Cytology of Follicular Dendritic Cell Sarcoma on Intraoperative Touch Imprint Smears
- A Case Report -

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Follicular dendritic cell (FDC) sarcoma is a neoplastic proliferation of FDCs. Because its cyto logic findings can vary widely, both the cytomorphology and histopathology of FDC sarcoma can impose a significant diagnostic dilemma. We present cytologic features of FDC sarcoma assessed by intraoperative touch imprint. Intra-abdominal lymphadenopathies were noted in a 54-year-old male with hepatitis B-virus associated liver cirrhosis. In contrast to cytologic features of classical FDC sarcoma, the tumor cells featured a large epithelioid or Reed-Sternberg cell-like shape scattered in a background with abundant inflammatory cells, which led to a mistaken diagnosis of malignant lymphoma. However, in accordance with cytologic features previously described in the literature, the tumor cells were characterized by a fragile cytoplasm with cytoplasmic processes in dendritic or reticulated patterns reminiscent of the ultrastructural features of FDC. Cytoplasmic features rendering nuclei with a tendency to form clusters or syncytial aggregates associated with reactive lymphocytes appear to be the most valuable finding in diagnosis of FDC sarcoma.

Key Words : Dendritic cell; Follicular; Sarcoma; Cytology; Lymph nodes

CASE REPORT

A 54-year-old male with hepatitis B-virus associated liver cirrhosis presented with multiple intra-abdominal lymphadenopathies. There was no peripheral lymphadenopathy or constitutional symptoms. Abdominal PET-CT scan disclosed multiple intraabdominal lymphadenopathies in the porta hepatis, peripancreatic, and paraaortic spaces. The patient underwent exploratory laparoscopic surgery. A lymph node in the porta hepatis was excised and submitted for intraoperative consultation. The lymph node measured 2.5 × 2 cm, and showed a whitish tan, bulging-out cut surface. For cytologic evaluation, touch imprint smears were acquired from the cut surface of the lymph node. Ethanol-fixed smears and air-dried smears were prepared for hematoxylin and eosin, Giemsa, and Papanicolaou stain. Based
on touch imprint smears and frozen sections, an erroneous diagnosis of malignant lymphoma was rendered. Ancillary studies with immunohistochemistry and ultrastructural evaluation of formalin fixed paraffin embedded tissue were subsequently conducted, and the case was diagnosed as FDC sarcoma. The patient was treated with radiation therapy, and 24 months afterward, he is now well without local recurrence or distant metastasis.

Cytologic findings

All cytologic smears exhibited high cellularity with a dimorphic cell pattern, and exhibited individually scattered large tumor cells in a background of many inflammatory cells that included an abundance of small lymphocytes, some plasma cells, and a few eosinophils. Tumor cells had a large epithelioid or Reed-Sternberg cell-like shape, with round to oval nuclei with delicate nuclear membranes, pale open chromatin, occasional prominent nucleoli, and scanty cytoplasm (Fig. 1). Mitotic figures were frequently observed. Some tumor cells with an oval to spindle shape appeared as semicohesive clusters and were intimately associated with many small lymphocytes. Tumor cells showed a tendency for nuclear clustering (Fig. 2A). Characteristically, some tumor cells appeared to have a fragile cytoplasm with an ill-defined cytoplasmic border and bi- or multipolar elongated cytoplasmic processes (Fig. 2B). Cytoplasmic processes with dendritic and reticulated patterns were reminiscent of those of normal FDC cells (Fig. 2C). These cytoplasmic features were also appreciated in the tumor cells in syncytial aggregates that were intimately associated with reactive lymphoid cells (Fig. 2D).

Histologic, immunohistochemical, and ultrastructural findings

Histologic sections showed a lymph node replaced by a multinodular tumor with a rim of compressed nodal tissue present in the peripheral portion. The tumor was comprised of single and loose clusters of large epithelioid or Reed-Sternberg-like cells in a background of abundant chronic inflammatory cells, including some plasma cells and a small number of eosinophils (Fig. 3). Some tumor cells appeared to be binucleated or multinucleated. Necrotic foci and frequent mitotic figures (more than 1/10 high power fields), including atypical form, were identified. On immunohistochemistry, the tumor cells were negative for lymphoid and epithelial markers, S-100, CD1a, and ALK1.

In situ hybridization with EBER (EBV-encoded RNA) was negative. Tumor cells were negative for CD21, CD23, and CD68 (KP1). The proliferation index assessed by Ki-67 immunostain was approximately 40%. Ultrastructural examination showed complex cytoplasmic processes similar to those of FDCs (Fig. 3A, inset). Finally, a diagnosis of FDC sarcoma was made by demonstration of many large cells showing strong cytoplasmic expression of clusterin (by courtesy of Dr. JKC Chan) along with staining in dendritic cell processes (Fig. 3B, inset).

