TURKISH JOURNAL of ONCOLOGY

Turk J Oncol 2025;40(3):252–256
doi: 10.5505/tjo.2025.4542

LETTER TO THE EDITOR

Poor Response to Chemotherapy in a Newly Diagnosed Metastatic Intraabdominal Follicular Dendritic Cell Sarcoma: A Call for Alternative Treatment Strategies

Derya KOYUN,[1] Seher YÜKSEL,[2] Işınsu KUZU,[2] Muhit ÖZCAN[1]

[1]Division of Hematology, Department of Internal Medicine, Ankara University Faculty of Medicine, Ankara-*Türkiye*
[2]Department of Pathology, Ankara University Faculty of Medicine, Ankara-*Türkiye*

Dear Editor,

Mesenchymal-derived follicular dendritic cells (FDCs) are essential for antigen presentation to B cells, stimulating their proliferation and differentiation.[1] Follicular dendritic cells (FDCs) reside in the germinal centers of B cell follicles and are pivotal in the germinal center reaction through their interactions with other cells.[2] Follicular dendritic cell sarcoma (FDCS) is characterized by a diverse neoplastic proliferation of spindle-shaped to ovoid cells that exhibit the morphological and phenotypic traits of follicular dendritic cells. This condition was first identified and described by Monda et al.[3] in 1986. Upon microscopy, FDCS exhibits fascicular, storiform, whorled, and diffuse patterns with eosinophilic cytoplasm. Lymphoplasmacytic infiltration is commonly present in tumor tissue. FDCS usually exhibits a low mitotic index, and the Ki-67 proliferation index is often below 25%. FDCS cells express CD21, CD23, CD35, clusterin, CXCL13, and podoplanin and contribute to the reactivity of FDCS for S100, smooth muscle actin, and CD68 by analysis of immunohistochemical staining profiles.[4,5] FDCS have the exact prevalence of both genders, mainly affecting middle-aged adults (median age 50 years; range 9–90). FDCS involves nodal and extranodal sites, especially the liver, spleen, and gastrointestinal tract, or combined.[5,6] Overall survival rates decline by approximately 50% in metastatic disease, but not depending on the stage of the disease.[6,7] Larger tumor (≥6 cm), intraabdominal involvement, high mitotic rate (≥5 mitoses in 10 HPF), cellular atypia, and coagulative necrosis are indicative of a poor prognosis.[6,7] FDCS clinical features and standard treatment approach are indefinite. We know that only one FDCS in the duodenum has been reported.[8] This report presents an extranodal intraabdominal (duodenal) FDCS with liver metastasis and analyzes the response to treatment, morphology, and immunophenotype characteristics.

A 52-year-old woman with a history of type 2 diabetes was admitted to our center in July 2021. She presented with a two-month history of abdominal pain, unintentional weight loss of 10 kg, and night sweats. Her family history was unremarkable. The patient's general physical exam and all laboratory studies, including tumor marker levels, were within normal limits. A computed tomography (CT) scan revealed a well-defined, 8×4.5 cm solid mass with suspicious 3.8 cm lymph node involvement in the left paraaortic area. The mass in the head of the pancreas, which showed enhancement, appeared to originate from the duodenum. It spread on the left side of the aortic bifurcation—a metastatic 1.6×2 cm subcapsular nodule on the liver in segment IV. The 18-FDGPET/CT showed increased uptake in the two masses, corresponding to those described on CT (abdomen (SUV_{max}:25); liver (SUV_{max}:13.9)) (Fig. 1). The patient had a laparoscopic excisional biopsy performed on the central mass.

