

tumour cell adhesion in diffuse carcinomas. Our data on cytoplasmic/nuclear β -ct expression support also the hypothesis that activation of the Wnt/ β -ct signalling pathway occurs in a subset of gastric carcinomas.¹ Finally, we observed a significant association between cytoplasmic/nuclear over-expression of β -ct and mixed carcinoma histotype, which we had previously shown to carry a guarded prognosis.^{2,5} It would be interesting to know whether or not the same applies to the series of Grabsch *et al.*¹

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Foamy cell mesothelioma

Sir: Tumours arising from serosal surfaces have a broad spectrum of morphological appearances. Malignant epithelial mesothelioma is typically composed of cells with abundant eosinophilic cytoplasm, disposed in a tubulo-papillary, solid or microcystic pattern, but variants with pleomorphic cells, deciduoid cells, small cells, vacuolated cells and clear cells have been described.^{1–6} We report a malignant epithelial mesothelioma of the pleura in which part of the tumour cells had an

abundant foamy cytoplasm, a pattern deceptively bland and largely unrecognized among pathologists.

The patient, a 56-year-old woman, smoker and with no history of asbestos exposure, presented with thoracic pain and dyspnoea. A chest X-ray and a total body computed tomography scan showed a left pleural effusion, with no lesions in other locations. A thoracentesis and a thoracoscopy were performed. The latter revealed several nodules of variable dimensions, involving the parietal pleura, the diaphragm and the pericardium. Multiple biopsies were obtained. The patient underwent palliative therapy but died of disease 6 months after diagnosis. No autopsy was required.

Histologically (Figure 1), thoracoscopic biopsies showed a solid and tubulo-papillary tumour, irregularly infiltrating a desmoplastic and myxoid stroma. Neoplastic cells were large, with round vesicular nuclei and prominent nucleoli. Mitotic activity was low. Cytoplasm was abundant and mostly eosinophilic; however, in about 40% of the neoplastic cells it was clear and foamy. The eosinophilic and the foamy elements merged imperceptibly. They both contained periodic acid–Schiff-positive cytoplasmic granules, which disappeared following diastase digestion. Immunohistochemically (Figure 2), both components were strongly reactive for cytokeratin AE1/AE3, calretinin and CD10, and negative for CEA, BER-EP4, B72.3, CD68, CD15 and TTF-1. Electron microscopic examination (Figure 3), performed on dewaxed paraffin blocks, showed clear, multivacuolated neoplastic cells with numerous long and slender microvilli of the mesothelial type, coated with proteoglycan particles.

This case represents a pleural tumour with the classical histological, immunohistochemical and

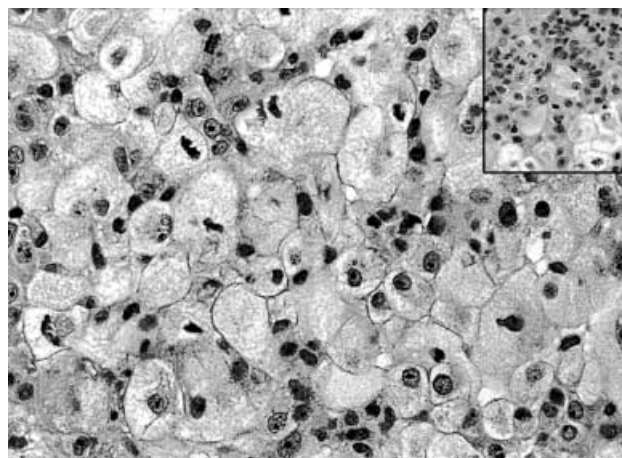


Figure 1. Part of the tumour is composed of large cells, with abundant foamy cytoplasm. Foamy cells merge with solid sheets of eosinophilic elements (insert). H&E.

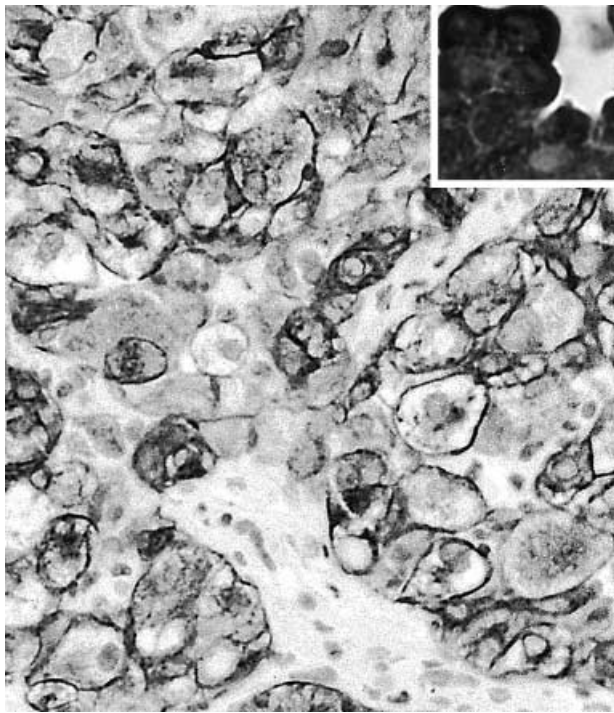


Figure 2. Both foamy and eosinophilic cells are strongly positive for CD10 and calretinin (insert). ABC.



