

## Extranodal Interdigitating Dendritic Cell Sarcoma Presenting in the Pleura: A Case Report

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Interdigitating dendritic cell sarcoma (IDCS) is an extremely rare neoplasm arising from the antigen-presenting cells of the immune system. This disease usually involves the lymph nodes, and rarely, extranodal sites may be affected. The authors report a case of extranodal IDCS presenting in the pleura. A 32-yr-old man presented with progressive chest pain. Imaging studies showed diffuse pleural thickening with pleural effusion. Morphological and immunohistochemical analysis of an incisional biopsy of the pleura were consistent with a diagnosis of IDCS; tumor cells were positive for S100 and CD45, but negative for CD1a, CD21, CD35, B cell and T cell markers. The patient was administered chemotherapy, but died of progressive disease. Although its incidence is extremely rare, this case suggests that extranodal IDCS should be considered in the differential diagnosis of undifferentiated neoplasms and that immunohistochemical staining be performed using appropriate markers.

**Key Words:** Dendritic Cell Sarcoma; Interdigitating; Pleura

### INTRODUCTION

Dendritic cells participate in the immune system as antigen-presenting cells. Four different types of dendritic cells exist in lymph nodes, namely, histiocytic, fibroblastic, interdigitating, and follicular cells. Their main function is the presentation of antigens and the generation and regulation of the germinal center reaction. Follicular dendritic cells participate in the immune system by presenting antigens for B cells and by stimulating B cell proliferation and differentiation. These cells are localized to areas of B cells in the germinal centers of lymphoid follicles. Interdigitating dendritic cells participate in the immune system by stimulating T lymphocytes and are found in the T cell areas of peripheral lymphoid tissues (1-3).

Dendritic cell neoplasms are rare tumors, though they are being recognized with increasing frequency. They were previously classified as lymphomas, sarcomas, or histiocytic neoplasms. However, the World Health Organization (WHO) classified dendritic cell neoplasms into five groups: Langerhans cell histiocytosis (LCH), Langerhans cell sarcoma (LCS), interdigitating dendritic cell sarcoma/tumor (IDCS), follicular dendritic cell sarcoma/tumor (FDSC), and dendritic cell sarcoma, not specified otherwise (4). IDCS are infrequent neoplasms, and therefore, a limited number of cases have been reported. Although most arise in lymph nodes, rare cases of IDCS have

been described in extranodal sites, such as the spleen, small intestine, nasopharynx, skin, testis, ovary, urinary bladder, and tonsils (5-12).

Here, we report a case of extranodal IDCS presenting in the pleura, a hitherto unreported site.

### CASE DESCRIPTION

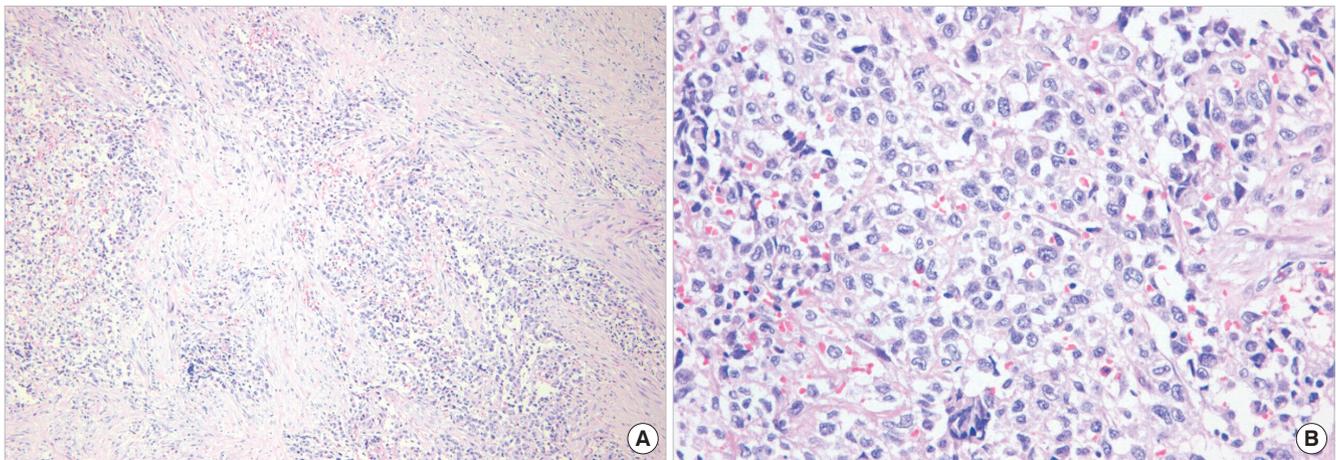
On October 1st, 2009, a 32-yr-old man visited the outpatient clinic with a 1-month history of progressively worsening blood-tinged sputum and chest pain. He had no relevant previous medical history. The patient had worked in a small educational institute for three years, and was currently working as a company employee. However, he denied exposure to asbestos. On physical examination, hepatosplenomegaly and peripheral lymphadenopathy were absent, but a chest examination revealed retraction and tenderness of the left chest wall. Laboratory testing revealed hemoglobin 12.3 mg/dL, white cell count 11,100/ $\mu$ L, and platelet count  $519 \times 10^3$ / $\mu$ L. Blood chemistry findings revealed an alanine aminotransferase 42 IU/L, aspartate aminotransferase 94 IU/L, and lactate dehydrogenase 451 IU/L. Computed tomography (CT) of the chest showed irregular pleural thickening and pleural effusion in the left lung (Fig. 1). An incisional biopsy of pleura was performed, and histologic findings suggested a malignant undifferentiated tumor. Microscopically,

