Angiosarcoma of bone marrow with unusual expression of chymase: diagnosis in a trephine biopsy specimen

Angiosarcoma is a very rare vascular neoplasm, comprising less than 1% of all sarcomas. Involvement of the bone marrow is distinctly uncommon and almost invariably seen in patients with disseminated disease. Primary angiosarcoma of the bone/bone marrow, however, is extremely rare and, to the best of the authors knowledge, has not been reported to be diagnosed in a trephine biopsy.¹

A 77-year-old woman presented with acute back pain. A mastectomy had been performed for carcinoma of the left breast 16 years previously. Her past medical history was otherwise unremarkable. On physical examination, the patient showed hemisensory loss of the left leg. MRI and radionuclide bone scan revealed a large tumour mass and a pathological fracture of the left iliac bone. A trephine biopsy was removed from the left iliac crest for histological confirmation of a suspected bone marrow carcinosis. The biopsy disclosed sheets of large pleomorphic tumour cells almost completely replacing the normal bone marrow architecture (fig 1). The tumour cells were found to be round to ovoid with pleomorphic nuclei and prominent nucleoli. The main growth pattern of the tumour was solid and only partly tubular. Focally, the tumour was composed of irregular channel-like spaces lined by epithelioid tumour cells (fig 1).

Immunohistochemical investigations revealed that neoplastic cells strongly expressed vimentin and CD31 (fig 2), while expression of other endothelial-related markers like CD34 and FVIII-related antigen was much less intensive. Moreover, the tumour cells were found to react strongly with antibodies against vascular endothelial growth factor (VEGF) and mast cell chymase (fig 2). The tumour cells did not express detectable amounts of CD25, KIT protein (CD117), and mast cell tryptase. Epithelial (EMA, TTF1, KL-1) and lymphocytic (CD5, CD10, CD20, CD23, CD30, and CD79), antigens were absent. Based on this unusual immunophenotype, the diagnosis of an angiosarcoma of bone marrow was established.

Primary angiosarcoma of the bone represents a challenging diagnosis in bone marrow biopsies, especially in poorly vasoformative tumours, as in the present case.² The differential diagnosis includes a variety of neoplasms ranging from undifferentiated large-cell carcinoma and other subtypes of sarcoma to malignant melanoma and blastic haematopoietic neoplasms.

Expression of VEGF in angiosarcomas has been reported previously.³ The strong expression of chymase—as in our case—has yet not been demonstrated in this tumour. Therefore, we examined tissue samples from five archival cases of angiosarcoma and found expression of chymase in three of them.

Functional properties of the serine protease chymase, which is expressed in normal/reactive mast cells, are not fully elucidated. In endothelial cells, chymase may play an important role in the

development of vascular proliferation via induction of angiotensin II formation.⁴ Moreover, it has been suggested that chymase could mediate apoptosis in smooth muscle cells through a mechanism involving degradation of pericellular fibronectin and disruption of focal adhesions.⁵

In conclusion, it may be speculated that chymase might play a role in the tumourigenesis of angiosarcoma and could be added as a marker in the immunohistochemical investigation of these rare malignancies.

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doi: 10.1136/jcp.2006.045427

Accepted 15 December 2006

Competing interests: None declared.

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Carinal leiomyoma: a cause for acute respiratory distress

Leiomyomata of the respiratory tract are rare neoplasms with an incidence of 0.34%, almost exclusive occurrence in adults and a slight female preponderance.¹ Similar lesions are exceptionally encountered in children and a remarkable feature is their occurrence on a background of immunodeficiency states and concomitant Epstein-Barr virus (EBV) infection.² We report multi-centric leiomyomata in a young patient; HIV status was not known, but immuno-markers for EBV were negative.

