Interdigitating Dendritic Cell Sarcoma of the Duodenum With Rapidly Fatal Course

A Case Report and Review of the Literature

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• Interdigitating dendritic cell sarcoma is an extremely rare malignancy derived from antigen-presenting cells. Dendritic cells constitute a heterogeneous group of cells, which includes Langerhans cells, dermal dendrocytes, follicular dendritic cells, and interdigitating dendritic cells present in lymphoid and nonlymphoid organs. We report the case of a 36-year-old woman who presented with epigastric pain, projectile vomiting, and significant weight loss. Upper gastrointestinal endoscopy showed a duodenal lesion; a biopsy of the lesion was taken and was diagnosed as sarcoma. She underwent a Whipple procedure. A final diagnosis of interdigitating dendritic cell sarcoma was made, with liver and peripancreatic lymph node involvement. The patient deteriorated rapidly and died 4 months later. Although interdigitating dendritic cell sarcoma of the duodenum is extremely rare, we think it should be included in the differential diagnosis of unusual spindle cell tumors with a rich lymphocytic infiltrate.

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The patient was a 36-year-old, unmarried woman who presented with epigastric pain, epigastric fullness, dysphagia to solid food, projectile vomiting, and weight loss. On physical examination we noted epigastric tenderness, but no palpable lymph nodes, jaundice, or organomegaly were identified. Ultrasound of the patient's abdomen showed intrahepatic biliary ductal dilatation, as well as enlarged porta hepatis lymph nodes. Endoscopic retrograde choledochopancreatography revealed a large ulcerated lesion in the second part of duodenum. Biopsies of the mass were taken and submitted for histopathologic evaluation. An initial diagnosis of spindle cell sarcoma was made. Computed tomographic scan showed a large mass in the area of the head of the pancreas, with multiple enlarged lymph nodes in the porta hepatis and perigastric and peripancreatic regions. Liver function tests showed elevated alkaline phosphatase, alanine aminotransferase, and lactate dehydrogenase levels. Her past medical history included a thyroidectomy, tonsillectomy, and appendectomy. Tissue diagnosis from previous surgeries was not available.

PATHOLOGIC FINDINGS

Intraoperatively, the pancreas was free of tumor. The tumor was palpable in the duodenum with enlarged lymph nodes in the porta hepatis. The liver also showed a few suspicious nodules. A Whipple procedure was done, with liver biopsies and sampling of para-aortic and porta hepatis lymph nodes. A frozen section was performed and reported as spindle cell sarcoma. A Whipple resection comprising the distal portion of the stomach, duodenum, and head of pancreas was examined. Grossly, an ulcerated, ovoid, firm mass was noted in the second part of the duodenum with extension into the muscularis propria. The cut surface of the mass was tan. The lymph nodes also showed a homogeneous tan-white cut surface. Microscopically, the duodenal tumor demonstrated prominent spindle cell morphology with large vesicular nuclei and inconspicuous nucleoli with whorled and fascicular growth patterns, in addition to focal epithelioid areas (Figure 1). In the lymph nodes, the tumor cells were more epithelioid with foci of spindle cell appearance (Figure 2). The tumor showed a large number of CD3-positive lymphocytes (T cells) and a few eosinophils. The tumor cells consistently expressed S100 protein (Figure 3) and vimentin in the duodenum, liver, and lymph nodes. CD45 (Figure 4) and CD68 (Figure 5) were weakly positive. Smooth muscle actin was positive only in the duodenal lesion (Figure 4) and negative in the liver and lymph nodes (Table 1). Electron microscopy showed no evidence of Birbeck granules or lysosomes (Figure 6). A final diagnosis of interdigitating dendritic cell sarcoma (IDCS) was made.

Two months after her surgery, the patient presented with cervical lymphadenopathy, and biopsies proved involvement by tumor. Her general condition deteriorated rapidly and she died within 2 months. Autopsy was not performed.

