

Small intestine perforation due to metastatic uterine cervix interdigitating dendritic cell sarcoma: a rare manifestation of a rare disease

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Abstract

Interdigitating Dendritic Cell Sarcoma (IDCS) is an infrequent dendritic cell tumor which mainly affects the lymphatic system. Intestinal metastasis from uterine IDCS is extremely rare. Here we report a case of a 76-year-old female presenting with vaginal bleeding and acute abdomen. The final diagnosis revealed a small bowel perforation due to metastatic involvement from uterine cervix IDCS. In this paper, we report the clinical manifestation, computed tomography and histopathological findings helpful for the accurate diagnosis of this rare tumor.

Introduction

Interdigitating Dendritic Cell Sarcoma (IDCS) is an extremely rare neoplasm. According to the World Health Organization (WHO) dendritic cell neoplasms are classified into five groups: Langerhans Cell Histiocytosis (LCH), Langerhans Cell Sarcoma (LCS), Interdigitating Dendritic cell Sarcoma/Tumor (IDCS/T), Follicular Dendritic Cell Sarcoma/Tumor (FDCS/T), and Dendritic Cell Sarcoma.¹ Dendritic cells are antigen-presenting cells and play crucial role in the immune system, especially in generating and regulating the germinal cell reaction. The subtype Interdigitating Dendritic Cells stimulate T lymphocytes and are found in the T cell areas of the lymphoid tissue. IDCS mainly occurs in the lymph nodes; however extranodal involvements such as nasopharynx, skin, testis, ovary, urinary bladder, tonsils, small intestine, and pleura have been previously described.² Here we report an uncommon case of extranodal

IDCS primarily affecting the uterine cervix, associated with metastatic involvement of the small intestine which presented with vaginal bleeding and acute abdomen due to bowel perforation.

Case Report

A 76-year-old female presented to our emergency room with vaginal bleeding, epigastric abdominal pain and constipation. The vaginal bleeding appeared 3 weeks before the admission. Medical history was significant for essential hypertension, diabetes mellitus controlled with oral drugs, cerebrovascular accident and cholecystectomy. Family history was negative for malignancy. At presentation, the patient had unremarkable vital signs. Her laboratory tests were normal except for anemia with 10.8 g/dL hemoglobin. Her physical examination revealed a soft, non-tender abdomen without a palpable abdominal mass. A small umbilical hernia without incarcerated content was also detected. There was no evidence of masses, fecal impaction, blood or melena at the digital rectal examination. Gynecologic examination detected an irregular mass originating from the uterine cervix and obliterating the upper vagina. The patient was admitted to the gynecology department for further evaluation.

For anatomical information and staging, thoracic, abdominal and pelvic CT scan was performed. The CT scan of thorax was normal. Abdominal CT revealed a 25×20 mm homogeneous soft tissue mass in close proximity to a small bowel loop (jejunum) (Figure 1). In addition, a large heterogeneous solid mass in the uterine cervix and vagina was noted (Figure 2). There was no evidence of ascites, intraperitoneal dissemination or lymphadenopathy.

During the hospitalization the patient underwent a colposcopy and multiple biopsies were taken from the distal cervix and proximal vagina, area involved with the mass. Neoplastic markers including: AFP-B, CEA-B, CA 153-B, CA 125-B and CA19.9 were within the normal limits. While waiting for the pathologic results, she was discharged with follow-up in the outpatient clinic. Four days later, and before getting the pathologic results the patient again presented in the emergency room with acute severe generalized abdominal pain, that was more prominent in the center and upper abdomen. She had fever, tachycardia (105 beats per minute) and normal blood pressure. Her abdominal examination revealed generalized tenderness, rigidity, guarding and rebound. Her laboratory tests were within the normal limits except for leukocytosis and neutrophilia. After adequate fluid resuscitation she was taken to the operation room for explorative laparotomy. The operation findings were

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pus in the peritoneal cavity, perforated small intestine neoplastic mass about 70 cm distally to the Treitz ligament, small uterine, tumor involving the cervix without any dissemination to the abdominal cavity. She underwent small bowel resection with about 10 cm macroscopic free margins, and hand-sewing double layer anastomosis was performed. After adequate irrigation of the peritoneal cavity the abdomen closed by anatomical layers. Pathological examination showed homogeneous white tissue that infiltrates the bowel wall and forms two nodular masses within the mesentery. Microscopic examination showed a poorly differentiated malignant neoplasm with variably epithelioid or spindle cytomorphology (Figure 3). The tumor cells have elongated tapering or else plump vesicular nuclei and indistinct palely eosinophilic cytoplasm. The biopsy from the region of the cervix is substantially more pleomorphic than the one in the small bowel and there is extensive necrosis. Immunostains performed on the small bowel mass showed focally strong positivity for keratin CAM 5.2 and also pan-keratin, while CD34, SMA, LCA, CD45Ro, CD163 MART-1 and desmin are negative with only some weak focal and likely non-specific positivity for MITF. Furthermore, the S-100 stain highlights the fact that many of the neoplastic cells have elongated dendritic cytoplasmic processes (an appearance which

would be unusual in either Malignant Peripheral Nerve Sheath Tumors (MPNST) or Melanoma). However, finally, what appears to be quite convincing positivity for CD4 in the spindle-shaped cells has been identified. In these circumstances, the findings correspond to IDCS. A few days later the patient was discharged with a recommendation for oncogynecologic and surgical follow-up in the outpatient clinic.

