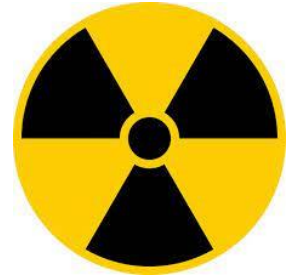




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CLINICAL DATA, PATHOLOGICAL FINDINGS, AND IMAGING FEATURES OF FOLLICULAR DENDRITIC CELL SARCOMA IN THE MEDIASTINUM: CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Follicular dendritic cells sarcoma (FDC sarcoma) are mesenchymal-derived dendritic cells located in B-follicles, where they play a pivotal role in triggering and maintaining B-cell adaptive immune response. It is an uncommon tumor with few reported cases. Using pathological tests, we investigated the computed tomography (CT) appearance, positron emission tomography-computed tomography (PET-CT), and pathological findings in a 43-year-old woman diagnosed with mediastinal FDC sarcoma which usually overlaps with lymphoma. Previous literature reports on FDC sarcoma were reviewed. FDC sarcoma should be considered in asymptomatic patients with mediastinal lymph node lesions with a diameter of more than 1cm and appears as an ill-defined mass with an arborising pattern of necrosis. The complement receptor CD21(+) is an immunohistochemically specific marker for determining the pathological diagnosis of FDC sarcoma. This case report aims to highlight imaging features to facilitate this rare entity's diagnosis and treatment options.

Keywords: Follicular Dendritic Cell Sarcoma; Computed Tomography; Positron Emission Tomography-Computed Tomography; Mediastinum.

Introduction

Follicular dendritic cell sarcoma (FDC sarcoma) is a rare malignancy that originates from follicular

dendritic cells featuring antigen-presenting activities.[1] Although the tumour has been found in both lymph nodes and extra-nodal sites, it is very scarce

in the mediastinum, with approximately 40 cases so far reported in the English literature.[1] Histologically, FDC sarcoma comprises neoplastic follicular dendritic cells and close-combined lymphoid cells.[2] Although FDC sarcoma affects lymphoid tissues, it accounts for less than 1% of all lymphoid neoplasms with an extra-nodal origin. This tumour is an extremely rare malignant neoplasm that mostly occurs in extra-nodal sites (79.4% of cases) and lymph nodes (15.1%); in about 7%-10% of cases, it is associated with hyaline-vascular Castleman disease.[4] The FDC sarcoma was first reported by Monda et al. in 1986. [5] The complement receptors (CD21 and CD35), these two FDC sarcoma markers, were shown to be highly and diffusely positive in tumour cells[1]. However, there have been a few cases described in the literature. This tumour behaves less like a malignant lymphoma and more like a low-grade soft tissue sarcoma. This tumour are often misdiagnosed and confused with others lymph node lesions in clinical practice. This tumour presents with lymph node disease in 31% of patients, extra-nodal disease in 58%, and both nodal and extra-nodal disease in 10%.[2] This report aims to alert radiologists about radiological features of the FDC sarcoma marker by multiple mediastinal lymph nodes lesion with necrosis. The CT features and pathological findings of a case of FDC sarcoma in the mediastinum were described. The finding of this report will improve the accuracy of FDC sarcoma diagnosis.

Patient and Methods:

Patients at our hospital

The Affiliated Hospital of Yan'an University's institutional review board approved this study and the patient's informed consent was obtained. Clinical data and Pathological examination results from the first patients diagnosed with extranodal lymphoid follicles of FDC sarcoma were collected. Tissue sections of FDC sarcoma were obtained and reviewed by a senior histopathologist. Each lesion's CT characteristics, including its location, shape, size, margins, attenuation in the plain and contrast-enhanced CT images, lesion enhancement pattern, and Positron Emission Tomography-Computed Tomography (PET-CT)

features, were reviewed independently by two radiologists with more than ten years of post-training experience.

Image acquisition

CT scan : The patient turned over and held her breath. For the chest CT scans, the GE Health Optima 660 and Lightspeed CT devices were utilised. The following scan parameters were selected: standard lung window level was 530-430 HU, window width was 1400-1600 HU, slice interval was 5 mm, acquisition slice thickness was 0.625 mm, scanning duration was 5 s. The window's width was 300–350 HU, and the mediastinal window level was 35–40 HU. The scanned area stretched from the thoracic cavity's entrance to the posterior costophrenic angle. The image was assessed after scanning to ensure that the inspection was successful and the image quality was adequate for diagnosis.

