Thoracic follicular dendritic cell sarcoma - an outlandish presentation of a rare tumour with review of literature

Vinay V[1], Saraansh Bansal[2], Pallavi Purwar[2], Ravindra Kumar Dewan[2], Paras Verma[1], Shalini Mullick[3], Mallika Dixit[4], B Rama Phanindra[2], Kanishk Siddhartha[2]

[1]Department of Tuberculosis and Respiratory Diseases, National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi; [2]Department of Thoracic Surgery, National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi; [3]Department of Pathology, National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi; [4]Department of Pathology, Core Diagnostics-Gurgaon, Haryana, India

Correspondence: Dr Vinay V, Department of Tuberculosis and Respiratory Diseases, National Institute of Tuberculosis and Respiratory Diseases (NITRD), Room no 29, 3rd floor, Doctors Quarters, Sri Aurobindo Marg (Near Qutab Minar), New Delhi 110030, India.
Mobile: +91.9740451097 / +91.7019508857.
E-mail: docvinayv@gmail.com

Key words: follicular dendritic cell sarcoma, primary pulmonary, endobronchial spread, pneumonectomy, diagnostic dilemma.

Contributions: all authors, study concept, definition of intellectual content; VV, BS, PP, RKD, PV, literature research; VV, BS, PP, PV, SM, MD, manuscript preparation; VV, BS, PP, SM, MD, BRP, KS, manuscript editing; All the authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Availability of data and materials: all data underlying the findings are fully available.

Ethics approval and consent to participate: no Ethical Committee approval was required for this Case Report by the Department, because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patient included in this study.

Consent for publication: patient has given the written informed consent to use his personal data for the publication of this case report and any accompanying images.

Acknowledgements: we would like to extend our heartfelt gratitude to the team of CORE DIAGNOSTICS, New Delhi and Gurgaon for assisting in diagnosing this case.

Received: 25 June 2022.
Accepted: 8 September 2022.
Early view: 20 September 2022.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Licensee PAGEPress, Italy
Monaldi Archives for Chest Disease 2023; 93:2360
doi: 10.4081/monaldi.2022.2360

Abstract

Follicular dendritic cell sarcoma is a rare low grade malignant neoplasm that arises from follicular dendritic cells in lymphoid tissue germinal centres and accounts for 0.4% of all soft tissue sarcomas. It is extremely rare to have pulmonary follicular dendritic cell sarcoma with endobronchial extension and as an anterior mediastinal mass with mediastinal lymph node involvement. We present the case of a 34-year-old male non-smoker who had been experiencing chest pain for three months. A lobulated left peri-hilar mass with endobronchial spread into the left main bronchus and mediastinal lymphadenopathy was identified on chest CT. The bronchoscope-guided cryobiopsy of the endobronchial mass was inconclusive. After a thorough multidisciplinary discussion, the patient underwent left sided pneumonectomy, mediastinal mass resection, and systematic lymph node dissection. Histologic examination using immunohistochemistry revealed follicular dendritic cell sarcoma.

Introduction

Follicular dendritic cell sarcoma (FDCS) is a rare, low-grade malignancy derived from follicular dendritic cells (FDC) that serve as accessory cells to the lymphoid system. It was initially described in 1986 by Monda *et al*. [1]. Primary and secondary lymphoid follicle germinal centres contain FDC, which are responsible for presenting antigens to B cells in order to facilitate their maturation [2]. FDCS has no gender predisposition and occurs commonly in adults with unclear pathogenesis. It can occur in both nodal and extra-nodal sites containing FDC [3]. Because of its rarity, diagnostic challenges and misdiagnosis, it is often not considered as a differential diagnosis of a spindle cell neoplasm. There's no well-designed treatment for this rare tumour and the role of adjuvant therapy remains questionable. Here, we report a rare case of thoracic FDCS with lung involvement and endobronchial extension, a separate anterior mediastinal mass and mediastinal lymphadenopathy successfully treated by pneu-

monectomy with anterior mediastinal mass resection and mediastinal lymph node dissection.