COMMENT

Interdigitating dendritic cell tumors are very rare, and to our knowledge, only 43 cases have been reported in the

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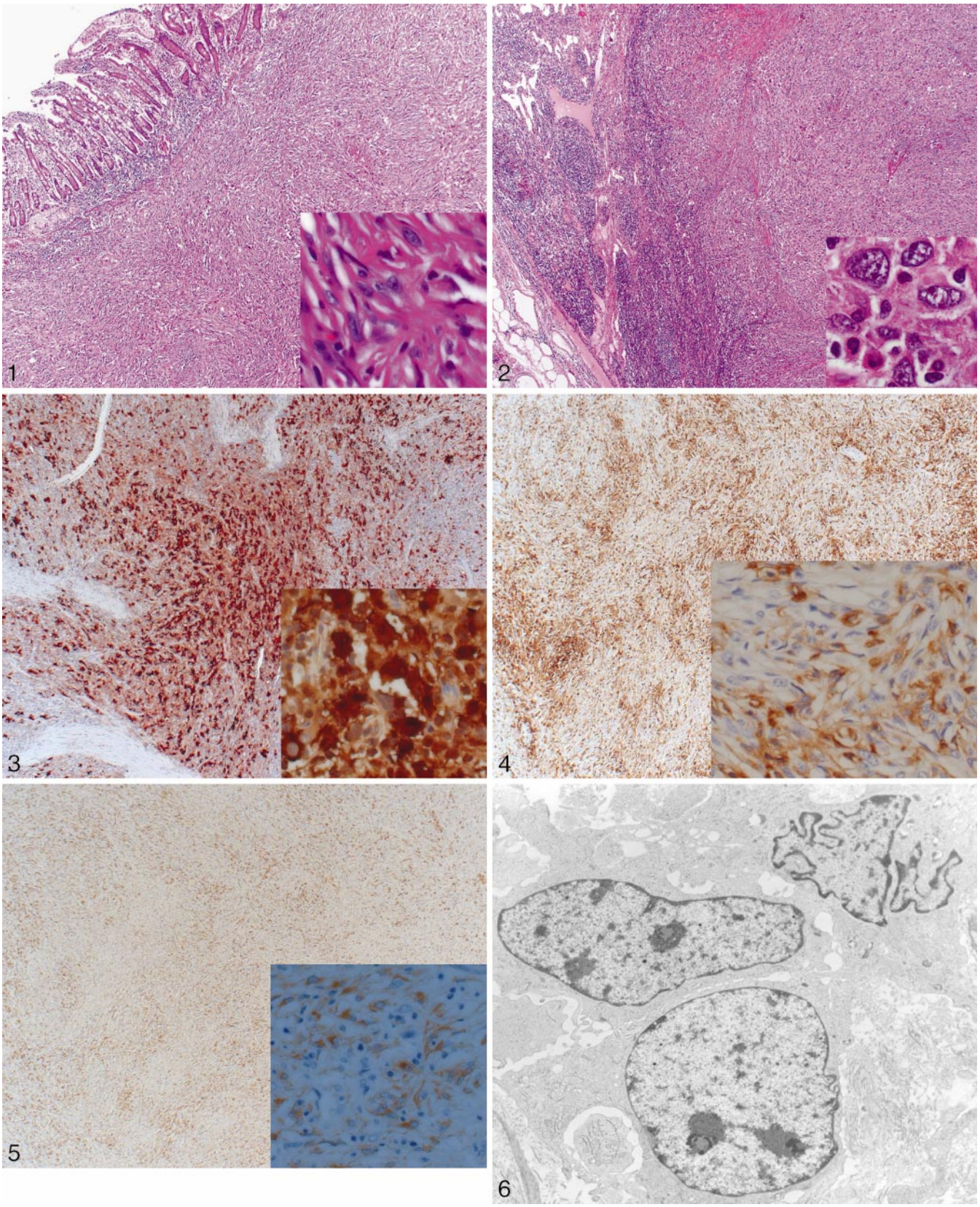

Figure 1. *Low-power view of duodenal tumor (hematoxylin-eosin, original magnifications ×5 and ×40 [inset]).*

Figure 2. *Epithelioid cells in lymph node (hematoxylin-eosin, original magnifications ×5 and ×100 under oil [inset]).*