PET/CT scan: Before the assessment, the patient was instructed to fast for at least 6 hours, and serum glucose levels under 160 mg/dL were verified. The Gemini 64 TF scanner (Philips, The Netherlands) was used for PET/CT scanning 40–60 min after 2-deoxy-2- [(18) F] fluoro-D-glucose ([(18) F] FDG) intravenous delivery (3.7–4.4 MBq/kg). Prior to PET scanning, multi-detector spiral CT images were acquired with an acquisition time of 1.5 minutes/bed position while shallow breathing using a Philips Gemini TF 16 PET/CT scanner. The vertex to the upper thighs made up the scan field. A technique for ordered-subset expectation smaximisation was used to recover PET data. Attenuation correction and anatomic localisation were done using CT data. SYNTEGRA software was used to display co-registered images (Philips).

Results from PET/CT and CT were interpreted by two skilled radiologists and nuclear medicine specialists in a blinded manner. By identifying a region of interest (ROI) around the primary tumour on the transaxial slices, standardised uptake value (SUV)_{max} and its average SUV_{avg} were calculated using the equation tumour activity concentration/injected dose/body weight. Primary tumour SUV_{max} divided by the liver

SUV_{max} and the aorta blood pool SUV_{max}, respectively, were used to define SUV_{T/L} and SUV_{T/A}. Regions that have an SUV difference of greater than 0.5 or 1.0 between the predicted and the actual PET/CT image were considered abnormal.

Literature review

A literature search in the English language was done to find case reports and case series of FDC sarcoma. PubMed, MEDLINE, Google Scholar, and the Cochrane Library were all searched between 2005 and 2022. The terms mediastinum dendritic cell sarcoma, lymph node cell sarcoma, and lymph node dendritic cell sarcoma were used as keywords. If relevant, the case report data were incorporated and examined. Each case report included the first author, publication year, patient number, patient's age, gender, symptoms, size, side, necrosis, and calcification.

Results:

Clinical data

A 43-year-old woman with mediastinum lymph node enlargement was diagnosed with mediastinal FDC sarcoma after ten days of back pain and shortness of breath. Physical signs were within normal limits, and no other contributing factors were identified. The tumour cells markers were immunoreactive for CD21(+), LCA (+), Vim (+), CD68(+), Ki67(+50%), and CD 163(+). From 2005 to 2022, 24 FDC sarcoma cases were reported in English, each with comprehensive details (Table 1). This research documented and examined 25 FDC sarcoma cases, including the one described above. Table -1 shows previously published literature for FDC sarcoma patients. The patient's average age was 43.6 years (range: 18-78 years, with 10 men and 15 women).

CT findings

Multiple ill-defined edge nodular masses in the superior anterior mediastinum were visible on unenhanced CT images of the chest. The largest one measured 3.9 × 4.0 × 4.4 cm on CT and showed heterogeneous soft-tissue attenuation with central hypo-dense lesion (Fig 1A). The size of the masses

was measured on axial, coronal or sagittal views then the averages was taken. The masses showed peripherally ring-like enhanced solid and central low-dense necrotic components. For administration of Omnipaque 300, using GE Healthcare with a dual-head pump injector, 80mL were injected intravenously at a flow rate of 3.0 mL/s (Fig 1B). PET-CT found excessive consumption of radioactivity in the mediastinum lymph nodes (Fig 1C).

Table 1 summarises the CT results of 24 cases. Ten (10) lesions were found in the mediastinum (41.66%), eleven (11) in the abdomen (45.83%), two (2) in the neck (8.32%), and one (1) in the axilla (4.16%). In 24 confirmed cases, the lesions' average size was 7.8 cm (range: 4.2 to 15 cm). The tumours were ill-defined round and ovoid masses with or without internal attenuation. The lesions' inner contents showed markedly heterogeneous attenuation due to necrosis on contrast-enhanced images, as observed in 58.33 % (14/24) of the cases. Calcification was found in some of the patients (33.33 %; 8/24).

Pathological findings

The storiform pattern and fascicles of the tumour's spindle-shaped cells were observed under a microscope. Eosinophilic cytoplasm was found in tumour cells. The malignant cells showed extensive nuclear pleomorphism. Around the tumour cells, lymphocytic infiltration was also seen (Fig. D&E). Rarely mitotic figures, necrosis, and cellular atypia were seen. To identify the patient's lesion prior to surgery, an ultrasound-guided fine-needle biopsy was carried out on the nodule with the largest diameter. Histopathology revealed a small round cell neoplasm, which was thought to be lymphoma. LCA (+), CD21 (+), Ki-67 (+80%) were immunohistochemically positive, while CK (-), CD20(-), CD30(-), PC (-), CD138(-), CD7 (-), PAX-5(-), CD43(-), MPO were negative. Multiple nodules fused into an irregular–white mass in the anterior mediastinum were discovered intraoperatively. Due to the mass's adhesion to the left brachiocephalic vein, pericardium, superior vena cava, and aorta, complete resection was difficult. The resected specimens' post-operative