Discussion

Interdigitating dendritic cell sarcomas are very rare neoplasm arising from the dendritic cells. Less than two hundreds cases have been

reported, with only about 50 cases of IDCS reported in the English literature.^{3,4} IDCS presents mostly in the lymph node. However, extranodal involvements have been reported.^{2,4-11} IDCS usually presents at mean age of 51 years and is more frequent in males (male/female ratio 19:12).⁶ Size ranges between 1 and 6 cm. It has the potential to infiltrate adjacent tissues with macroscopic hemorrhage and necrosis and in one third of the reported cases, IDCS had aggressive behavior.

IDCS should be differentiated from the other subtypes (LCH, LCS, and FDSC) as well as from melanoma, and fibroblastic reticular cell tumors. The recognition of extranodal IDCS requires a high index of suspicion because of its rarity. The diagnosis of any one of these entities can rarely be achieved from

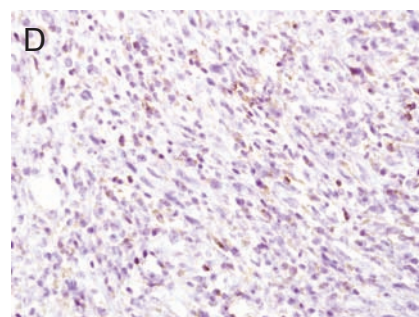
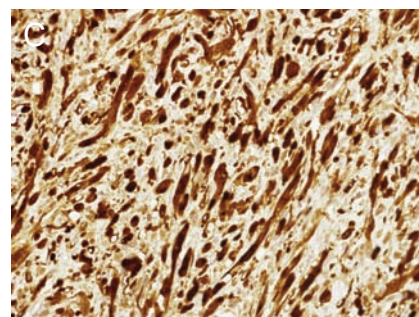
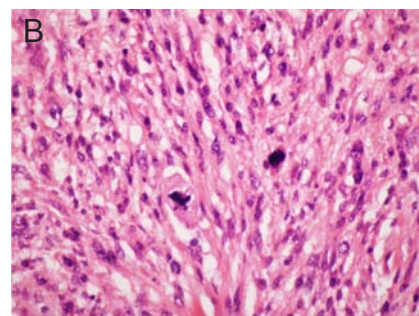


Figure 3. A) Macroscopic picture shows the gross appearance of the small intestinal tumor. The mass is composed of homogeneous white tissue that infiltrates the bowel wall and forms two nodular masses within the mesentery; B) Histological photomicrograph of the tumor showing spindle and epithelioid cells with variable degrees of atypia and polymorphism (Hematoxylin and eosin stain; x600); C) Photomicrograph shows tumor cells with strong and diffuse cytoplasmic and nuclear reactivity for S-100 protein immunostain; D) Photomicrograph shows tumor cells with cytoplasmic reactivity for CD4 immunostain.



Axial contrast-enhanced computed tomography (CT) images through upper abdomen A, B) and coronal multiplanar reconstruction CT image C) show a round soft tissue mass (arrow) in close proximity to small bowel loop (jejunum) consistent with metastatic involvement from interdigitating dendritic cell sarcoma (IDCS) of the uterine cervix



Figure 2. A) axial, B) coronal and C) sagittal contrast-enhanced computed-tomography images through lower abdomen and pelvis demonstrate a large solid mass at the uterine cervix and vagina (M). There is no evidence of ascites, intraperitoneal dissemination or lymphadenopathy. R denotes rectum; UB denotes urinary bladder; U denotes uterus.

clinical and light microscopic information alone, and immunohistochemical and ultrastructural studies can contribute to discriminating between them. Criteria for diagnosing IDCS include: appropriate macroscopic morphology (although varying in their gross appearance, the dendritic cell neoplasms are usually well circumscribed, nodular and solid masses, with tan-gray or white color), microscopic interdigitating junctions with ATPase activity, S-100 and HLA-DR positivity, and CD1a negativity.

Aberrant keratin staining is not unusual in dendritic cell neoplasms and this is the best explanation for an S-100 positive/CD4-positive neoplasm with dendritic cytoplasmic processes. Sarcomas of this type more often have the morphology seen in the bowel mass and most often associated with a relatively low-grade clinical course. The appearance in the cervical mass, however, suggests that this particular case may be more aggressive. One out of four lymph nodes was involved by the sarcoma.

In localized disease, surgical resection has been the mainstay treatment with variable outcomes depending on the disease extension. Disease-free survival (DFS) can reach up to more than 3 years. Relapses mostly occur within 3 years. DFS can reach up to 9 years after surgical resection of a local recurrence. Adjuvant radiotherapy and neo-adjuvant radiotherapy and chemotherapy had good results. Furthermore, adjuvant radiotherapy prolonged the DFS according to few reports.

While metastatic at presentation or with relapse, the disease has poor prognosis. Metastectomy may prolong the DFS. Several chemotherapeutic regimens have been tried including CHOP, ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine), DHAP (dexamethasone, cisplatin, high-dose cytar-

bine), EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin), ICE (ifosfamide, carboplatin, etoposide), and cisplatin/epirubicin with limited response.¹

In our case, the patient had poor prognosis due to locally advanced cervical disease, metastasis to the small intestine with perforation, lymph node involvement and microscopic aggressive appearance. She was referred to the oncology department for neo-adjuvant radiotherapy and chemotherapy and re-evaluation for gynecologic surgery.

Conclusions

IDCS is an extremely rare tumor and it requires a high index of suspicion for accurate diagnosis, especially in extra-nodal involvement. Awareness of this tumor and the use of immunohistochemical stains with appropriate markers are crucial for a correct diagnosis. Surgical resection is the mainstay treatment for localized disease. The role of adjuvant, neo-adjuvant chemotherapy and radiotherapy in metastatic disease still not clearly defined.

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