A tumor was detected upon microscopic examination. The tumor also infiltrated one lymph node. The tumor cells were spindle and ovoid cells arranged in a storiform pattern containing a large eosinophilic cytoplasm with round-irregular vesicular nuclei containing

Received: February 22, 2025
Accepted: March 15, 2025
Online: September 03, 2025

Accessible online at:
www.onkder.org

Dr. Derya KOYUN
Ankara Üniversitesi Tıp Fakültesi,
İç Hastalıkları Anabilim Dalı,
Hematoloji Bilim Dalı,
Ankara-Türkiye
E-mail: dr.deryakoyun@hotmail.com

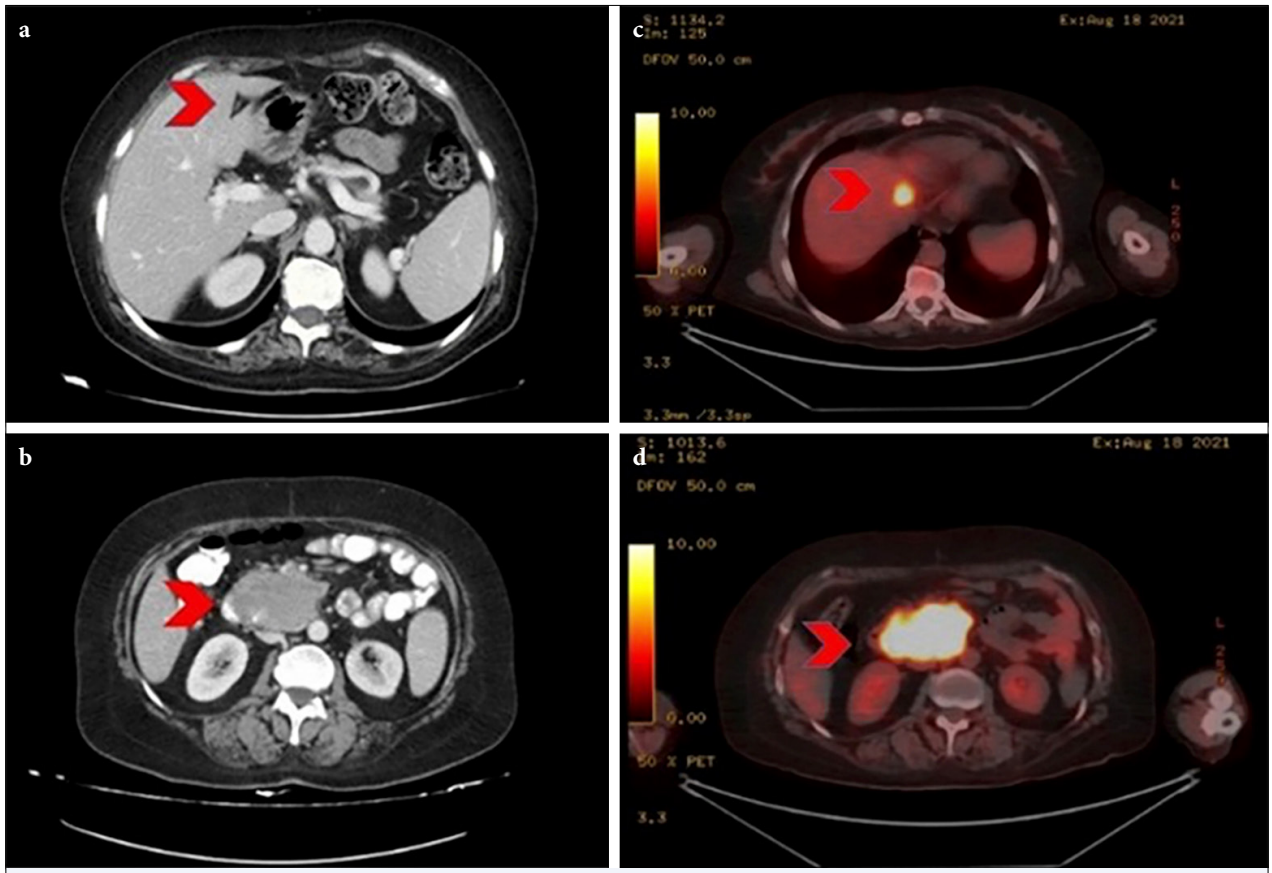

Fig. 1. (a) Abdominal CT imaging showing a metastatic nodule in the liver and (b) a large solid mass arising from the dudenum in the right upper quadrant, (c) pre-chemotherapy 18-FDGPET/CT showing liver metastasis and (d) intraabdominal infiltration.
CT: Computed tomography; 18-FDGPET/CT: 18F-fluorodeoxyglucose positron emission tomography.