histopathology examination revealed mature lymphocytes and spindle cells (Fig 1D). Cells were highly positive for CD21(+), LCA (+), Vim (+), CD68(+), Ki67(+50%), CD 163(+), (Fig 1E), but negative for S100(-), HMB45(-), SMA (-), CD 35(-), CK19(-), CD30 (-), ALK (-), CK7 (-), CK (-), EMA (-), CD3 (-), CD20 (-), TDT (-), CD5 (-), and CD117. These observations aided in the identification of FDC sarcoma. In the published literature, immunohistochemistry was used on samples from 20 patients, and the common marker was CD21(+).

Treatments and prognosis

After surgery, our case study patient received routine post-operative chemotherapy, including cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) at a standard dose, as well as daily clinical follow-up. A post-operative contrasted CT scan ensures the anterior mediastinal lymph nodes have been entirely removed. FDC sarcoma appeared to have distal metastasis in bilateral supraclavicular and axillary lymph nodes (Fig-1F). Then the antineoplastic protocol was modified to bevacizumab, topotecan, ifosfamide, and carboplatin chemotherapy for three circles and DT50Gy/25 times radiotherapy, which resulted in partial remission.

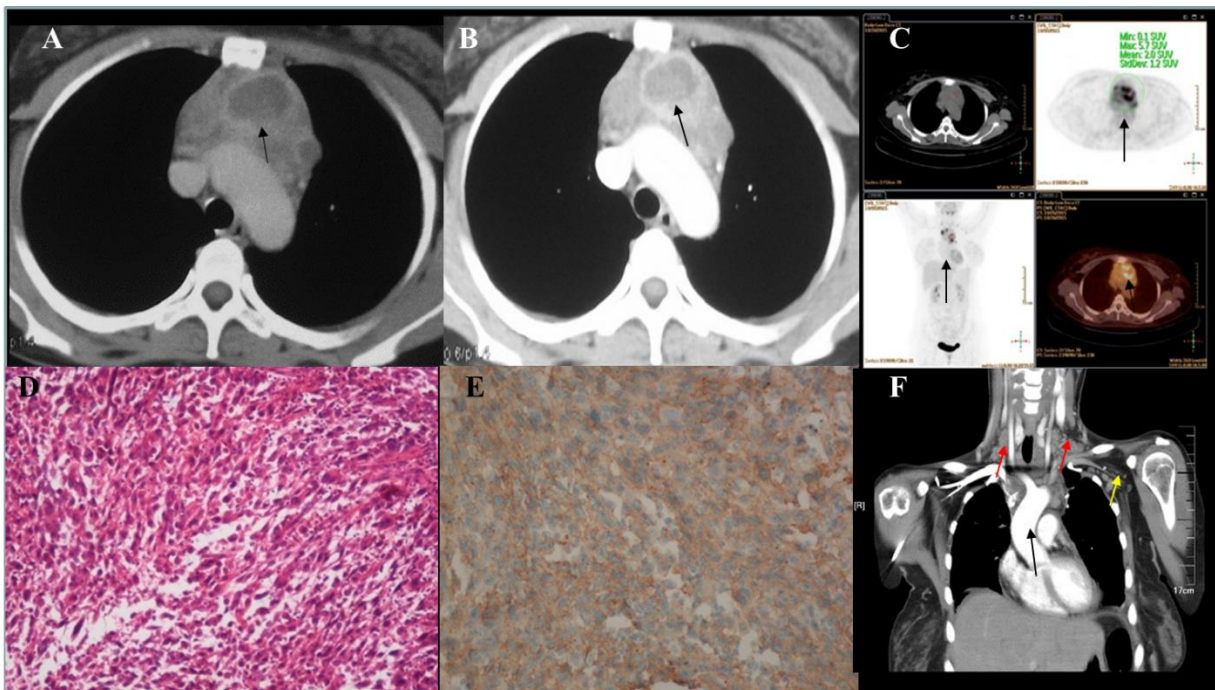


Figure 1: Asymptomatic mediastinal follicular dendritic cell sarcoma in a 43-year-old woman. (A): Unenhanced CT image of thorax revealing ill-defined anterior mediastinal mass (black arrow). (B): Contrast-enhanced CT image showing marked heterogeneous enhancement of the mass (black arrow) with a sarborising pattern of necrosis. (C): Positron emission tomography-computed tomography (PET-CT) demonstrated high levels of radioactivity in the mediastinum (black arrows) with a minimum of 0.1 SUV, maximum of 5.7 SUV, mean of 2.5 SUV, and standard deviation of 1.2 SUV. (D): Pathology assessment showed mature-appearing lymphocytes and spindle cells that were arranged (H & E staining, original magnification, $\times 200$). (E): Immunohistochemistry assessment showed mature-appearing lymphocytes and spindle cells that were arranged (original magnifications $\times 200$). (F): post-operative contrast enhances CT scan confirming the complete excision of the anterior mediastinal (black arrow), bilateral supraclavicular lymph nodes (blue arrows), axillary lymph nodes (yellow arrow) were enlarged follicular dendritic cell sarcoma

Table 1: Summarised data of 23 Cases of follicular dendritic cell sarcoma in the literature

No.	Authors	Years	PN	Sex	Age(y)	Main complain	Size (CM)	Location	Presence of calcification or necrosis
1.	Tonath A. Leipsicet al.	2005	1	M	43	intermittent chest pain	13×10×6	mediastinum	calcifications