the tumor showed an infiltrative growth pattern with a desmoplastic stroma. The tumor cells had oval to spindle nuclei, and indented nuclei were frequently observed. The chromatin was

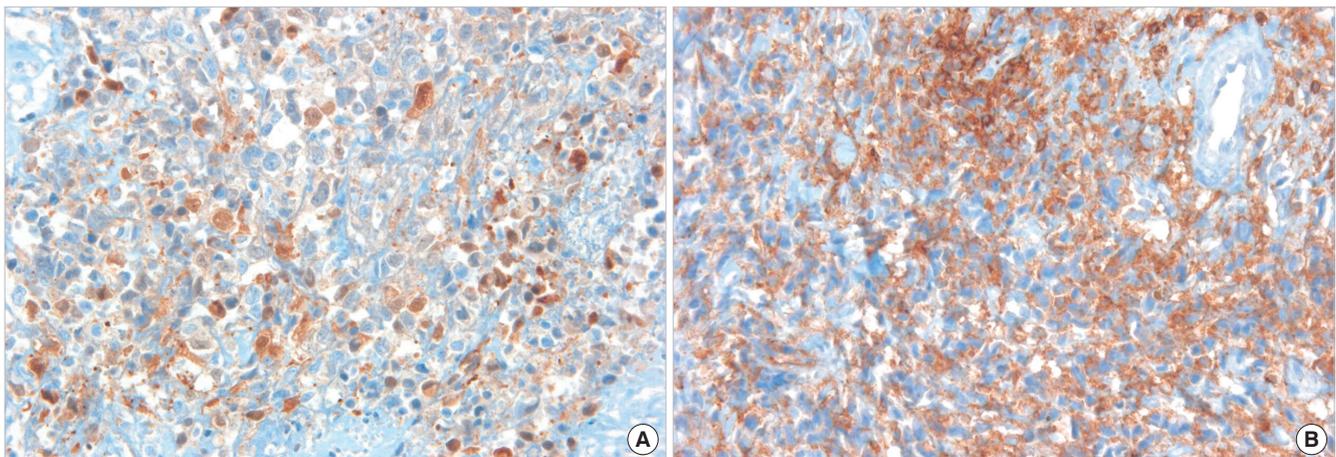


**Fig. 1.** Computed tomography of the chest showed irregular pleural thickening and pleural effusion in the left lung.

often vesicular with inconspicuous nucleoli. The cytoplasm of the tumor cells was abundant and slightly eosinophilic with an indistinct border (Fig. 2). In addition, immunohistochemistry was performed on the Benchmark automated immunostaining system (Ventana Medical System, Tuscon, AZ, USA). The monoclonal antibodies used were the following: S100 (1:800; Dako, Glostrup, Demark), vimentin (1:200; Dako), CD45 (1:100; Leica, Newcastle-upon-Tyne, UK), CK (1:600; Leica), myeloperoxidase (1:200; Leica), HMB45 (1:150; Leica), CD1a (1:20; Leica), CD20 (1:200; Leica), CD21 (1:60; Leica), CD23 (1:100; Leica), CD31 (1:300; Leica), CD34 (1:20; Leica), CD56 (1:150; Leica), CK5 (1:300; Leica), WT-1 (1:40; Leica), calretinin (1:100; Leica), CD68 (1:600; DiNonA, Iksan, Korea), CD3 (1:300; Neo, Fremont, USA), CD35 (1:50; Cell marque, Rocklin, CA, USA), and CK6 (1:50; Thermo, Fremont, CA, USA). Immunohistochemistry showed that the tumor cells were positive for S100, CD45 (Fig. 3), vimentin, and CD68, but negative for cytokeratin (epithelial cell marker), myeloperoxidase (myeloid cell marker), HMB45 (melanoma marker), CD1a (LCS marker), CD3 (T-cell marker), CD20 (B-cell marker)