Figure 3. *S100 protein in lymph node (original magnifications ×5 and ×40 [inset]).*

Figure 4. *CD45 weak positivity in duodenal tumor (original magnifications ×5 and ×40 [inset]).*

Table 1. Results of Immunohistochemical Staining in Duodenal, Liver, and Lymph Node (Metastatic) Tumor*

	Lymph Node	Liver	Duodenum	Antibody Manufacturers
ALK-1	−	−	−	Dako, Denmark
Bcl-2	−	ND	−	Dako
CD1a	−	−	−	Ventana, Tucson, Ariz
CD2	−	ND	−	Ventana
CD3	−	−	−	Cell Marque, Hot Springs, Ark
CD15	−	−	−	Cell Marque
CD20	−	−	−	Dako
CD21	−	−	−	Dako
CD30	−	−	−	Dako
CD34	−	−	−	Dako
CD35	−	ND	−	Dako
CD45	±	±	±	Dako
CD68	±	±	±	Dako
CD117	−	−	−	Dako
Desmin	−	−	−	Dako
EMA	−	−	−	Dako
Fascin	+	ND	−	Ventana
HMB-45	−	ND	−	Ventana
MSA	−	ND	−	Dako
Pan-keratin	−	−	−	Ventana
S100	+	+	+	Dako
SMA	−	−	+	Dako
Vimentin	+	+	+	Ventana

* ALK indicates anaplastic lymphoma kinase; ND, not done; EMA, epithelial membrane antigen; MSA, muscle-specific actin; SMA, smooth muscle actin; plus sign (+), positive; minus sign (−), negative; and plus/minus sign (±), weakly positive.

world literature to date.[1] The age range for this tumor is 6 to 77 years, and it is more common in adult males.[2] The patients may present with lymph node enlargement or extranodal disease, such as in the nasopharynx, salivary glands,[3] paraspinal area,[1] chest wall,[1] urinary bladder, spleen, or testis.[4] Based on the functional, ultrastructural, and morphologic features, monocytes and related cells can be divided into 2 major categories: phagocytes and dendritic cells. The dendritic cells include (*a*) the follicular dendritic cell of the germinal center of lymph nodes; (*b*) the Langerhans cell of the skin, cervix, vagina, stomach, and esophagus; (*c*) the interstitial dendritic cell, representing the counterpart of Langerhans cell in parenchymal organs (with the exclusion of brain and cornea); (*d*) the indeterminate cell; and (*e*) the interdigitating dendritic cell of the T-zone of lymph node.

The International Lymphoma Study Group reviewed 61 cases of histiocytic and accessory dendritic tumors.[2] They found that 93% of the cases of histiocytic/dendritic cell

Table 3. Combined Immunophenotypic and Morphological Classification of Histiocytic and Dendritic Cell Neoplasms[2]

I. Macrophage/histiocytic neoplasms
  A. Histiocytic sarcoma
II. Dendritic cell neoplasms
  A. Langerhans cell tumor
  B. Langerhans cell sarcoma
  C. Interdigitating cell tumor/sarcoma
  D. Follicular dendritic cell tumor/sarcoma
III. Unclassifiable

