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Follicular dendritic cell sarcoma of small intestine with aberrant T-cell marker expression

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**Note:** The document appears to be text-heavy and contains a table with multiple entries. However, due to the nature of the content, it is challenging to extract meaningful insights or convert it into a readable format without context. The table likely contains detailed information related to the study or findings, but without additional context, it's difficult to provide a coherent summary.
Follicular dendritic cell sarcoma of small intestine with aberrant T-cell marker expression.

FDC sarcoma with T-cell marker (26 letters)

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Follicular dendritic cell sarcoma (FDCS) is an uncommon neoplasia usually occurring in lymphoid tissue. Herein we present a case of FDCS of the small intestine with positivity for T-cell antigen, simulating T-cell lymphoma. An 82-year-old man consulted a doctor for epigastric pain of one-week duration. Imaging study revealed a mass in the small intestine. Malignant lymphoma was suspected because of high serum levels of soluble interleukin-2 receptor, and resection of the tumor was performed. Microscopically, the tumor was comprised of large pleomorphic cells with reactive small lymphocytes. Most of the nuclei of the tumor cells were round or ovoid-shaped, and some of the tumor cells also showed spindle-shaped nuclei. Although the tumor cells were diffusely positive for CD45RO and CD4 immunohistochemically, negativity for pan-T-cell markers and CD56 were unusual for T-cell lymphoma of intestinal origin. Additional immunohistochemical study demonstrated that the tumor cells were positive for follicular dendritic cell markers including CD23, CD35 and CAN.42, and diagnosis of FDCS was made. To our knowledge, this is the first case of FDCS aberrantly expressing CD45RO, and FDCS expressing T-cell markers can be a pitfall for diagnosis of FDCS. (190 words)

<Key words>
Dendritic cell sarcoma, follicular
Intestine, small
Lymphoma, T-cell
[Introduction]
Follicular dendritic cell sarcoma (FDCS) is a tumor composed of spindle or oval cells with follicular dendritic cell differentiation. Usually, their morphology and immunohistochemical features are distinct from those of non-Hodgkin lymphomas. In this report, we present FDCS in an elderly man with pleomorphic histology and T-cell marker expression, simulating T-cell lymphoma.

[Clinical summary]
The patient was a previously healthy 82-year-old Japanese man. He visited a hospital for epigastric pain of one-week duration. Physical examination revealed a firm mass in the upper part of the abdomen. Abdominal CT scan showed focal obstruction of the small intestine by thickening of the intestinal wall. Contrast enema using an ileus pipe demonstrated severe stenosis at 50 cm distal to the Treitz ligament. The serum level of soluble interleukin-2 receptor was elevated to 1470 U/ml (normal range, 145-519 U/ml). A malignant lymphoma of small intestine was suspected, and partial resection of the jejunum was performed. After the operation, he was received adjuvant chemotherapy (CHOP) for 3 months and there was no evidence of recurrence at 12-month follow-up.

[Pathological findings]
Macroscopically, a mass measuring 10 x 10 cm in greatest dimension was seen in the jejunum extending throughout the wall of the intestine. Cut surface demonstrated a well-circumscribed, gray-white solid tissue with focal hemorrhage (Figure 1).

Microscopically, the tumor consisted of large pleomorphic cells, mainly forming diffuse sheets. Focal coagulative necrosis was found (Figure 2). The large cells had faintly eosinophilic cytoplasm and pleomorphic nuclei with coarse chromatin and distinct nucleoli. Nuclear pseudo-inclusion, binucleated and multinucleated nuclei were also present. Mitotic figures
were numerous (50 counts / 10 high power field) (Figure 3). In the background of the tumor cells, interspersed small lymphocytes were evident, and some of them were seen around the blood vessels. Lymphoid follicles were recognizable in some areas of the tumor. Regional lymph node involvement of the tumor with sparing of some lymph follicles was also noted.

The results of immunohistochemistry are summarized in Table 1. The tumor cells were focally (5%) positive for pan-B-cell marker CD20, and diffusely positive for CD45RO (Figure 4), a T-cell marker, as well as CD45RB. But the tumor cells did not show positivity for pan T-cell markers including CD3 and CD5. The tumor cells were diffusely positive for CD4 (Figure 4), CD68, and vimentin, and showed immunoreactivity for follicular dendritic cell markers including CD23, CD35, and CNA.42 (Figure 5). They were focally positive for S-100 protein and negative for CD21 (Figure 5) and D2-40. Ki-67 index was 90%.

In situ hybridization for Epstein-Barr virus encodes small RNA (EBER) { INFORM EBER probe (CE) (Roche)} failed to show positive cells. In clonal analysis, genomic DNA was extracted from paraffin-embedded tissue and T-cell receptor (TCR) γ gene rearrangements were studied by PCR. The amplified DNA yielded a polyclonal smear pattern on electrophoresis.

