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Intraperitoneal Follicular Dendritic Cell Sarcoma: Role of Chemotherapy and Bone Marrow Allotransplantation in Locally Advanced Disease?

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ABSTRACT: We describe a case of a 44 year-old woman diagnosed with follicular dendritic cell sarcoma (FDCS). FDCS is a very rare disease affecting the dendritic antigen presenting cells and is often misdiagnosed. Surgery is considered the best treatment modality, followed by chemotherapy. In our case, surgical excision was not possible, therefore the patient received two lines of chemotherapy followed by bone marrow allotransplantation, then a third line of chemotherapy with a complete metabolic response seen on PET/computed tomography (CT) follow-up 29 months later. A review of the literature has been performed.

KEYWORDS: intraperitoneal, follicular dendritic cell sarcoma (FDCS), chemotherapy, bone marrow allotransplantation

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Introduction

Follicular dendritic cell sarcoma (FDCS) is a neoplastic proliferation of spindled to ovoid cells showing morphologic and phenotypic features of follicular dendritic cells and was firstly described by Monda in 1986.[1] Only few case reports and retrospective series have been published.[2–15] FDCS mainly affects head and neck lymph nodes.[16] Intraperitoneal location of FDCS is a very uncommon discovery and is associated with a particularly aggressive clinical course.[2,13]

In this report, we present a case of advanced intraperitoneal FDCS treated successfully with chemotherapy and bone marrow allotransplantation.

Case Report

A 44 year-old woman with no known previous medical history, presented with a painless periumbilical mass, associated with intermittent constipation. An abdominal computed tomography (CT) was performed and showed a homogeneous enhancing mass in the lesser omentum, 5 cm in diameter and located in front of the pancreas. Another subhepatic heterogeneous enhancing mass of 5.9 × 8.6 × 7 cm was also detected and a retroperitoneal lymph node without involvement of adjacent structures, suggestive of lymphoma (Fig. 1A and B). The 18-FDGPET/CT showed two hypermetabolic masses, corresponding to those described on CT, with multiple retroperitoneal and right iliac hypermetabolic lymph nodes (Fig. 2). A laparoscopic excisional-biopsy of the main mass was performed to confirm the suspicion of lymphoma diagnosis. Macroscopically, an encapsulated nodular mass measuring 8.5 × 5.5 × 5.5 cm was identified. Histopathologic assessment of the resected specimen showed clusters of small lymphocytes and epithelioid cells with eosinophilic cytoplasm and indistinct borders (Fig. 3A). We note sheets of ovoid cells with vesicular nuclei and pale eosinophilic cytoplasm. We note also mitotic activity, syncitial appearance, and the presence of interspersed lymphocytes (Fig. 3B). Immunohistochemical staining showed cells that were strongly positive for the FDCS marker CD23 (Fig. 3C) and negative for