neoplasms could be classified with 6 paraffin-based markers: CD68, LYS, CD1a, CD21, CD35, and S100 protein. The remaining cases (7%) were resolvable with added morphologic and ultrastructural features (Table 2). They divided these tumors into macrophage/histiocytic, dendritic cell, and unclassifiable neoplasms (Table 3). In that study, they examined a total of 4 cases of IDCS. The terms *interdigitating dendritic cell sarcoma* and *interdigitating dendritic cell tumor* are used interchangeably to describe these cases. The International Lymphoma Study Group review study[2] did not set defined criteria to differentiate interdigitating dendritic cell tumor from IDCS, and actually the 4 cases that they reviewed were lumped under 1 category (interdigitating dendritic cell tumor/IDCS). The neoplastic cells of IDCS are large, fusiform spindle cells with indistinct cell borders, oval central nuclei, finely dispersed chromatin, and small but prominent nucleoli. Occasional multinucleated cells are found. The neoplastic cells often show a storiform or whorled, fascicular growth pattern. The key morphologic finding suggesting this diagnosis is the paracortical location of IDCS within the lymph node (in nodal IDCS cases). These tumors show consistent expression of S100 protein. Expression of CD1a, CD21, and CD35 is absent and CD68 expression is variable. CD45 may be immunopositive. Ultrastructurally, IDCS may show complex interdigitating cytoplasmic processes; however, no Birbeck granules are seen. In our case, the microscopic appearance in the duodenum was spindly with whorled and fascicular growth patterns, in addition to focal epithelioid areas. In the lymph nodes, the tumor cells were more epithelioid with foci of spindle cell appearance. In all locations, the background of the tumor showed a large number of CD3-positive (T-cell) lymphocytes. The tumor cells consistently expressed S100 protein and vimentin in the duodenum, liver, and lymph nodes. Reactivity for CD45 and CD68 was weakly positive, while smooth muscle actin was pos-

Table 2. Immunophenotypic Features of Histiocytic and Dendritic Cell Neoplasms[2]*

	CD68	LYS	CD1a	S100	CD21	CD35
Histiocytic sarcoma	+	+	−	±	−	−
Langerhans cell tumor/sarcoma	+	±	+	+	−	−
Interdigitating cell tumor/sarcoma	±	−	−	+	−	−
Follicular dendritic cell tumor/sarcoma	±	−	−	±	+	+

* Plus sign (+) indicates positive reaction; minus sign (−), negative; plus/minus sign (±), weakly positive.

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Figure 5. *CD68 weak positivity in duodenal tumor (original magnifications ×5 and ×40 [inset]).*

Figure 6. *Electron microscopy shows rounded and spindly cells with interdigitating processes and no Birbeck granules.*

itive only in the duodenal lesion and negative in the liver and lymph nodes.

The differential diagnosis of these tumors includes inflammatory pseudotumor, follicular dendritic cell sarcomas,[5,6] malignant Langerhans cell histiocytosis, and anaplastic large cell lymphoma. In addition, a whole range of sarcomas may be included in the differential diagnosis, including malignant fibrous histiocytoma, fibrosarcoma, leiomyosarcoma, and rhabdomyosarcoma. One has to pay close attention to morphology, immunohistochemistry, and ultrastructural features.[1] Inflammatory pseudotumor, in contrast to IDCS, shows no morphologic atypia or aggressive growth pattern, and a polymorphic cell population is usually present.[5] Follicular dendritic cell sarcoma may have a similar appearance, especially with respect to the whorled growth pattern of spindle cells; however, CD21 and CD35 positivity is evident in the neoplastic cells.[2] Strong clusterin staining also is observed in follicular dendritic cell sarcoma.[7] Malignant Langerhans cell histiocytosis is CD1a positive and shows Birbeck granules ultrastructurally. Anaplastic large cell lymphomas are usually positive for CD30 and epithelial membrane antigen. In addition, there may be anaplastic lymphoma kinase positivity. One should always consider melanoma, which is also positive for S100, in the differential diagnosis. However, melanoma is also often positive for HMB-45 and shows melanosomes ultrastructurally. In the duodenum, the more common gastrointestinal stromal tumor (CD117 positive) has to be excluded.

There is no consensus on a standard chemotherapeutic regimen for IDCS. Patients with this malignancy have been treated with chemotherapy regimens with variable response, and treatments generally are unsuccessful. Olnes et al[8] reported a case of IDCS treated with 6 cycles of ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) chemotherapy regimen that showed complete response.

In summary, we report a case of a 36-year-old woman presenting with abdominal pain and a large duodenal tumor. A diagnosis of IDCS was made based on the overall microscopic, immunophenotypic, and ultrastructural features. In addition to S100 protein and vimentin, the tumor expressed CD45 and CD68. It is a rare tumor in an uncommon site,[9] and in this article we reviewed the classification, diagnosis, and differential diagnosis of dendritic cell tumors and IDCS.

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