment on the morphology of the normal myometrium are less well documented. A case is reported of a 42 year old woman with a history of menorrhagia in whom a combination of degenerative and atrophic changes resulted in a histological appearance resembling diffuse leiomyomatosis.

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Keywords: Leiomyomatosis, gonadotrophin releasing hormone analogue.

Gonadotrophin releasing hormone (GnRH) analogues are used in the management of patients with uterine leiomyomas. Reduction in leiomyoma volume occurs following GnRH analogue administration, possibly because of atrophy of smooth muscle cells.1 Changes in cellularity, necrosis, and haemorrhage have been described in leiomyomas following treatment with GnRH analogues,1–4 but the range of histopathological changes resulting from the administration of GNRH analogues has yet to be fully defined. Here, we report a case in which features suggestive of diffuse leiomyomatosis were present in a hysterectomy specimen following administration of goserelin, a GnRH analogue.

Case report
A 42 year old woman had been attending the gynaecology clinic for four years with a history of menorrhagia. Examination at initial presentation revealed a small mobile uterus. She was started on a cyclical progesterone but defaulted from follow-up. Two years later, the patient presented with acute urinary retention and was found to have an enlarged uterus with fibroids. She also complained of menorrhagia; endometrial curretage was performed yielding normal secretory endometrium. She was started on a progesterone
B cell signet-ring cell lymphoma of bone marrow.

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