2.	Lagaruet al.	2007	1	M	30	Dyspnea	11 ×11.5	mediastinum	necrosis
3.	Kiryu et al.	2009	3	2F 1M	56& 60& 78	Asymptomatic	4 ×2.3 8× 5.0& -	spleen	necrosis
4.	Manil subesingheet al.	2011	1	F	52	weight loss	-	mediastinum	calcifications
5.	Paulo N martin et al.	2011	1	F	53	abdominal pain& fever	-	liver	necrosis
6.	Qiulong-hua et al.	2011	2	M F	47& 28	chest pain &malaise	7.5×4& 7× 10	mediastinum &lesser curvature	necrosis
7.	Jung-soo et al.	2012	1	M	31	left Para pharyngeal swelling	4.7× 4.5×1.9	left neck	calcifications
8.	Doone Bennett et al.	2012	1	F	61	Dyspnea	6.8× 5.3	left lung	calcifications
9.	Stefen martin et al.	2013	1	M	76	Dyspnea	8× 10× 10	mediastinum	calcifications
10.	Rizzotto et al.	2014	1	M	57	Asymptomatic	6.4 ×4.4	mediastinum	necrosis
11.	G. liberaleet al.	2014	1	F	44	Asymptomatic	8.5× 5.5	subhepatic	necrosis
12.	Kirtibushan	2014	1	M	37	low-grade fever &weight loss	8.9× 8.5× 8. o	mediastinum	necrosis
13.	Suwendparkait et al.	2015	3	3F	24 &50& 27	1. diffuse abdominal pain 2. hemoptysis 3. asymptomatic	6.4× 5.3 ×3& 5.5× 4.3× 4.0& 4.2 ×3.4× 2	1. mesenteric 2. Cervical 3. pelvis	necrosis
14.	Yuan ma et al.	2015	2	M F	24& 24	intermittent pain &65 days of delayed menstruation, respectively	2.1× 3& 15× 15× 10	axilla & lesser curvature	necrosis& calcification
15.	Ryo Miyoshi et al.	2016	1	F	18	Asymptomatic	8.0×6.5×4.0	posterior mediastinum	necrosis& calcification
16.	AparnaMullangath Prakasan el al.	2016	1	M	39	Skin vesicles over the left forearm voice change & weight loss.	6 ×3.8	anterior& middle mediastinum	not mention
17.	Tao Lu	2019	1	F	49	Repeated ptosis of her eyelids, oral ulcers, and erosions	6 × 5	Pancreatic tail	well-defined round solid mass with central necrosis
18	Ting Zhang et al.	2020	1	F	48	Asymptomatic	5.7_4.2	Thyroid	Heterogeneously enhanced mass (necrosis)

Discussion:

Pathogenesis and clinical presentation

An FDC sarcoma is a rare tumour that develops from both primary and secondary lymphoid follicles. The Follicular Dendritic cells are crucial to the immune system's response since they act as antigen-presenting cells for the B-cell compartment.[1] Immunohistochemical characteristics that respond positively in CD21, CD23, and CD35 markers were employed to detect the tumour.[5,8,9] The majority of those affected were young to middle-aged people, with an average age of 43.8 years and a range of 14 to 76 years. The tumour may have no sex predilection.[10,11] A coalescent nodal mass is the most typical symptom, and the head and neck are the most often affected areas by extra-nodal diseases. The liver, gastrointestinal tract, spleen, and oral cavity, among other locations, have all been reported to have FDC sarcoma.[10]

