Follicular Dendritic Cell Sarcoma Presenting as a Submucosal Tumor of the Stomach

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Follicular dendritic cell (FDC) sarcoma is an uncommon tumor of FDC origin, although more than 50 cases have been reported in the English literature to date. Follicular dendritic cells are antigen-presenting cells that normally form meshworks in lymphoid follicles, and FDC sarcomas in general recapitulate both the histologic and ultrastructural findings and the immunophenotypic profile of FDCs. This tumor affects mainly the lymph nodes, but it also involves extranodal sites in about one third of cases.

REPORT OF A CASE

A 45-year-old man presented with melena and dizziness of 3 weeks’ duration. Physical examination and laboratory tests were unremarkable except for mild anemia; his serum carcinoembryonic antigen level was normal. Fiber-optic gastroscopy and an abdominal computed tomographic scan revealed a 4-cm fungating mass with a central ulceration on the antrum of the posterior wall of the stomach. Radical subtotal gastrectomy was performed, based on the pathologic diagnosis of spindle cell sarcoma from gastroscopic biopsy specimens. The patient was well without evidence of disease 10 months after surgery.

PATHOLOGIC FINDINGS

The specimen received was a resected stomach containing a 5 × 4.5-cm fungating mass. The mass was located on the antrum of the posterior wall, and a deep, central ulceration coated by necrotic tissue was present (Figure 1). On cut sections, the mass was well demarcated and had a grayish-white flesh cut surface. The tumor was almost wholly located in the submucosa abutting the muscle proper.

Microscopically, the well-demarcated tumor, which was mainly located in the submucosa but had focal infiltration into the mucosa, was composed of plump, oval to spindle-shaped cells arranged in sheets and interlacing fascicles (Figure 2). Although areas of short fascicles of spindle-shaped cells that formed a vague storiform pattern were present, most of the tumor cells had plump eosinophilic cytoplasm with ill-defined cell borders forming a patternless diffuse growth. The tumor cell nuclei were oval to round and had a vesicular chromatin pattern (Figure 3); some multinucleated tumor cells were also present. Focal nuclear pleomorphism and scattered mitotic figures (average, 3 mitoses/10 high-power fields) were observed.

The tumor cells characteristically were intermingled with many lymphocytes, and in some areas a perivascular cuff of lymphocytes was also present (Figures 2 and 3). Tumor metastasis was present in 1 of the resected para jejunal lymph nodes.

Sections from the routinely processed paraffin-embedded tissue were examined immunohistochemically using the labeled streptavidin-biotin peroxidase method (LSAB 2 kit, Dakopatts, Glostrup, Denmark). The antibodies tested included CD21, CD23, CD35, CD45, CD68 (KP1), CD68 (PG-M1), CD3, L26, α-smooth muscle actin, vimentin, desmin, S100 protein, epithelial membrane antigen, HMB-45, CD31, and neuron-specific enolase (Dakopatts); cytokeratin (AE1/AE3), synaptophysin, and factor XIIIa (BioGenex, San Ramon, Calif); CD34 and CNA.42 (Immuno-tech, Westbrook, Me); and c-kit (C-19; Santa Cruz Biotech-
nology, Santa Cruz, Calif). Antigen retrieval by trypsin for CD21, CD35, and cytokeratin, and by microwave for other antibodies except for α-smooth muscle actin, synaptophysin, S100 protein, and neuron-specific enolase were performed before incubation with antibodies. An in situ hybridization study for Epstein-Barr virus-encoded (EBER1) mRNA was performed using the probe and detection system from Novocastra (Newcastle upon Tyne, United Kingdom). Tumor cells expressed membrane and cytoplasmic immunoreactivity for FDC markers (CNA.42, CD21, CD23, and CD35) (Figure 4). Cytoplasmic expression of epithelial membrane antigen, CD68 (KP1), α-smooth muscle actin, vimentin, and factor XIII were also present, and focal nuclear and cytoplasmic immunoreactivity for S100 protein was detected. Most of the lymphoid cells were T cells expressing polyclonal CD3, with a minor population of B cells expressing L26. No immunoreactivity was demonstrated for CD45, CD3, L26, desmin, HMB-45, neuron-specific enolase, synaptophysin, cytokeratin, CD31, CD34, and c-kit in the tumor cells. CD68 (PG-M1) was expressed only in reactive dendritic cells within the tumor. The nuclear signal for EBER1 mRNA was not detected by the in situ hybridization method.

