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Malignant lymphoma mimicking metastatic adenocarcinoma

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We report a case of malignant lymphoma of the inguinal lymph node exhibiting gland-like structures and abundant fibrillary matrix, mimicking cytologically and histologically a metastatic adenocarcinoma. The only clue to the possible lymphomatous nature of the lesion was immunohistochemical study proving that this represented a B-cell non-Hodgkin's lymphoma, staining positively for leukocyte common antigen, L26(CD20), IgG and kappa light chain, supported by ultrastructural findings of filiform cytoplasmatic processes on the surface of tumor cells. We conclude that the possibility of malignant lymphoma should not be disregarded even when a tumor shows gland-like structures or cohesive growth pattern.

Key words: lymphoma, non-Hodgkin's; adenocarcinoma, diagnostic pitfall

Introduction

An unexpected malignant process in the lymph nodes, especially in instances where microscopic changes are not sufficiently informative to decide whether the malignant cells show epithelial, mesenchymal or lymphoid phenotype, is a frequent problem facing surgical pathologist. The presence of glandular formations in metastatic tumors is strongly suggestive of the diagnosis of metastatic adenocarcinoma. When rosette-like formations and abundant fibrillary matrix in poorly differentiated tumors are dominant, the diagnosis of neural tumors such as neuroblastoma or ganglioneuroblastoma are favored. In this report we describe a unique case of a malignant lymphoma with gland-like structures and abundant fibrillary matrix.

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Case report

A 63-year-old female was observing a slowly growing lump in her left groin for 11 months. The swelling was interpreted by a surgeon as a hernia. Due to the acute pyelonephritis and transient renal insufficiency, the patient was admitted to a general hospital, where an aspiration biopsy of the inguinal tumor was performed and interpreted as a metastatic process of unknown origin. After admission to the Institute of Oncology, Ljubljana, an additional, 5.5 cm infiltrate of the left retroperitoneum was disclosed by laparoscopy. An excisional biopsy of a left inguinal lymph node was performed.

Materials and methods

Formalin and methacarn-fixed, paraffin embedded tissue sections were stained with hematoxylin and eosin, Giemsa, periodic acid Shiff and Kreyberg.

Immunohistochemical staining was carried out on paraffin-embedded sections using the avidin-biotin-peroxidase complex technique with antibodies to keratin wide spectrum, vimentin, alpha-smooth muscle actin, S-100 protein, leukocyte common antigen(LCA), T-markers CD3, CD43, CD45RO, B-markers CD 20, CD22, MB2, Ig, kappa and lambda light chains, and activation marker CD30. The immunohistochemical staining was done with appropriate positive controls.

For electron microscopic analysis, wet tissue fixed in 10% neutral formalin was used. It was washed in phosphate buffer at Ph 7.2, postfixed in buffered osmium tetroxide, and embedded in Epon LX-112. Thin sections were stained with uranyl acetate and lead citrate and examined with an Opton 9 electron microscope.

Results

The resected tissue was a solitary, enlarged lymph node, measuring $4.5 \times 4.0 \times 3.0$ cm. On the cut surface, the tissue was homogenous, pink, partially nodular. Necrosis was not evident.

Histologically, most of the lymphoid tissue was replaced by tumor cells forming cords, nests, several layers thick, with some solid areas and gland-like structures within the myxoid stroma (Figure 1). The residual small germinal centers were surrounded by neoplastic cells, with their mantles often infiltrated. In some areas tumor cells were dissociated in between prominent capillaries. The tumor cells were round to oval, with eosinophilic or clear cytoplasm. The nuclei were irregular, pleomorphic, sometimes multilobated, with one to several distinct nucleoli. In the cells of gland-like structures, the nuclei were situated peripherally.

The overall impression of the tumor resembled that of a metastatic, poorly differentiated adenocarcinoma with poorly developed myxoid stroma. However, stains for mucin and keratin were negative. In contrast, the tumor cells showed definite membrane positivity for LCA (Figure 2) and CD20 (Figure 3). The cells also showed monotypic staining pattern for IgG with a definite kappa ligh chain excess, thus confirming their B lineage. Staining for CD 22 and MB2 was negative. The fibrillar matrix, expressed mostly within gland-like spaces, also stained strongly with LCA and CD20. T-Cell

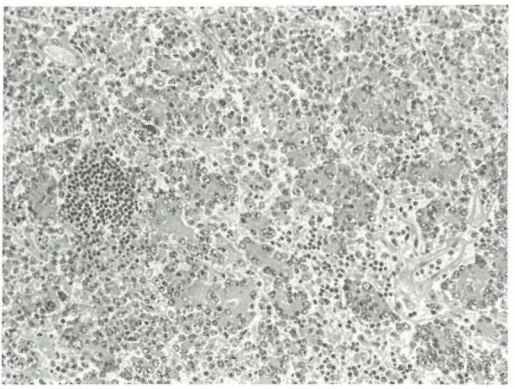

Figure 1. Lymph node almost diffusely replaced by solid and gland-like tumor cell clusters, separated by pale hypocellular areas with distinct capillaries.

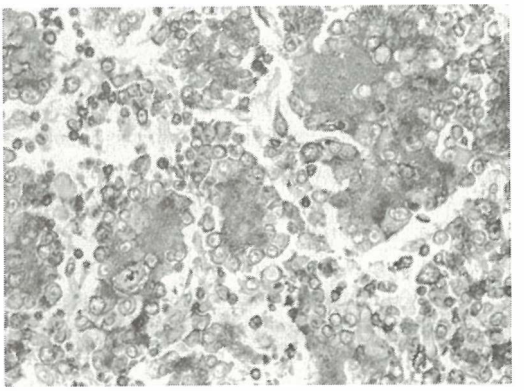

Figure 2. Clusters of tumor cells show membrane staining for leukocyte common antigen (CD 45 RB). Deeply stained central fibrillary matrix additionally supports the wrong impression of gland-like formations.