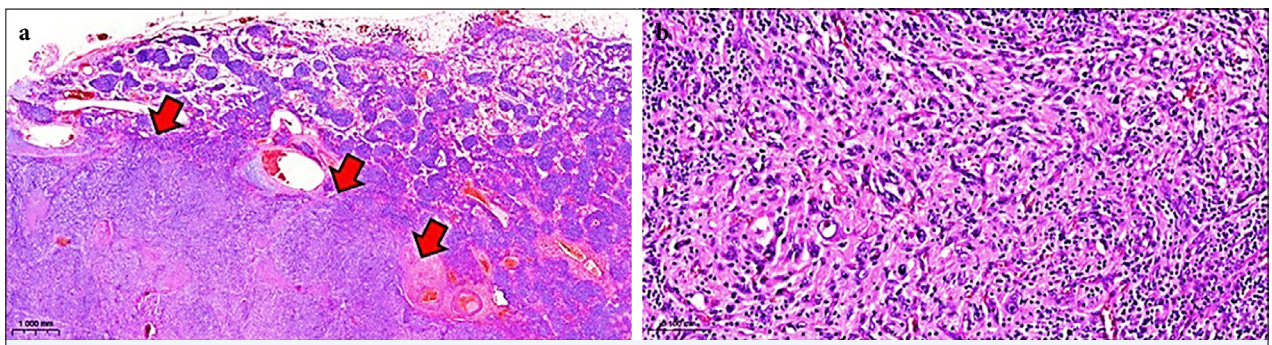

Fig. 2. (a) The tumor in lymph node is observed (red arrows). (b) The tumor cells characterised by storiform organisation, vesicular irregular or rounded nuclei, large eosinophilic cytoplasm and visible nucleoli.

prominent nucleoli (Fig. 2). Small, scattered lymphocytes and plasma cells were present among tumoral cells. Mitosis was not observed. Necrosis was absent. In immunohistochemical staining, tumor cells were positive for CD21, D2-40, fascin, and clusterin (Fig. 3). The tumour cells were negative for CD45, CD3, CD20, CD38, CD15, Pax5, CD30, CD34, S100, ERG, EMA, CD23, CD15, ALK-1, HHV8, desmin, smooth muscle actin, LMW+HMWCK (cocktail). In situ hybridization for Epstein-Barr (EBV) was negative. There was a population of CD3-positive T, CD20, Pax5-positive B lymphocytes, and CD38-positive plasma cells.