Ultrastructural examination of the paraform-embossed tissue demonstrated long and thin interdigitating cytoplasmic processes and desmosomal cell junctions between adjacent cell processes (Figure 5).

**COMMENT**

In this report, we describe a hitherto unreported presentation of a rare tumor, which was identified as FDC sarcoma by the results of histopathologic, immunohistochemical, and ultrastructural studies. Follicular dendritic cells, interdigitating dendritic cells, and Langerhans cells are the major nonphagocytic antigen-presenting accessory cells of the immune system. They reside in different compartments of the immune system and differ in their functional, morphologic, and immunophenotypic aspects. Each of these cells can give rise to proliferative lesions. Among these, Langerhans cell histiocytosis is the most common and well known, whereas FDC and interdigitating den-
Figure 5. The long, slender, interweaving cytoplasmic processes locally connected by desmosomal cell junctions (uranyl acetate–lead citrate, original magnification ×42 000).

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...thyroid follicular structures. However, it can be distinguished by its tendency to have an infiltrative margin and by the presence of more obvious nuclear pleomorphism. In addition, areas of cytoke...
positive carcinoma should be present, and immunoreactivity to FDC markers (CD21, CD23, and CD35) has not yet been reported in sarcomatoid carcinoma. Lymphocyte-rich undifferentiated carcinoma was excluded in a similar way.

Although malignant fibrous histiocytoma is unusual in the stomach,18 the presence of spindle cells in a storiform pattern and multinucleated tumor giant cells raised the possibility of malignant fibrous histiocytoma. The lack of marked cytologic atypia and the expression of lineage-specific markers precluded this diagnosis.19 Malignant melanoma could be excluded by the expression of FDC markers and the absence of melanosomes and HMB-45 expression.

Interdigitating reticulum cell (interdigitating dendritic cell) sarcoma is another type of neoplasm of reticular dendritic cell origin, and it shares some histologic, immunophenotypic, and ultrastructural features with FDC sarcoma. Fewer cases of interdigitating dendritic cell sarcoma have been reported than for FDC sarcoma,1 and this lesion can also present as an extranodal mass, including in the gastrointestinal tract.20,21 Although there is some overlap of immunophenotypic profiles, the presence of FDC markers and the lack of CD45 expression excluded the diagnosis of interdigitating dendritic cell sarcoma. Spare intracytoplasmic organelles and interdigitating cytoplasmic processes are common ultrastructural features, but interdigitating dendritic cell sarcoma does not show desmosomes.

The majority of the reported cases of FDC sarcomas have no known etiologic or predisposing factors. Hyaline-vascular Castleman disease sometimes demonstrates proliferating and dysplastic FDCs, and a number of cases of FDC sarcomas complicating Castleman disease have been reported, which suggests a hyperplasia-dysplasia-neoplasia sequence of FDC sarcoma in some cases.22-25 Scattered mucosa-associated lymphoid tissue with secondary lymphoid follicles (probably induced by Helicobacter pylori infection) was present in the resected stomach, but dysplastic FDCs were not observed in the follicles. Although Epstein-Barr virus has been demonstrated in selected cases of FDC sarcomas,2,23,25 it is unlikely that this virus plays an important role as an etiologic agent, and our case did not reveal any nuclear signal on EBER1 mRNA in situ hybridization, which is the most specific and sensitive method for the detection of Epstein-Barr virus.

The biological behavior of this tumor is difficult to predict, but in general it is more akin to that of an intermediate-grade soft tissue sarcoma than a malignant lymphoma.25 An intra-abdominal location was reported to be associated with a particularly aggressive course, along with a high mitotic count (>5 mitoses/10 high-power fields), coagulative necrosis, and significant cellular atypia.23,24 Our case interestingly demonstrated perigastric lymph node metastasis, despite the early stage of the primary tumor. The patient was doing well 10 months after curative surgery, but his clinical course is uncertain because he has already demonstrated regional lymph node metastasis.

In summary, we have described the unusual case of an FDC sarcoma presenting as a gastric submucosal tumor in a 45-year-old man. This case highlights the occurrence of FDC sarcoma as a submucosal tumor of the gastrointestinal tract and demonstrates that FDC sarcoma should be considered in cases of c-kit- and CD34-immunonegative spindle or epithelioid cell tumors of the gastrointestinal hollow viscus, particularly if lymphocytes are minimally admixed intratumorally.

References