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Teaching Case

Retroperitoneal Follicular Dendritic Cell Sarcoma: A Case Report

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Introduction

Follicular dendritic cell sarcoma (FDCS) comprises 0.4% of soft tissue sarcomas.[1] It most commonly relapses in the lungs and liver.[2] In 1986, it was first described in a series of 4 case reports where management with wide local excisions and chemotherapy showed varying success.[3] There have been limited studies on outcomes. A retrospective study of 31 patients with FDCS did not show significant differences in 5-year overall survival (OS) for patients who received adjuvant radiation or neoadjuvant chemotherapy compared with surgery alone ($P = .58$).[4] For patients receiving adjuvant radiation, 30 to 63 Gy was delivered more than 30 to 35 fractions using intensity modulated radiation therapy.[4] However, treatment protocols and results were not stratified by primary tumor location, and only 42% of cases primarily involved the abdomen.[4] Another retrospective study on FDCS showed an association between consolidative adjuvant radiation therapy and improved local control, median progression-free survival, and OS; however, recurrences occurred in 14% of patients.[5] Thus, there remains a lack of data on the role of radiation therapy in FDCS, particularly in the abdomen. Here, we present a patient with retroperitoneal FDCS successfully managed with surgery and adjuvant radiation.

Case Report

A 49-year-old man presented with abdominal discomfort in April 2012 found to be secondary to diverticulitis on computed tomography (CT) scan. He reported full resolution of his complaints after completing a treatment course for diverticulitis, denying night sweats, fever, weight loss, or abdominal discomfort. However, the CT scan incidentally revealed a retroperitoneal mass that was further imaged with magnetic resonance imaging and positron emission tomography (PET)/CT demonstrating an FDG avid 4.1 × 3.5 cm lesion in the celiac axis region. He underwent a gross total resection with regional lymphadenectomy of 2 enlarged lymph nodes on July 31, 2012. Margins were negative and the specimen measured 4.0 cm in diameter. His postoperative course was notable only for delayed wound healing treated with a course of antibiotics.

Microscopic examination revealed a mass composed of loosely aggregated, heterogenous spindle cells interspersed with small lymphocytes and focal fibrosis (Fig 1). Immunohistochemical stains were positive for CD21 (Fig 1 B), D240, and CD35 (weak) but negative for CD1a, CD34, S100, and HHV8, consistent with follicular

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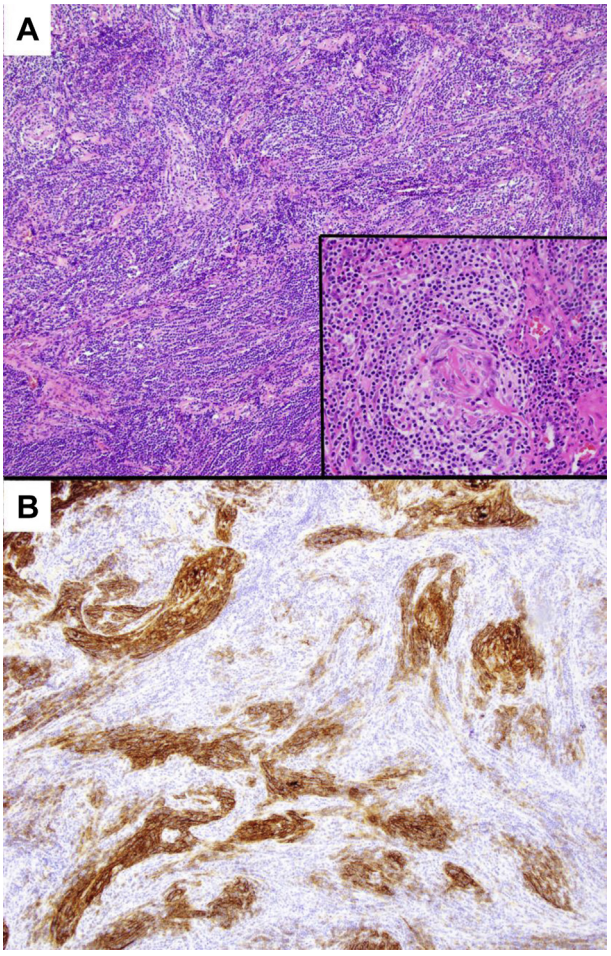

Figure 1 (A) In this photomicrograph, normal lymph node architecture is replaced by subtle fascicles and whorls of spindled cells that have elongated, ovoid nuclei with thin nuclear membranes, vesicular chromatin, and small, distinct nucleoli admixed with small lymphocytes. The fascicular architecture and cell morphology are features of follicular dendritic cell proliferations (hematoxylin and eosin stain, original magnification 100×). The inset displays one of several scattered involuted follicles with a hyalinized blood vessels that exit the follicles radially and with mantle zones displaying concentric ringing of lymphocytes. Such atypical follicular architecture represents Castleman Disease–like changes (hematoxylin and eosin stain, original magnification 200×). (B) A CD21 immunohistochemical stain is positive (brown precipitate) in the spindled cells, consistent with follicular dendritic cell differentiation, and highlights the fascicular pattern of the proliferation (original magnification 100×).

dendritic cell differentiation. A few partly hyalinized foci contained atretic follicles consistent with Castleman disease (CD)–type changes, particularly the hyaline vascular variant (Fig 1 A, inset). The 2 lymph nodes failed to show pathologic abnormalities. When integrating pathology with the clinical and radiographic picture, the best fit was determined to be FDCS likely associated with unifocal CD.