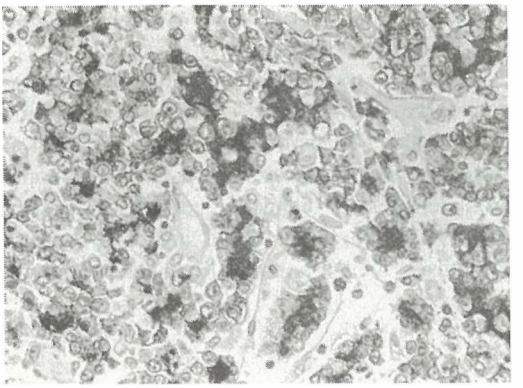

Figure 3. Tumor cells demonstrating strong reactivity for B-cell marker L26 (CD 20).

markers, actin, vimentin, S-100 protein and CD30 were all negative. Thus, the immunohistochemical studies clearly showed that the initial impression of metastatic carcinoma had been incorrect, and proved the condition to be a large cell non-Hodgkin's malignant lymphoma of B-cell lineage.

Ultrastructurally, the large lymphoid tumor cells displayed long, interdigitating cytoplasmic processes (Figure 4). These thin, filiform, branching projections filled intercellular spaces, but also a solitary intracytoplasmic lumen filled with the same type of projections was found within a lymphoma cell. Intercellular junctions were absent.

Follow-up

The patient was treated by chemotherapy according to CHOP regimen, followed by regional radiotherapy (TD 2100 cGy). A complete remission was achieved. The patient is alive and well 9 months after the diagnosis.

Discussion

Malignant non-Hodgkin's lymphomas can occasionally exibit unusual histological patterns, such as sinusoidal growth in anaplastic large cell lymphoma (ALCL), CD30 positive, resembling metastatic carcinoma,[1] spindle cells with

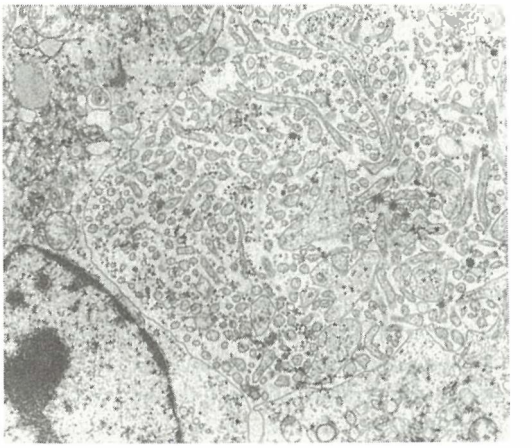

Figure 4. Lymphoid cell characterized by round nucleus, few organelles and profuse interdigitating villopodial projections along the cell surface (x 5000).

storiform pattern similar to that seen in sarcoma or malignant melanoma,[2] myxoid stromal changes and cord like cellular arrangement not unlike that in myxoid chondrosarcoma[3] or even signet cell differentiation simulating metastatic mucoid cell carcinoma.[4]

The gland-like structures with solid areas in a myxoid, vascularized stroma exhibited in this case were cytologically and histologically thought to be a poorly differentiated carcinoma metastatic to the lymph node, but negative stainings for mucins and cytokeratins ruled out this possibility.

The immunological studies proved fruitful in demonstrating the lymphoid nature of this neoplasm with definite membrane positivity for LCA and L26 (CD20) with IgG and kappa light chain clonality in the tumor cells.

Adenocarcinoma-like change is a previously unrecognized pattern of malignant lymphoma. It is well known, however, that ALCL, CD 30 positive, characterized sometimes with varying degrees of sinusoidal and subcapsular infiltration by large bizarre neoplastic cells might simulate other neoplasms, such as metastatic carcinoma,[5] but adenocarcinomatous pattern in such cases has not been observed so far.

The presence of an abundant extracellular mucoid matrix has not been considered to sup-

portive in the diagnosis of lymphoma until the reports by Chan[2] and Tse.[3] They described a case of anaplastic large cell Ki-1 lymphoma with myxoid matrix showing unusual sarcomatoid appereance and a case of B-cell malignant lymphoma in the soft tissue exhibiting prominent myxoid stromal changes. These authors claim that lymphoma tumor cells can elicit an exuberant myxoid change, probably by stimulating stromal cells. Contrary to their case of sarcomatoid lymphoma, where tumor cells were situated predominantly around the blood vessels, in the present case well defined perivascular cuffs were absent. Groups of tumor cells were situated randomly without any evidence of angiotropism lacking appereance that would suggest the diagnosis of lymphoma.

Histologically, the cytoplasm of the tumor cells merged into an abundant fibrillary matrix filling the central parts of gland-like and pseudo-rosette-like structures, but which was absent outside them. Similarly to the tumor cells, the fibrillary matrix stained with LCA and B-cell marker. Immunohistochemically and ultrastructurally, this case represents a type of filiform or anemone B-cell lymphoma which is characterized by multiple cytoplasmic projections on the cell surface.[6] It is interesting that in the current case, the cytoplasmic processes of the lymphoma cells were present almost exclusively in the center of cell groups thus forming the condensed eosinophilic fibrillary matrix which, seen on conventional histologic sections, was partially responsible for diagnostically misleading organoid histological picture. As most of the matrix was made of cell membrane material, it readilly stained with membrane leukocyte markers.

Given the wide range of histological appearances that malignant non-Hodgkin's lymphoma can assume, it is important and of clinical relevance not to exclude malignant lymphoma from differential diagnostic consideration even when the tumor shows gland-like or rosette-like structures or an apparently cohesive growth pattern.

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