**Fig. 2.** Pathologic features of an incisional biopsy of the pleura. (A) The growth pattern of the tumor is infiltrative with a desmoplastic stroma (H&E,  $\times 100$ ). (B) The tumor cells shows oval to spindle and indented nuclei and abundant cytoplasm with indistinct border (H&E,  $\times 400$ ).



**Fig. 3.** Immunohistochemistry showed that the tumor cells were positive for (A) S100 and (B) CD 45 ( $\times 400$ ).



**Fig. 4.** Corresponding positron emission tomography (PET)-CT image showed 18-fluoro-deoxyglucose (FDG) uptake (standardized uptake value, SUV, 10.5 and 9.8), by thickened pleura of the left hemithorax and the whole axial skeleton, which was compatible with malignant tissue.

er), CD21, CD23, CD35 (FDCS marker), CD31 (vascular endothelial cell marker), CD34 (myeloid stem cell marker), CD56 (neuroendocrine cell marker), CK5, CK6, WT-1, and calretinin (mesothelioma marker). The proliferation index (Ki 67) of the neoplastic cells was approximately 25%. A diagnosis of IDCS was made based on histological and immunohistochemical findings. The patient underwent a positron emission tomography (PET)-CT scan, which revealed 18-fluoro-deoxyglucose (FDG) uptake in the thickened pleura and whole axial skeleton (standardized uptake value (SUV); 10.5 and 9.8) compatible with malignant tissue (Fig. 4). Subsequently, the patient was treated with two courses of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) and one course of IMEP (ifosfamide, methotrexate, etoposide, prednisolone). However, the pleura-based masses were aggravated, and he died of progressive disease 3 months after diagnosis.

## DISCUSSION

Tumors arising from dendritic cells, such as, FDCS and IDCS, are very rare. Fewer than two hundreds of cases have been reported to date (4), and only 37 cases of IDCS have been reported in the English literature (5). IDCS usually is encountered in a lymph node, but extranodal IDCS is rare and can occur in a wide variety of sites (5-12). The recognition of extranodal IDCS requires a high index of suspicion because of its rarity. We present a case of extranodal IDCS in the pleura that was diagnosed using a combination of morphologic and immunophenotypic char-

acterizations. As far as we know, only one case of IDCS with pleural effusion has been reported, in which malignant pleural effusion occurred during disease course in a IDCS patient presented with multiple lymphadenopathies (13). Moreover, the reported case might not be IDCS due to its expression of surface CD1a in the tumor cells. To the best of our knowledge, this is the first case report to describe extranodal IDCS initially presented with diffuse pleural involvement.

The diagnosis was confirmed histologically on slides stained with hematoxylin and eosin and a wide panel of antibodies, which included probes recognizing antigens specifically expressed by follicular and interdigitating dendritic cells (2, 3). Neoplastic cells were large, fusiform spindle cells with indistinct cell borders, oval central nuclei, finely dispersed chromatin, and small but prominent nucleoli, and often formed a storiform or whorled, fascicular growth pattern. IDCS should be differentiated from FDCS, LCS, S100 positive histiocytic tumors, melanoma, and fibroblastic reticular cell tumors. Immunohistochemistry demonstrated neoplastic cells positivity for all histiocytic markers, including CD68, lysozyme, and macrophage transcription factor PU.1, and showed that the dendritic cell markers fascin and S100 were strongly expressed. However, they were negative for CD1a (LCS marker), CD21/23/35 (FDCS marker), CD20 (B cell marker), CD3 (T cell marker), and CD34 (myeloid stem cell marker) (5-8). Neoplastic cells in our case were strongly positive for S100 and negative for T cell, B cell, epithelial, and follicular dendritic cell markers.