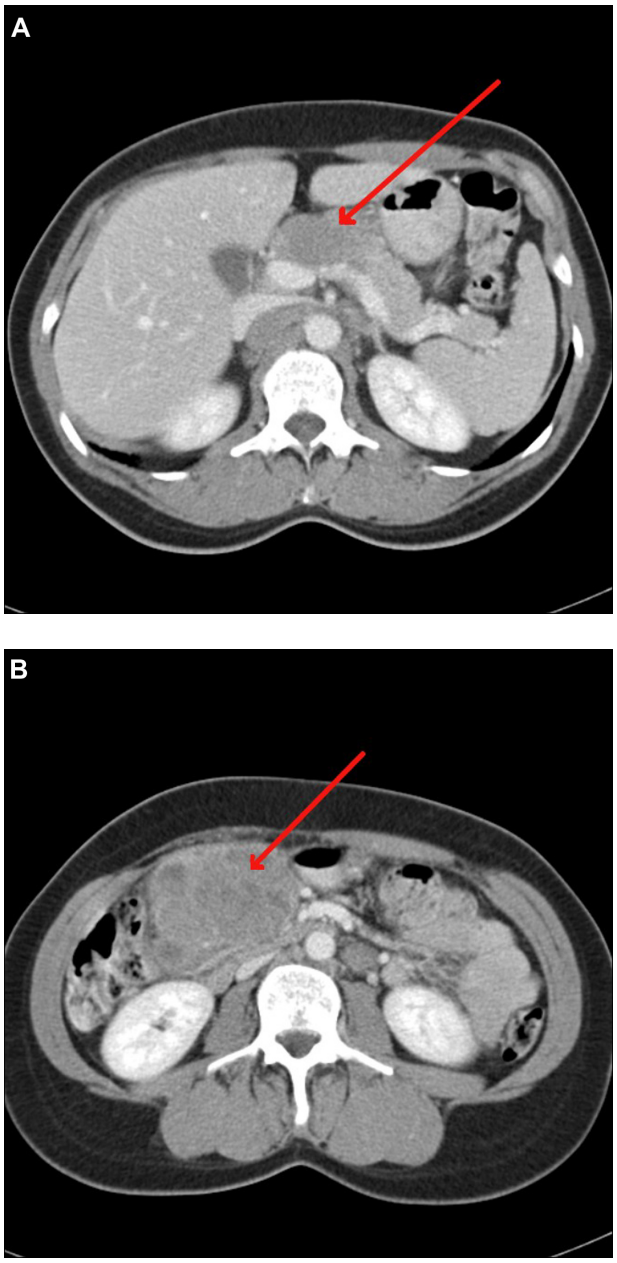

Figure 1. (**A**) Homogenous enhancing mass in the lesser omentum located in front of the pancreas. (**B**) Heterogeneous enhancing mass located below the liver.

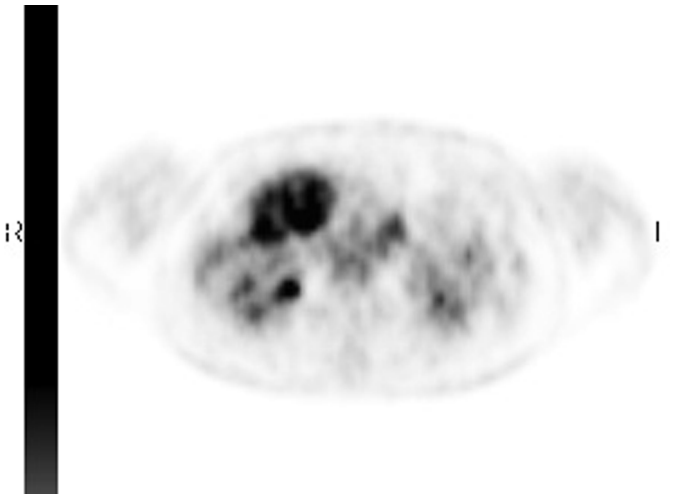

Figure 2. Pre-chemotherapy 18-FDGPET/CT showing multiple retroperitoneal and intra-abdominal infiltrations.

CD20, S-100-protein, and CD1a. ALK was also negative. No monoclonal rearrangement of the T-cell receptor gamma-chain, of immunoglobulin heavy-chain gene or of immunoglobulin kappa light-chain gene was revealed by PCR. These findings were considered diagnostic of FDCS. Multidisciplinary discussion of the case agreed on a classical lymphoma-based chemotherapy with cyclophosphamide, adriamycin, vincristine, and prednisone (CHOP, six courses).

The patient received six courses of chemotherapy. A post-chemotherapeutic 18-FDGPET/CT performed six months after diagnosis showed a partial metabolic response and a macroscopic mass was still visible on CT after the first four cycles (Fig. 4A), and a complete metabolic and radiologic response at the end of the first line (Fig. 4B and C). At nine months, recurrence was noted in the peripancreatic region on 18-FDGPET/CT. She was further treated by a second line chemotherapy with etoposide, cisplatine, ARA-C, and prednisone (ESHAP). The 18-FDGPET/CT performed after four courses showed a complete metabolic response. She received one more course of ESHAP followed by a bone marrow allotransplantation (BHS2 protocol). BHS2 is the reduced intensity conditioning regimen received by the patient consisted in (total lymphoid irradiations) TLI 8 Gy (80c Gy/day during 10 days) from day-11 to day-7 and from day-4 to day-0, and rabbit ATG (Thymoglobulin Genzyme) 1.5 mg/kg/day during five days from day-11 to day–7. GVHD prophylaxis consisted in cyclosporine (Neoral), six months post transplantation and mycophenolate mofetil acid, 1 gr bid (CellCept) during 45 days.[21]

At 24 months (eight months after bone marrow allotransplantation), another recurrence occurred at the same site on 18-FDGPET/CT. The patient received two lymphocytes infusions, from her previous donor, without therapeutic effectiveness. Then, we proceeded by administration of a third line chemotherapy with gemcitabine, navelbine, and dexamethasone. The 18-FDGPET/CT performed after four courses showed a partial metabolic response. She received two additional courses in consolidation.