Case Report

A 34-year-old, previously healthy, non-smoker male presented with complaints of chest pain for 3 months. He denied having any social or occupational risk factors for drug abuse or HIV. His physical examination revealed that he was afebrile, that his pulse rate, blood pressure and respiratory rate were all normal, and that he had no skin lesions or palpable lymphadenopathy. When the respiratory system was examined, decreased movements of the left hemithorax was observed, which was later confirmed by palpation. Trachea was central in position confirmed by palpation. The tactile vocal fremitus was decreased on left side of the chest. There was dullness on percussion of left infrascapular and interscapular region. Air entry was decreased on the left hemithorax over all the areas. Right hemithorax was normal on examination. Rest of the systemic examination was normal. Routine blood investigations were within normal limits and HIV antibody testing was negative. Chest X-ray revealed a left hilar mass (Figure 1A). CECT-thorax delineated a lobulated left peri-hilar mass (7.2 cm × 7.0 cm) with endobronchial spread into left main bronchus (Figure 1B). No significant abnormality was found on abdominal USG and electrocardiogram (ECG). Bronchoscopy revealed an endobronchial mass occluding the left main bronchus, cryobiopsy of the mass was inconclusive. A rigid bronchoscope-guided biopsy of the mass revealed pseudoinflammatory changes with no evidence of malignancy.

Whole-body positron emission tomography-computed tomography (PET-CT) was done to assess staging and resectability status. It showed a dense FDG avid large heterogeneously enhancing mass with internal necrosis in the left perihilar region measuring 7.4x7.2x8.4 cm (SUVmax 9.0) with endobronchial spread into left main bronchus and loss of aeration in left upper and lower lobe. FDG avid heterogeneously enhancing lymph nodes were noted in aorto-pulmonary window with SUVmax of 5.3 (Figure 1 C,D). After discussion with multidisciplinary team (MDD), it was decided to perform surgical resection.

After taking a written informed consent and pre-anaesthetic clearance, left pneumonectomy with systematic lymph node dissection was planned. A standard fourth intercostal space thoracotomy was performed. Intra-operatively, there was a large left sided mass involving the left main bronchus (Figure 2A) and the parenchyma with enlarged aorto-pulmonary window lymph nodes, and a separate anterior mediastinal mass (Figure 2B). The hilar dissection was unusually challenging owing to the large mass and inelasticity of the remaining lung with dense hilar adhesions. Left sided pulmonary artery and left superior and inferior pulmonary veins were divided using vascular staplers. After ensuring an adequate margin, the left main bronchus was divided using a bronchial