Turk J Oncol 2025;40(3):252–256
doi: 10.5505/tjo.2025.4542

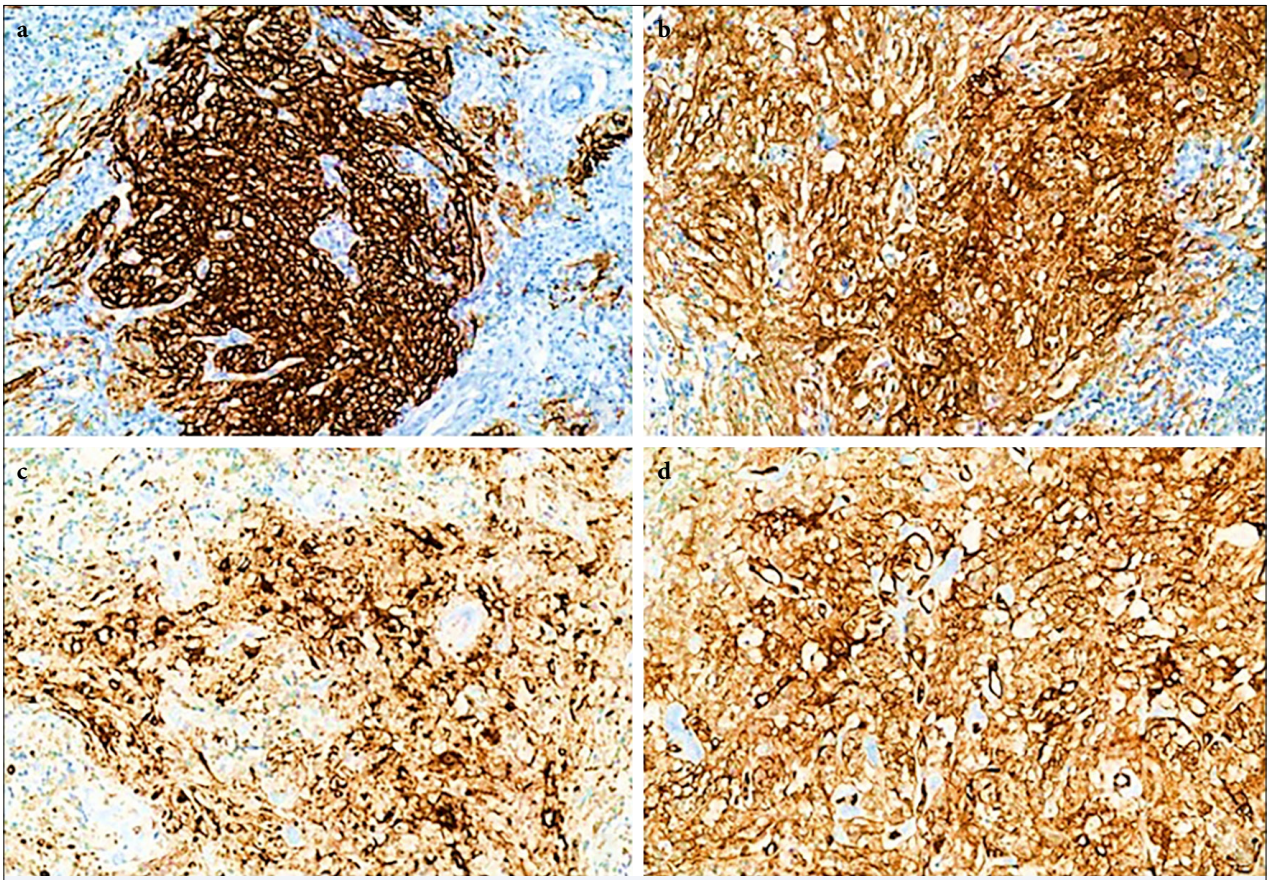

Fig. 3. In immunohistochemistry, infiltrative cells positive for CD21 (a), D2-40 (b), Clusterin (c), Fescin (d).

The patient was diagnosed with FDCS. Concurrent EBV viral load was negative in plasma, and the bone marrow was not involved. The presence of metastatic disease led to the decision not to pursue surgical therapy. The patient underwent chemotherapy using a combination of gemcitabine and docetaxel (Gemcitabine was given at a fixed-dose rate of 900 mg/m² through IV infusion on days 1 and 8, along with docetaxel at 75 mg/m² intravenously on day 8, every 21 days). This treatment was chosen based on its potential to target the rapidly growing tumor cells. After three cycles, the disease progressed rapidly with an increase in the size of the tumor with an enlarged 4.7×3.7 cm lymph node in the left parailiac area and additional mesenteric nodal metastasis in the CT scan.

In contrast, a concurrent PET/CT showed partial metabolic disease (abdomen SUV_{max}: 16.1; liver SUV_{max}: 10.4). PD-L1 was negative (rare expression in inflammatory infiltrate cells), so administration of nivolumab with a planned switch. Cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone (CHOEP) chemotherapy were administered as a second-line treatment. After one cycle, the patient had grade 4 fatigue, hypotension, melena, and dropping hemoglobin. Upper gastrointestinal (GI) endoscopic findings include a blood-filled stomach and multiple deep-bleeding duodenal ulcerations. The patient underwent a Whipple (pancreaticoduodenectomy) procedure. A severe life-threatening hemorrhage occurred 2 days postoperatively, and unfortunately, she died five months following her FDCS diagnosis.