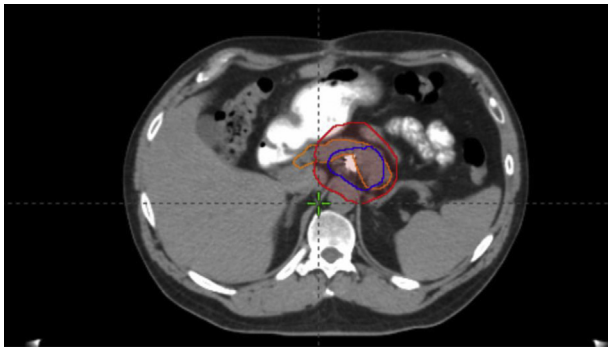

Figure 2 Mapping of the treated lesion based on the patient's preradiation therapy abdominal computed tomography scan. Orange = pancreas; red = planning target volume; blue = gross tumor volume SUV 3.5.

After resection, the patient followed up with hematology-oncology, which led to multidisciplinary discussions. FDCS has been thought to fall along a spectrum from Hodgkin lymphoma to typical sarcoma, although it might more closely resemble low-grade soft tissue sarcomas than lymphoma.[6] A restaging PET/CT and bone marrow biopsy were both negative. Based on literature, however, the patient possessed risk factors for local recurrence including abdominal location and surgical excision alone as primary therapy. Owing to his lack of residual disease and risk factors, hematology-oncology deferred management to radiation oncology.

According to literature, adjuvant radiation improved local control in both lymphoma and sarcoma patients. Based on 2 available case series, the patient was started on a 5.5-week radiation regimen to the preoperative PET-defined gross tumor volume with a 1.5-cm margin superiorly and inferiorly and a 1.0-cm margin radially. This region received 50.4 Gy in 28 fractions using 6 MV photons in a volumetric-modulated arc therapy technique (Fig 2). Dose constraints to organs at risk are shown in Table 1. He received radiation from October 22 to November 30, 2012, nearly 3 months after his excision. He tolerated this without side effects beyond grade 1 diarrhea and grade 1 nausea at the beginning and end of treatment, respectively, per Common Terminology Criteria for Adverse Events.

At 1-month follow-up, his clinical status was returning to baseline. Hematology-oncology opted to observe him given the definitive nature of the radiation. A PET/CT performed 2 months afterward revealed mildly increased uptake (SUV 2.5) in a subcutaneous nodule along the abdominal incision, interpreted as scar tissue. At 6- and 8-month follow-ups, he was back to baseline without weight loss, night sweats, lymphadenopathy, or pain. His Karnofsky Performance Status at these follow-ups was 100%. A repeat PET/CT 9 months afterward was negative for

Table 1 Dose constraints for designated organs at risk

Organ at risk	Volume	Dose limit
Left kidney	100%	≤15 Gy
Left kidney	50%	≤20 Gy
Left kidney	25%	≤25 Gy
Right kidney	100%	≤15 Gy
Right kidney	50%	≤20 Gy
Right kidney	25%	≤25 Gy
Liver	50%	≤30 Gy
Liver	25%	≤45 Gy
Small bowel	50%	≤45 Gy
Spinal cord	100%	≤45 Gy
Stomach	100%	≤55 Gy
Esophagus	100%	≤55 Gy

malignancy. The patient was subsequently lost to follow-up.

Discussion

Here, we report a case of FDCS that was successfully treated with resection and adjuvant radiation. FDCS is a rare malignancy, with only 51 cases described in the English literature from 1986 to 1998.[7] Our patient, a 49-year-old man, fits the observed demographic of FDCS, which has a median age of diagnosis of 47 years old and no sex preference.[8] However, his disease was in the abdomen, whereas FDCS predominantly involves cervical lymph nodes.[9]

Management formerly consisted of definitive surgical excision with or without adjuvant treatment. Monda et al first reported 4 FDCS cases that all presented as painless unilateral cervical adenopathy.[3] Of these cases, 1 was lost to follow-up, and another was successfully managed with a local excision. The other 2 experienced recurrences; one had a successful repeat wide local excision, and the other underwent repeat excisions and 5 rounds of adjuvant chemotherapy only to experience abdominal metastasis. She succumbed to her disease.