Figure 3. Long slender and branching microvilli coated with proteoglycan particles. TEM.

ultrastructural features of malignant epithelial mesothelioma,¹ in which a portion of the neoplastic cells had abundant foamy cytoplasm. This phenomenon, akin to the foamy gland carcinoma of the prostate⁷ and pancreas,⁸ is unusual in mesothelioma. Spriggs *et al.*⁹ described three mesotheliomas in which samples of pleural effusion showed foamy macrophage-like neoplastic mesothelial cells; however, the subsequent histological specimens revealed mesotheliomas of

traditional histology, with no foamy elements. Mikuz *et al.*¹⁰ found rare neoplastic foamy cells in a well-differentiated papillary mesothelioma of the tunica vaginalis testis. Rare mesotheliomas composed of clear cells have been reported:^{1,5,6,11,12} however, at least from the illustrations provided by the authors, the cytoplasm of the neoplastic population seems to be more uniformly clear and empty, lacking the foamy and microvesicular pattern present in our case. Finally, Kitazawa *et al.*¹³ published a malignant peritoneal mesothelioma with foamy cells, in which the latter were reactive stromal histiocytes, not neoplastic mesothelial elements.

In our case, because of the tissue-recovery procedure, electron microscopy was unable to access the nature of the cytoplasmic inclusions; however, collections of lipid droplets, glycogen or round vesicles such as those recently described in pancreatic adenocarcinoma with foamy gland pattern⁸ are the most likely candidates.

The most important points are to recognize the malignant nature of foamy cell mesothelioma, and to differentiate it from other clear cell neoplasms, particularly metastatic renal carcinoma, which can occasionally mimic the clinico-radiological presentation of pleural mesothelioma.¹⁴ In this regard, the strong positivity of the tumour cells in our case for CD10, an antibody known to react with about 90% of renal cell carcinomas, could have been misleading. However, CD10 is positive in 18% of mesotheliomas.¹⁵ Attention to the clinico-radiological findings, the presence of areas of more traditional mesothelioma, and the use of a limited immunohistochemical panel, enable the correct diagnosis.

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Primary natural killer cell lymphoma of skeletal muscle

Sir: Natural killer (NK) cell lymphoma is a rare but highly aggressive malignancy, recently categorized as a distinct clinicopathological entity in the World Health Organization (WHO) classification of haematolymphoid malignancies.¹ Pathologically, neoplastic NK cells are usually small to medium in size with a variable degree of nuclear atypia, and possess azurophilic cytoplasmic granules. Tumour cells tend to infiltrate and destroy blood vessels (angiocentricity), and zonal tumour necrosis is often found.^{2–4} Immunophenotypically, the tumour cells are characteristically CD2+, surface CD3–, cytoplasmic CD3ε+, and CD56+. Genotypically, the T-cell receptor (TCR) gene is in germ-line configuration, and clonal Epstein–Barr virus (EBV) infection of the tumour cells is virtually invariable.^{2–4}

Clinically, NK cell lymphomas can be classified into different categories depending on the initial sites of involvement. In the majority of cases, the tumours initially involve the nasal or upper aerodigestive areas and are referred to as nasal NK cell lymphomas.^{2–4} A minority involve primarily non-nasal areas, such as the skin, liver, spleen, testis, and gastrointestinal tract, and are referred to as non-nasal (nasal-type) NK cell lymphoma.^{5–7} Rarely, the lymphoma can be disseminated with infiltration of multiple organs at presentation. As the peripheral blood may also be involved, the disease is referred to as NK cell lymphoma/leukaemia.⁸ In the WHO classification of lymphoid malignancies, nasal/non-nasal NK cell lymphomas are categorized as extranodal NK/T-cell lymphoma, nasal type; and NK cell lymphoma/leukaemia as aggressive NK cell leukaemia (ANKL).²

Although NK cell malignancies at different anatomical sites are pathologically similar, they are often clinically distinct. Nasal NK cell lymphomas are usually localized at presentation, and rarely if ever metastasize to the liver, spleen or bone marrow, even in terminal cases.^{3,4} In non-nasal NK cell lymphomas, terminal systemic dissemination occurred in fewer than 10% of cases.⁵ However, in ANKL systemic dissemination is the presenting feature. Quintanilla-Martinez and Jaffe recently commented on the relationship of this rare aggressive form with the nasal/non-nasal types, and noted both similarities and differences between these subtypes.⁹ We report a patient with primary NK cell lymphoma of the skeletal muscle, which highlighted some of the problems in classifying NK cell malignancies anatomically.

A 34-year-old woman presented to a regional hospital with intermittent fever and painless right forearm swelling. The serum creatinine kinase was elevated (270 U/l, reference 34–138 U/l), and a diagnosis of polymyositis was made. She was treated intermittently with corticosteroids, which led to resolution of the fever and the forearm swelling. However, on withdrawal of steroids, the arm swelling and fever recurred. Magnetic resonance imaging showed quite severe involvement of the right forearm muscle compartments (Figure 1A,B). A muscle biopsy was interpreted as showing polymyositis. Steroids were administered again, which resulted in a resolution of the arm swelling. However, the fever persisted and the patient became jaundiced. On referral, the patient was febrile, jaundiced, and quite ill. There was no forearm swelling, lymphadenopathy or organ enlargement. A full blood count showed haemoglobin 8.9 g/l, leucocyte count $9.4 \times 10^9/l$, and platelet count $97 \times 10^9/l$. The serum lactate dehydrogenase was elevated (2637 U/l, reference 200–360 U/l),