DISCUSSION

FDC sarcoma is typically diagnosed by histology based on immunoreactivity to at least one of the FDC markers (CD21, CD23, CD35, and clusterin) or electron microscopic examination.
Fig. 2. Touch imprint smear showing tumor cells with nuclear clustering and dendritic cytoplasmic processes. (A) There is a tendency for nuclear clustering of tumor cells. (B) Tumor cells have characteristic cytoplasm with bi- or multipolar elongated cytoplasmic processes. (C) The cytoplasmic processes with dendritic and reticulated pattern are similar to those of FDC cells. (D) The dendritic cytoplasmic processes are noted in syncytial tissue fragment.

Fig. 3. Histologic, electron microscopic, and immunohistochemical findings. (A) The tumor comprises singles and loose clusters of very large cells in a background of abundant small lymphocytes and plasma cells (inset: A low power electron micrograph shows complex cytoplasmic processes). (B) The large cells are pleomorphic and show oval or irregularly folded nuclei, distinct nucleoli and variable amount of cytoplasm with ill-defined cell border (inset [by courtesy of Dr. JKC Chan]: Tumor cells show strong cytoplasmic expression of clusterin along with staining in the dendritic cell processes).
However, expression of FDC markers can be focal, and ultrastructural features can mimic other dendritic cell tumors, which can impose diagnostic difficulties.

Classical FDC sarcoma is characterized by dual populations of cells, attributed by neoplastic proliferation of large spindled to ovoid cells with various pleomorphisms in a background of abundant reactive chronic inflammatory cells. Classic cytopathologic findings for FDC sarcoma feature solid sheets or fascicular whirl-like patterns of large oval to spindle cells in a background of inflammatory cells. In contrast, the imprint smears of the present case showed many tumor cells with epithelioid or Reed-Sternberg cell-like shapes dispersed in a background of inflammatory cells, which can be misleading, and result in erroneous diagnosis of lymphoid malignancy in preference to Hodgkin inflammatory cells. In addition, some tumor cells forming cohesive clusters and syncytial aggregates were suggestive of a syncytial variant of nodular sclerosis Hodgkin lymphoma. In addition, some tumor cells forming cohesive clusters and syncytial aggregates were suggestive of a syncytial variant of nodular sclerosis Hodgkin lymphoma.

Retrospectively, however, we recognized fragile cytoplasm in tumor cells with elongated cytoplasmic processes with nuclei that demonstrated the tendency to form clusters or syncytial aggregates. Cytoplasmic processes of tumor cells were better appreciated, particularly in tumor cells that were intimately associated with reactive small lymphocytes, providing a striking contrast in differential diagnosis between FDC sarcoma and Hodgkin lymphoma.

Bhatia et al. recently reported on the cytomorphology of spindle cell variants of diffuse large B-cell lymphoma (DLBCL) mimicking the large oval to spindle cells of FDC sarcoma. Dendritic cytoplasmic processes in fibrillary or reticulated patterns, however, are unusual for lymphoid malignancy. Attention should be paid to the cytoplasmic features of the recapitulating complex interweaving the cytoplasmic processes of normal FDC, which can provide a clue to differential diagnosis between FDC sarcoma versus DLBCL.

The inflammatory pseudotumor (ITP)-like type of FDC sarcoma usually occurs in extranodal intraabdominal tissue, and is commonly associated with EBV infection, and usually shows rare mitotic figures and decreased expression of conventional FDC markers. Although there is no significant difference in cytologic features between the classical type and the IPT-like type of FDC sarcoma, our case resembled the ITP-like type in that tumor cells were accompanied by prominent reactive lymphoid cells and negativity for most FDC markers, except for clusterin. However, our case showed frequent mitotic figures and negativity for EBER-in situ hybridization.

Epithelial growth factor receptor (EGFR) is expressed in most FDC sarcomas, except for those with poorly differentiated appearance or high grade morphologic features. Our case was negative for EGFR, which could be associated with high grade morphology, including severe cytologic atypia, mitotic rate, presence of necrotic foci, and high Ki-67 labeling index.

In conclusion, we described touch imprint cytology of FDC sarcoma mimicking malignant lymphoma for emphasis of cytoplasmic processes in fibrillary or reticulated patterns, which can provide a clue in differential diagnosis between malignant lymphoma and FDC sarcoma.

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