Since then, limited progress has been made in elucidating an optimal treatment regimen. Many clinicians have treated FDCS based on recommendations for high-grade soft tissue sarcomas where resection is the cornerstone of management. The literature indicates a 40% risk of recurrence and 28% risk of metastasis, prompting consideration of adjuvant therapy.[8] Fonseca et al performed a review of 51 FDCS cases in the literature. Twelve of the 31 patients who underwent surgical resection alone experienced relapse compared with 2 of the 8 patients who also received radiation therapy; the 6 radiation patients who remained disease-free had a median disease-free survival of 36 months. This raised the idea that adjuvant radiation therapy could decrease recurrence.[7]

Adjuvant chemotherapy has been more controversial. In a case series of 17 patients, 7 patients were treated with adjuvant chemotherapy regimens most commonly featuring CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone).[10] Four experienced progression or recurrence within 2 years.[10] Meanwhile, 2 patients treated with neoadjuvant CHOP experienced >95% tumor response and symptomatic improvement, respectively.[10] Despite limited data, there may be a higher benefit to neoadjuvant systemic therapy. However, definitive diagnosis requires surgical pathology. CHOP is a standard lymphoma regimen, and advanced soft tissue sarcoma regimens such as CYVADIC (cyclophosphamide, vincristine, doxorubicin, dacarbazine) and gemcitabine and docetaxel have also been used.[10-12] Higher intensity regimens may protect against progression, but outcomes with chemotherapy require more systematic comparisons to those without.

Indications for radiation are also controversial. A pooled analysis of FDCS case reports found no significant difference in OS in patients who received adjuvant radiation therapy compared with surgery alone ($P = .474$).[13] However, neoadjuvant radiation therapy has resulted in good outcomes. One patient received 57.5 Gy to the oropharynx before a wide excision with radical neck dissection; they were disease free 4.5 years afterward.[10] There are currently no treatment guidelines by the National Comprehensive Cancer Network. This is further complicated by variables such as tumor size >6 cm, >5 of 10 high-power fields mitotic count, and cellular atypia, which all have prognostic significance and lend a more heterogeneous import to FDCS.[13]

Of the patients with isolated local FDCS who received adjuvant radiation, there seems to be a threshold for effectiveness. One study evaluated 13 FDCS patients who received adjuvant radiation therapy to the resection bed with an additional 1 to 2 cm margin; they received a median dose of 50.4 Gy (range, 35-66 Gy) with significantly improved progression-free survival and OS compared with gross total resection only.[5] Local relapses occurred in 2 patients who had received 39.6 Gy and 45 Gy of radiation.[5] Taken together, these findings imply that higher dosages could increase effectiveness. This mirrors the findings of our patient, who received 50.4 Gy of intensity modulated radiation therapy.

Also, our patient's histopathologic findings underscore a potential link between FDCS and CD.[14] CD is a benign lymphoproliferative disorder involving interleukin 6.[15] It can be classified as either multicentric or unicentric, and the hyaline vascular variant comprises 90% of unicentric CD.[16] Ten percent to 20% of patients with FDCS have been found with the hyaline vascular variant of CD (HVCD), as with our patient.[1] Demographically, however, he does not fit the average CD parameters featuring a female predominance and younger age range.[17]

Since 1986, there have limited cases of FDCS with CD, and the majority were intra-abdominal and involved

HVCD.[8] This is consistent with our patient. Chan et al published the first case report of a patient with FDCS transforming from HVCD. He had initially presented with a nasopharyngeal mass that was biopsied showing HVCD with focal FDC overgrowth.[18] Years later, the mass recurred, and biopsy revealed FDCS in the setting of focal HVCD. After undergoing excision, 3 cycles of adjuvant CHOP, and a nasopharyngectomy, the patient was disease-free at 3-year follow-up.[18] However, this case differs from ours in disease locality, and thus management cannot be directly extrapolated.

Hwang et al described a case of concurrent abdominal CD and FDCS where a patient had a 5-cm peripancreatic lymph node revealed as FDCS in a background of focal residual CD.[8] This was resected and she underwent adjuvant radiation therapy consisting of 45 Gy over 5 weeks with no recurrence at 9 month follow-up. Our patient was similarly diagnosed with abdominal FDCS with features suggestive of CD, and he also underwent 50.4 Gy of adjuvant radiation therapy and was disease-free at 9 months. These cases demonstrate that for intra-abdominal HVCD and FDCS, adjuvant radiation therapy in the range of 45 to 51 Gy has a potential benefit, although the degree is uncertain owing to a lack of controls and loss to follow-up. Radiation therapy is potentially sufficient as the sole adjuvant therapy, which is advantageous because it has fewer side effects compared with chemotherapy. Our patient did not develop toxicities beyond class 1 nausea and vomiting.

In summary, this is a rare case of intra-abdominal FDCS with features of HVCD that was successfully managed with surgical excision and adjuvant radiation therapy. With new cases, studies elucidating the role of radiation therapy are recommended.

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