FDCS is a rare low-intermediate grade neoplasm occurring at different body parts. Data has been limited since 1986. Only several case reports and a series of FDCS have been published. The median tumor size in the literature was 7 cm (range, 1–22 cm), and most patients have bulky disease.[6,7] The disease arises predominantly in extranodal involvement (isolated 79.4% or with nodal involvement 5.5%).[5] The most commonly involved nodes were included, respectively, abdominal 31% and cervical 29%.7 Extranodal FDCS in the duodenum is extremely rare and has been reported in a case report.[8] Our data differs from this case with a concurrent nodal involvement.

Patients with extranodal disease have poor outcomes.[7] There is still a lack of effective treatment management for cases that recur or metastasize.

Surgery, chemotherapy, radiotherapy (RT), or combinations of these treatments have been proposed for FDCS. The gold standard treatment for patients with resectable, localized disease is surgery (gross total resection). Of the patients treated with surgical resection and consolidative RT, progression-free survival (PFS) and overall survival (OS) improved; however, adjuvant or neoadjuvant chemotherapy had no more benefits.[7,9] Some studies indicate that adjuvant radiotherapy does not significantly improve survival rates in cases of localized disease.[6,9]

In patients with metastatic and/or unresectable disease, systemic chemotherapy regimens include CHOP, ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine), ICE (ifosfamide, carboplatin, etoposide), can be used. Other sarcoma-based regimens like gemcitabine with taxanes (gem-tax) have been successful.[7,10,11] Objective responses were observed in two patients with FDCS metastatic to the liver who received gemcitabine and docetaxel treatment.[11] Also, another patient with FDCS and pulmonary metastasis responded significantly with this regimen, and no recurrence occurred within 5 years.[12] In a study by Jain et al.,[7] 10 of 28 patients of FDCS received gem-tax and were associated with an ORR of 80%. The median response duration was 13.4 months (range 3–83 months), and they suggested a gem-tax regimen in the front line for patients without eligibility for surgery.[7] However, in our case, a combination of gem-tax did not benefit disease control. Bulky, intraabdominal, and extranodal disease characteristics may be linked to a poor prognosis and treatment failure in the patient. Although our patient has liver metastasis, most studies show that the disease stage does not indicate a relationship with survival.[6,7]

Tyrosine kinase inhibitors can effectively control the disease with unknown mechanisms (pazopanib, imatinib, sorafenib, sunitinib, brivanib, and sirolimus).[9,13] This might be an unknown loss of negative genetic alteration in the NF-κB regulatory pathway (BIRC3, NFKBIA, TRAF3, SOCS3, TNFAIP3).[14] CDKN2A and TP53 genes are the most frequent oncosuppressor genes.[14,15] The BRAFV600E mutation was identified in 18.5% of patients with FDCS.[16] A case of FDCS shows biological association with castleman disease, and PDGFRB N666S mutation was discovered.[15] High expression percentage of PD-L1 and PD-L2 has been detected in FDCS (PD-L1 50%, PD-L2 55%) and PD-L1 expression can respond to immune checkpoint inhibitors.[17,18] We considered the off-label use of nivolumab in our case.

To conclude, we report a case of bulky, metastatic, intraabdominal, nodal, and extranodal FDCS with poor outcomes and no benefit from intensification of therapy. In the future, considering the genetic environment and interactions will help us understand the causes of this rare entity's heterogeneous outcomes, and novel, practical, targeted therapies will be encouraged for treatment success.

The case was reviewed and approved by the Ankara University Human Research Ethics Committee (Date: 10.12.2021, Approval No.: İ11-688-21).

Conflict of Interest: All authors declared no conflict of interest.

Financial Support: None declared.

Use of AI for Writing Assistance: No AI technologies utilized.