18-FDGPET/CT performed after six courses showed a complete metabolic response.

At the 29-month follow-up, she presented with a complete metabolic response.

Discussion

FDCS belong to dendritic cell sarcoma group with interdigitating dendritic cell sarcoma (IDCS) and fibroblastic reticular cell tumor (FRCT).

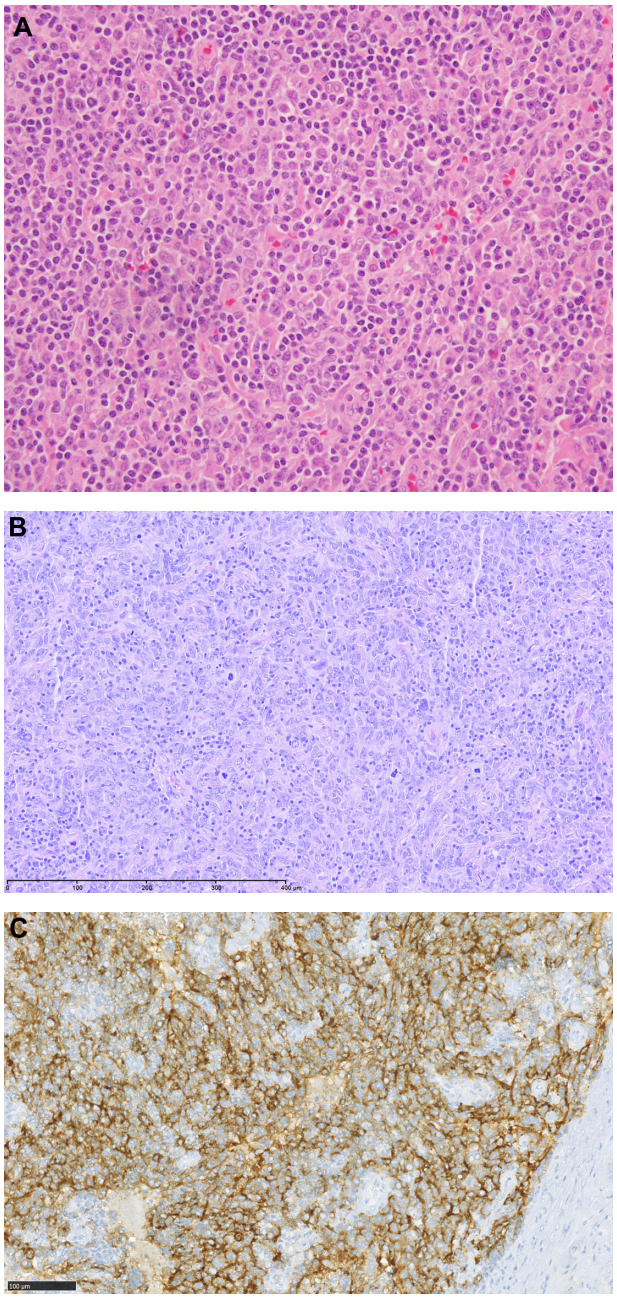

Figure 3. (**A**) Clusters of small lymphocytes and epithelioid cells with eosinophilic cytoplasm and indistinct borders. (**B**) Sheets of ovoid cells with vesicular nuclei and pale eosinophilic cytoplasm. Note the mitotic activity, syncitial appearance, and the presence of interspersed lymphocytes. (**C**) CD23 immunostaining, × 40.