A final diagnosis of FDCS was made on these findings.

[Discussion]

FDCS is a neoplasm consisting of spindle to ovoid cells, which closely mimics various types of tumors and tumor-like lesions. Typically, they are nodal in origin, but extranodal involvement including the small intestine has been reported1. In case of intestinal FDCS, the major differential diagnosis includes gastrointestinal stromal tumor (GIST) and primary intestinal lymphomas. In this case, GIST was easily excluded by a lack of expression of CD34 and c-kit in the tumor cells. Expression of T-cell markers, including CD4 and CD45RO, however, might have lead to a diagnosis of T-cell lymphoma of intestinal origin. Enteropathy-type T-cell lymphomas among Japanese are type 2 in most cases, and are phenotypically characterized by positivity of CD8 and CD562. Peripheral T-cell lymphoma, not otherwise specified, often
demonstrates CD4 with frequent loss of CD5 or CD7. However, complete loss of pan-T-cell markers is unusual for T-cell lymphoma. In our case, the possibility of aberrant expression of T-cell antigens in a non-lymphoid tumor was considered. Infiltration of small lymphocytes, especially around the blood vessels, suggested the possibility of FDCS.

For investigation of undifferentiated neoplasm, including FDCS in the differential diagnosis is important since follicular dendritic cell markers are usually not included in the first panel of antibodies. To diagnose FDCS, at least one FDC marker (CD21, CD35, CD23, KiM4p and CNA.42) should be positive and CD1a should be negative. For lymphoid markers, CD20 and CD45(LCA) have been reported to be occasionally positive, while CD3, a pan-T-cell marker, is consistently negative. Our case suggests that even some T-cell associated antigens can be demonstrated in FDCS.

Although CD4 is a co-receptor acting in the activation of T-helper cells by the MHC class II antigen restricted pathway, CD4 expression is not restricted to T lymphocytes. Langerhans' cells, plasmacytoid dendritic cells/monocytes and true histiocytic sarcomas are known to be positive for CD4. Likewise, CD45RO, recognized by antibody UCHL-1 and once widely used as a T-cell marker on paraffin sections, can be expressed in histiocytic tumors. Actually, both CD4 and CD45RO lack lineage specificity and are commonly expressed by histiocytic sarcoma. Additionally, our case expressed CD68, one of the most available histiocytic markers. For diagnosis of histiocytic sarcoma, however, dendritic cell markers should be negative and other histiocyte-specific markers such as lysozyme or CD163 are usually expressed. In this case, the tumor cells were negative for CD68, and CD163 was not available. Differential diagnosis from the CD4+ blastic plasmacytoid dendritic cell neoplasm would be straightforward, because of non-hematodermic distribution, more sarcomatous morphology, and negativity for immunoreactive CD56 in this case.

Chan et al. reported that mitotic rate of FDCS is usually between 0 and 10/10HPF and Ki-67 labeling index are between 1 and 25% (mean 13%). In contrast, our case showed high proliferative index (mitotic rate of 50/10 high power fields and Ki-67 labeling index of 90%). As poor prognostic factors of FDCS, significant cytologic atypia, extensive
coagulative necrosis, a high proliferative index, large tumor size (> 6cm) or intraabdominal location are documented\textsuperscript{3}, and our case meets the all factors. Moreover, to the best of our knowledge, there have been 7 reported cases of primary gastrointestinal FDCS\textsuperscript{9-15}, and 6 among the 7 showed recurrence and/or metastasis. In our case, regional lymph node metastasis is found. Considering those findings, we think that our case is a high-grade malignancy, and that careful follow-up is needed.

In summary, we present a case of FDCS of small intestine origin. Expression of CD45RO was a feature that has not been previously reported. Including follicular dendritic cell markers into immunohistochemical panel and awareness of key histologic features such as perivascular distribution of small lymphocytes and residual lymphoid follicles in the tumor were crucial for diagnosis of FDCS. Possibility of FDCS with unusual phenotypic expression should be considered in undifferentiated neoplasms with a mixed population of lymphocytes.
<References>


Figure 1: The cut surface of the tumor demonstrating a clear border and spreading throughout the wall of the small intestine.

Figure 2: Diffuse proliferation of the tumor cells with focal necrosis. HE section, original magnification x10.

Figure 3: Tumor cells showing abundant faint eosinophilic cytoplasm and pleomorphic nuclei. Occasional mitotic figures are seen. HE section, original magnification x40.

Figure 4: The neoplastic cells are diffusely positive for CD45RO and CD4, original magnification x80

Figure 5: The neoplastic cells are positive for CD23, CD35 and FDC, and negative for CD21, original magnification x20.
<table>
<thead>
<tr>
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<th>Clone</th>
<th>Source</th>
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<th>Results</th>
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(++) indicates diffusely (5% or more) positive; (+) indicates focally (< 5%) positive; (-) indicates completely negative.