A young patient had presented to the emergency medical services with sudden exacerbation of breathlessness and cough that had been present for nearly 6 months. Clinical examination suggested collapse of the left lung and foreign body aspiration. Radiological investigations revealed left lung collapse, right lung hyperinflation and occlusive carinal and left main bronchial masses. Thereafter, there

Figure 1 Angiosarcoma of bone marrow. (A) Trephine biopsy specimen with almost complete replacement of the normal bone marrow architecture by large sheets of pleomorphic tumour cells (H&E). (B) A focus of irregular channel-like spaces lined by epithelioid tumour cells is seen at higher magnification.

Figure 2 Immunohistochemical investigations revealed that neoplastic cells strongly express CD31 (A) and mast cell chymase (B).

Figure 1 Sessile polypoidal friable carinal tumour with tumorous occlusion of both the main bronchi. Note collapsed left lung and hyperinflated right lung. Inset: smooth right bronchial mucosa after scooping out the tumour fragment.

was sudden respiratory distress and the child died.

Autopsy revealed a 2×1.8×1.7 cm, sessile, polypoidal, soft, whitish-yellow exceedingly friable tumour in the carina and left main bronchus (fig 1). The left lung was collapsed, firm with a dark brown cut surface. An unattached friable piece of tumour (0.9×0.4 cm) was present in the lumen of the right main bronchus. Removal of the right bronchial luminal fragment revealed smooth and glistening underlying mucosa (fig 1,

inset). The right lung was voluminous, oedematous and haemorrhagic. On histology, a benign spindle cell tumour, arranged in intersecting fascicles, was seen to originate from the carinal smooth muscles (fig 2). The cells were stained red by Masson trichrome stain, with a strong immunoreactivity for smooth muscle actin, and were non-reactive to EBV antigen (EBNA) and CD117. No tumour was seen elsewhere.

Predisposing factors for bronchopulmonary leiomyomata in adults have not been well documented. In sharp contrast, in children, immunodeficient states have served as fertile grounds for benign and malignant smooth muscle proliferations.² Chadwick *et al*³ first described pulmonary leiomyoma in three HIV-positive children; prior to their report, only eight children with such tumours had been reported.³ Since then, 18 cases have been described with HIV infection and other immunodeficient states.^{2,4} Ours will be the 19th patient. The role of EBV in smooth muscle tumourigenesis in immunocompromised conditions has been proved beyond doubt.^{2,4} In the reported case, the HIV status was not available. There were no features suggesting primary or acquired immunodeficiency. Immunohistochemistry was negative for EBV antigens. In an attempt to delineate the histogenesis, we used an immunostain for CD117, as the tracheo-bronchial tree is a foregut derivative. However, this was non-reactive. Benign endobronchial or parenchymal leiomyomata have always been described as "firm" or "hard". Surprisingly, this tumour

was extremely friable. A fragment had broken off from the main mass to occlude the right bronchus, which precipitated the fatal respiratory distress. Such a phenomenon, though not previously reported, should be borne in mind when diagnostic bronchoscopy is attempted. The tumours are amenable to surgical or endoscopic intervention. It is important to assess the HIV and EBV status when tumours are multifocal or involve extra-pulmonary sites.

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doi: 10.1136/jcp.2006.046136

Accepted 4 January 2007

Competing interests: None declared.

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CORRECTIONS

doi: 10.1136/jcp.2006.044719.corr1

There was an error in an author name in the July issue of the journal (Smellie WSA, Hampton KK, Bowles R, *et al*. Best practice in primary care pathology: review 8. *J Clin Pathol* 2007;**60**:740–8.) The correct name of the third author is R Bowley.

doi: 10.1136/jcp.2006.041251.corr1

There was an omission in an article published in the August issue of the journal (Lee DH, Lee GK, Kong S-Y, *et al*. Epidermal growth factor receptor status in anaplastic thyroid carcinoma. *J Clin Pathol* 2007;**60**:881–4.) The following statement should have been included: DHL and GKL contributed equally to this work.

Figure 2 (A) Interlacing bundles of spindle-shaped cells without pleomorphism or mitoses (H&E, ×400). (B) Strong positivity with smooth muscle actin (×400).