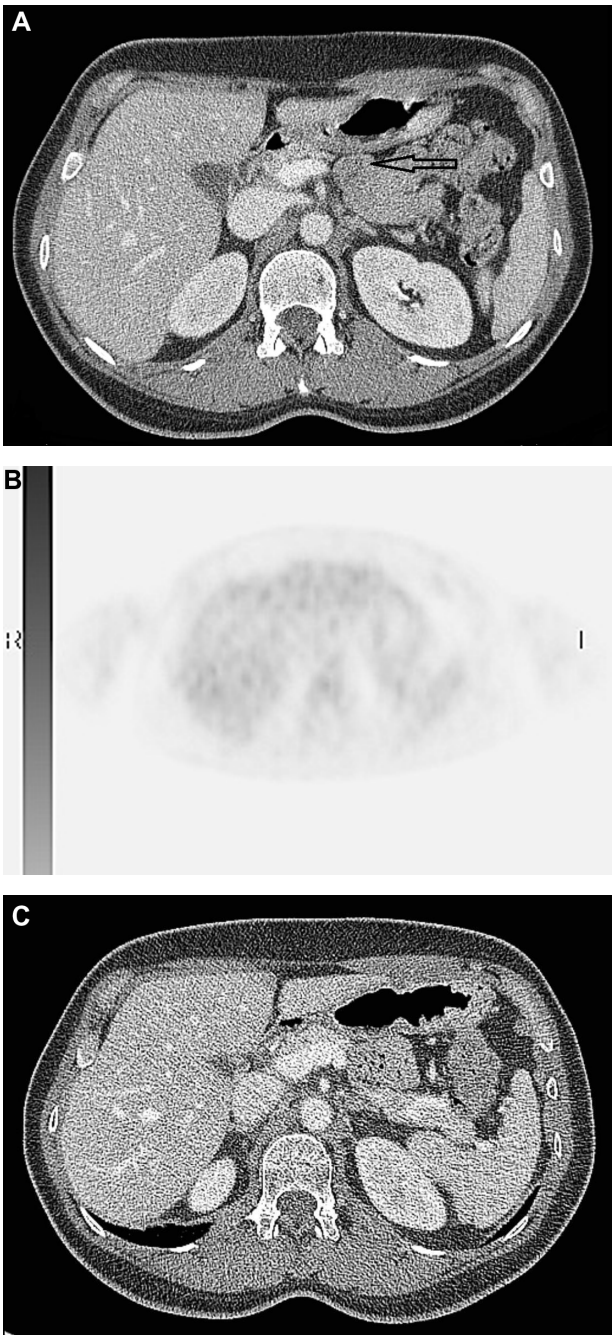

Figure 4. (**A**) Residual mass after the first four cycles. (**B**) Post-chemotherapy (first line) 18-FDGPET/CT showing complete metabolic response. (**C**) Complete radiologic response at the end of the first line of chemotherapy.

FDCS is a very rare neoplasm of antigen presenting cells of the B-cell follicles of lymphoid organs. FDCS affects mainly young adults without gender predilection.[2] Recurrence is frequent with local recurrence and distant metastases reported in about 40% of patients.[3] FDCS are probably underdiagnosed because of its rarity and uncommon histological features. At histology, differential diagnoses are thymoma-like, meningioma-like tumors and malignant fibrous histiocytoma. Immunohistochemical analyses are fundamental to confirm the diagnosis. Tumor cells show phenotype of non neoplastic follicular dendritic cells and are thus positive for markers CD21, CD23, and CD35.[2–4] In addition, they are usually positive for desmoplakin, vimentin, fascin, and HLA-DR. Tumors cells are variably positive for S-100-protein and CD68 and they are consistently negative for CD1a, lysozyme, myeloperoxidase, CD34, CD3, CD79a, CD30, HMB-45, and cytokeratins. Most of the cases reported in the literature have involved lymph nodes of the neck, mediastinum, and axilla. Approximately one third of the cases were located in

extranodal sites, such as liver, tonsil, and intra-abdominal soft tissue.[4–8,13] Intra-abdominal location is associated with higher recurrence, metastasis, or mortality rate.[2,3,13]

A recent literature review by Saygin et al reported 343 published cases of FDCS but no specific data are reported on intra-abdominal disease.[18]

Etiopathogenesis of FDCS remains unclear. A stromal cell derivation origin and a hematopoietic lineage origin have been proposed. Hwang So et al have reported a transformation of Castleman disease into an intra-abdominal FDCS.[19]

Table 1 shows the clinical features of the 17 cases of intra abdominal FDCS reported so far.[2–12,14,15] Complete surgical excision is mainly proposed for FDCS, but also for local resectable disease. According to small series and reviews, chemotherapy and radiotherapy have not yet proven their effectiveness for the treatment of FDCS.[2,3,18,20] In the present case, the perigastric mass did not seem completely resectable and there was retroperitoneal lymph node involvement. The disease was considered locally advanced. Advanced intraperitoneal FDCS is a very severe condition where treatment options are not well established.