Authorship Contributions: Concept – D.K.; Design – D.K.; Materials – D.K., S.Y., I.K., M.Ö.; Data collection and/or processing – D.K., M.Ö.; Literature search – D.K., M.Ö.; Writing – D.K., S.Y.; Critical review – D.K., S.Y.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Kairouz S, Hashash J, Kabbara W, McHayleh W, Tabbara IA. Dendritic cell neoplasms: An overview. Am J Hematol 2007;82:924–8.
2. Aguzzi A, Kranich J, Krautler NJ. Follicular dendritic cells: Origin, phenotype, and function in health and disease. Trends Immunol 2014;35:105–113.
3. Monda L, Warnke R, Rosai J. A primary lymph node malignancy with features suggestive of dendritic reticulum cell differentiation. A report of 4 cases. Am J Pathol 1986;122:562.
4. Lorenzi L, Döring C, Rausch T, Benes V, Lonardi S, Bugatti M, et al. Identification of novel follicular dendritic cell sarcoma markers, FDCSP and SRGN, by whole transcriptome sequencing. Oncotarget 2017;8:16463–72.
5. Facchetti F, Simbeni M, Lorenzi L. Follicular dendritic cell sarcoma. Pathologica 2021;113:316–29.
6. Saygin C, Uzunaslan D, Ozguroglu M, Senocak M, Tuzuner N. Dendritic cell sarcoma: A pooled analysis including 462 cases with presentation of our case series. Crit Rev Oncol Hematol 2013;88:253–71.
7. Jain P, Milgrom SA, Patel KP, Nastoupil L, Fayad L, Wang M, et al. Characteristics, management, and outcomes of patients with follicular dendritic cell sarcoma. Br J Haematol 2017;178:403–12.
8. Ferede A, O'Connor R, Stafford A, Swan N. Follicular dendritic cell sarcoma of the duode-

Turk J Oncol 2025;40(3):252–256
doi: 10.5505/tjo.2025.4542

num: An extremely rare entity. BMJ Case Rep 2018;2018:bcr2017221505.
9. Gounder M, Desai V, Kuk D, Agaram N, Arcila M, Durham B. Impact of surgery, radiation and systemic therapy on the outcomes of patients with dendritic cell and histiocytic sarcomas. Eur J Cancer 2015;51:2413–22.
10. Conry RM. Response of follicular dendritic cell sarcoma to gemcitabine and docetaxel: Report of two cases and literature review. Clin Sarcoma Res 2014;4:6.
11. Jain P, Patel KP, Futreal A, Gumbs C, Hu S, Bueso Ramos C, et al. Clinico-pathological characteristics, treatments and outcomes of patients with dendritic cell sarcoma (DS). Blood 2015;126:2700.
12. Esmati E, Kolahdouzan K. Metastatic follicular dendritic cell sarcoma treated with gemcitabine plus docetaxel with an outstanding survival: A case report and review of literature. Clin Case Rep 2021;9:473–6.
13. Shah P, Shah S, Agostino N. Disease response to pazopanib in follicular dendritic cell sarcoma. Case Rep Oncol 2020;13:1131–5.
14. Griffin GK, Sholl LM, Lindeman NI, Fletcher CDM, Hornick JL. Targeted genomic sequencing of follicular dendritic cell sarcoma reveals recurrent alterations in NF-κB regulatory genes. Mod Pathol 2016;29:67–74.
15. Massoth LR, Hung YP, Ferry JA, Hasserjian RP, Nardi V, Nielsen GP, et al. Histiocytic and dendritic cell sarcomas of hematopoietic origin share targetable genomic alterations distinct from follicular dendritic cell sarcoma. Oncologist 2021;26:1263–72.
16. Go H, Jeon YK, Huh J, Choi SJ, Choi YD, Cha HJ, et al. Frequent detection of BRAFV600E mutations in histiocytic and dendritic cell neoplasms. Histopathology 2014;65:261–72.
17. Xu J, Sun HH, Fletcher CD, Hornick JL, Morgan EA, Freeman GJ, et al. Expression of programmed cell death 1 ligands (PD-L1 and PD-L2) in histiocytic and dendritic cell disorders. Am J Surg Pathol 2016;40:443–53.
18. Lee MY, Bernabe-Ramirez C, Ramirez DC, Maki RG. Follicular dendritic cell sarcoma and its response to immune checkpoint inhibitors nivolumab and ipilimumab. BMJ Case Rep 2020;13:e234363.