Treatments administered have varied in accord with clinical context of the affected patients. In patients with localized disease, surgical resection has been the mainstay treatment. The roles of chemotherapy and radiotherapy have not been clearly defined. Several chemotherapeutic regimens have been tried including CHOP, ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine), DHAP (dexamethasone, cisplatin, high-dose cytarabine), EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin), ICE (ifosfamide, carboplatin, etoposide), and cisplatin/epirubicin with limited response (1, 3, 6). For the greater part, the agents used are combination chemotherapies designed for the treatment of lymphoma. Remission durations are usually short, and limited results for bone marrow transplantation are not encouraging (3). Our patient was treated using the CHOP and IMEP regimens, but eventually succumbed to disease progression.

This case highlights the diagnostic difficulties associated with rare tumors. Furthermore, its unusual location, extreme rarity, and the morphological similarities between IDCS and FDCS and with other poorly differentiated tumors can easily delay diagnosis. The possibility of IDCS with an unusual extranodal site should be considered when an undifferentiated neoplasm with a mixed population of lymphocytes is encountered.

We present a case of extranodal IDCS presenting with diffuse

pleural involvement. Awareness of this tumor, particularly in extranodal sites, and the use of immunohistochemical stains with appropriate markers are crucial for arriving at a correct diagnosis.

## REFERENCES

1. Fonseca R, Yamakawa M, Nakamura S, van Heerde P, Miettinen M, Shek TW, Myhre Jensen O, Rousselet MC, Tefferi A. *Follicular dendritic cell sarcoma and interdigitating reticulum cell sarcoma: a review. Am J Hematol* 1998; 59: 161-7.
2. Pileri SA, Grogan TM, Harris NL, Banks P, Campo E, Chan JK, Favera RD, Delsol G, De Wolf-Peeters C, Falini B, Gascoyne RD, Gaulard P, Gatter KC, Isaacson PG, Jaffe ES, Kluin P, Knowles DM, Mason DY, Mori S, Müller-Hermelink HK, Piris MA, Ralfkiaer E, Stein H, Su IJ, Warnke RA, Weiss LM. *Tumours of histiocytes and accessory dendritic cells: an immunohistochemical approach to classification from the International Lymphoma Study Group based on 61 cases. Histopathology* 2002; 41: 1-29.
3. Kairouz S, Hashash J, Kabbara W, McHayleh W, Tabbara IA. *Dendritic cell neoplasms: an overview. Am J Hematol* 2007; 82: 924-8.
4. De Pas T, Spitaleri G, Pruneri G, Curigliano G, Noberasco C, Luini A, Andreoni B, Testori A, de Braud F. *Dendritic cell sarcoma: an analytic overview of the literature and presentation of original five cases. Crit Rev Oncol Hematol* 2008; 65: 1-7.
5. Efuno G, Sumer BD, Sarode VR, Wang HY, Myers LL. *Interdigitating dendritic cell sarcoma of the parotid gland: case report and literature review. Am J Otolaryngol* 2009; 30: 264-8.
6. Gaertner EM, Tsokos M, Derringer GA, Neuhauser TS, Arciero C, Andriko JA. *Interdigitating dendritic cell sarcoma. A report of four cases and review of the literature. Am J Clin Pathol* 2001; 115: 589-97.
7. Kawachi K, Nakatani Y, Inayama Y, Kawano N, Toda N, Misugi K. *Interdigitating dendritic cell sarcoma of the spleen: report of a case with a review of the literature. Am J Surg Pathol* 2002; 26: 530-7.
8. Pillay K, Solomon R, Daubenton JD, Sinclair-Smith CC. *Interdigitating dendritic cell sarcoma: a report of four paediatric cases and review of the literature. Histopathology* 2004; 44: 283-91.
9. Luk IS, Shek TW, Tang VW, Ng WF. *Interdigitating dendritic cell tumor of the testis: a novel testicular spindle cell neoplasm. Am J Surg Pathol* 1999; 23: 1141-8.
10. Rupar G, Beham-Schmid C, Gallé G, Zigeuner R, Langner C. *Interdigitating dendritic cell sarcoma of urinary bladder mimicking large intravesical calculus. Urology* 2005; 66: 1109.
11. Banner B, Beauchamp ML, Liepman M, Woda BA. *Interdigitating reticulum-cell sarcoma of the intestine: a case report and review of the literature. Diagn Cytopathol* 1997; 17: 216-22.
12. Androulaki A, Giaslaktiotis K, Lazaris AC. *Interdigitating dendritic cell sarcoma/tumour of the tonsil. Br J Haematol* 2005; 131: 415.
13. Yamakawa M, Matsuda M, Imai Y, Arai S, Harada K, Sato T. *Lymph node interdigitating cell sarcoma. A case report. Am J Clin Pathol* 1992; 97: 139-46.