Since curative surgery was not possible for this patient, we opted for a medical treatment with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy (identical protocol as used for aggressive lymphomas). The choice of this regimen in our case was based on a literature review where the association of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) was widely used and showed its efficacy.[13] Other chemotherapeutic such as ICE (ifosfamid, carboplatin, etoposide), CHEOP, and ABVD (adriamycin, bleomycin, vincristine, dacarbazine) regimen have also been proposed.[14]

Given the bad prognosis of the disease, the recurrence after conventional chemotherapy and the availability of a familial donor, an allogeneic hematopoietic stem cell transplantation (HSCT) was decided following the report of a similar case in the literature.[17] No rituximab was added because of the negativity of CD20. Even though a macroscopic mass was still in place after four cycles of chemotherapy, with reduced FDG capitation, a complete metabolic and radiologic response was achieved after six courses of chemotherapy. This observation suggests that chemotherapy can be effective in locally advanced FDCS. Longer follow-up and further cases are definitely needed in order to draw any conclusion. However, six courses of CHOP chemotherapy might be considered an option for patients with unresectable FDCS lesions.

Table 1. Clinical features of intra abdominal FDCS reported in the literature.

REPORTED CASES	SITE OF TUMOR	INITIAL TREATMENT	CHEMOTHERAPY AGENT	OUTCOME
Perez-Ordoñez et al.[4]	Spleen	Resection	None	Unknown
	Peripancreatic tissue	Resection	None	Unknown
Loo[12]	Intra abdominal	Resection	None	Unknown
Han et al.[5]	Submucosal of the stomach	Resection	None	Disease free at 10 months
Hollowood et al.[6]	Small intestine	Resection	None	Recurrence at 6 months
	Head of pancreas	Resection	None	Disease free at 4 months
Chan et al.[2]	Wall of small intestine	Resection of small bowel	None	Recurrence at 6 months
	Head of pancreas	Subtotal resection	None	Died at 11 months
De Pas et al.[3]	Liver	Cholecystectomy-liver resection	None	Recurrence at 11 months
Skarin A[10]	Anterior abdominal wall	Resection followed by radiotherapy	None	Disease free at 8 months
Chan et al.[2]	Mesocolon and mesenteric lymph nodes	Debulking resection followed by chemotherapy	Protocol as used for aggressive lymphomas (no details)	Recurrence at 18 months
Sander et al.[7]	Spleen	Resection followed by chemotherapy	Adriamycin, isofosfamide, GCSF[a]	Died at 9 months
Yamakawa[11]	Omentum	Resection followed by chemotherapy	CHOP[b]	Died at 30 months
Geerts et al.[8]	Stomach and liver metastasis	Unknown	Unknown	Unknown
Chien-Feng[9]	Multiple abdominal tumors	Unknown	Unknown	Unknown
Chien Jerry et al.[19]	Omentum	Resection	Unknown	Unknown
Hwang Soon et al.[18]	Pancreas	Resection	None (Radiation alone)	Disease free at 9 months
Our case	Intra abdominal	Partial resection followed by chemotherapy	CHOP[b], ESHAP[c], Third line chemotherapy[d]	Disease free at 29 months

Notes: [a]Granulocyte colony-stimulating factor. [b]Cyclophosphamide, adriamycin, vincristin sulfate and prednisolone. [c]Etoposide, Cisplatine, ARA-C and Prednisone. [d]Gemcitabine, Navelbine, Dexamethasone.

Conclusion

FDCS is a rare entity, especially those located in the intraperitoneal cavity. The diagnosis must be kept in mind when confronted with uncommon histological features in lymphoid tissue. A complete metabolic response after six courses of CHOP was achieved in a patient with FDCS. Even though complete excision is currently known to be the best way to treat early stage FDCS, our case confirms other reports' suggestion that 'lymphoma-like' chemotherapy could be a good option in patients with advanced unresectable disease.

Author Contributions

Conceived and designed the experiments: GL. Analyzed the data: GL, KK. Wrote the first draft of the manuscript: GL. Contributed to the writing of the manuscript: KK, MAA, NSA. Agree with manuscript results and conclusions: GL, KK, MAA, NSA, IEN. Jointly developed the structure and arguments for the paper: GL. Made critical revisions and approved final version: GL, KK, MAA, NSA, IEN. All authors reviewed and approved of the final manuscript.

DISCLOSURES AND ETHICS

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

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