Imaging features and differential diagnosis

Sizes of FDC sarcoma observed during our study measured 3.9, 4.0 and 4.4 cm in longitudinal or transverse diameters. Several sizes of FDC sarcoma cases have been reported in the literature.[11] The average size of the 24 cases reported was 6.7 cm (range: 6 to 13 cm), with eight of the 24 lesions measuring between 6 and 15 cm in the abdomen. Two of them originated from cervical lymph nodes with a diameter of less than 6 cm, one from the axilla with a diameter of 6.8 cm, and two from the pelvis with a diameter of 4 cm. The outline or margin of tumours observed in this study were generally well-circumscribed. The tumour showed markedly heterogeneous attenuation, similar to our subject's mediastinal FDC sarcoma. In the literature, 16 of the 24 intra-abdominal cases (66.66%) had areas of gross intra-lesion necrosis or haemorrhage.[6] According to the authors, the CT

findings of an FDC sarcoma of the abdomen were described as a well-enhanced tumor with heterogeneous high-signal intensity mass on the T2 weighted image.[12] On the other hand, since necrosis is common in large tumours, extensive necrosis in the lesions may be related to tumour size.[13] Only a few research studies have focused on the vascularity of FDC sarcomas.[14] In our study, the hypervascularity was discovered after surgery, and after intravascular contrast media injection, a considerable demarcation was visible. These results might contradict with previous report that all FDC sarcomas are hypovascular.[15] In our study, the CT findings showed multiple enhanced lesions with a spattern of necrosis that was very similar to lymphoma, as reported previously.[7] However, a subset of FDC sarcomas has grown in or close to lymphoma foci. [15,16] As a result, radiologically distinguishing FDC sarcoma from lymphoma in the mediastinum may be difficult, necessitating further histopathology study. The mediastinal lymph node-involved FDC sarcoma appeared as a multiple ill-defined masses with necrosis. These characteristics can help differentiate FDC sarcomas from mediastinal metastatic carcinoma or lymphoma, which often have heterogeneous lesion attenuation due to central necrosis. Another previously mentioned mediastinal lymph nodes lesions in tuberculosis had calcification.[17] Calcification may allow distinguishing FDC sarcoma from more common Epstein-Barr virus-related mediastinal tumours. [18] Additionally, in the differential diagnosis for the CT findings in our patient, lymphoma, lymph node tuberculosis, and metastatic lymphadenopathy are all usual causes of bulky mediastinal masses that should be investigated. Some studies claimed that FDC sarcoma has radiological characteristics that are similar to lymphoma.[19] This patient's first diagnosis was lymphoma. Necrosis, on the other hand, is more common in FDC sarcoma than in lymphoma or distant metastasis.[20] Positivity for CD21, CD23, and CD35 is utilised in immunohistochemistry to make a differential diagnosis. [21] Three primary criteria and two minor criteria are used to diagnose FDC sarcoma. FDC sarcoma is defined in a variety of forms. (i) A ill-

defined mediastinal lymph node mass should be visible on a plain CT scan. (ii) The necrosis enhancement pattern on a contrast-enhanced CT image is heterogeneous (iii). CD21, CD23, or CD35 immunohistochemically positive. Minor criteria for FDC sarcoma include (i) asymptomatic early-stage presentation (unless there are pressure signs of dyspnea or dysphagia) and (ii) elevated radioactivity in the lesion on (PET-CT).

Treatment and outcome

The management of FDC sarcoma must take diagnosis accuracy and reliability into account. Complete surgical excision is the main treatment option for FDC sarcoma,[22] and adjuvant therapy (chemotherapy or radiation), which greatly improves survival rates.[23] Poor prognosis signs of a high mitotic activity include intra-lesion necrosis, a mass more than 6 cm, intra-abdominal lesions, and a high proliferative lesion.[3]

Conclusion

FDC sarcoma is not very common. The clinical and radiological characteristics of FDC sarcoma are not specific, and the lesions typically have ill-defined margins and fluctuate in size, according to our findings. This is the first instance of a tiny multiple FDC sarcoma being found in a asymptomatic patient with necrosis. When determining the differential diagnosis of mediastinal lymphoid tissue tumours, FDC sarcoma should be considered, especially if the diagnosis is ambiguous.

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Disclosure of Conflict of Interest

None

Authors' contributions. Conceptualization & writing the original draft, Yifan Wu, Yang Yang. Review: Abdoulaye Issotina Zibrila. Validation: Mazen Musa, Review & editing: Zhengxiang Zhang, Supervision and final validation: Mustafa Salimeen.

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