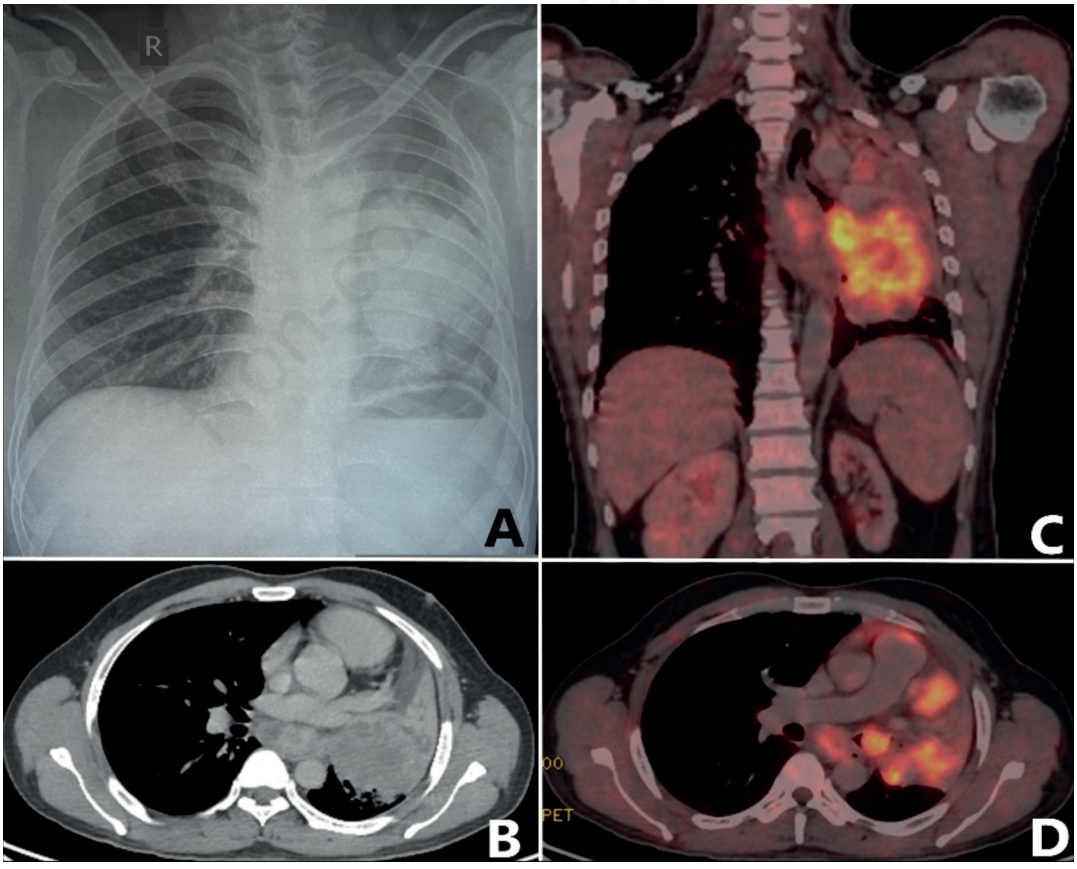

Figure 1. A) Chest X-ray (PA view). B) CT-thorax (axial view), revealing a lobulated left peri-hilar mass. C, Coronal view. D) Axial view PET-CT showing a dense FDG avid large heterogeneously enhancing mass in the left perihilar region with endobronchial spread into left main bronchus.

stapler and left pneumonectomy with extensive mediastinal lymph node dissection along with resection of the anterior mediastinal mass was performed. The intra-operative blood loss was approximately 700 ml and there were no post-operative complications. The patient was discharged on the 10th post-operative day.

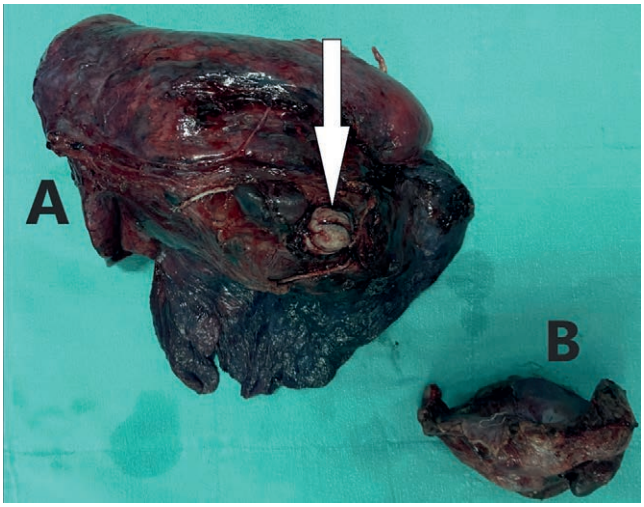

Figure 2. Left pneumectomy specimen (A) showing left lung hilar surface with mass protruding through the left main bronchus (white arrow) and anterior mediastinal mass (B).

A detailed histopathological analysis of the specimen was conducted (Figure 3). Grossly, there was a polypoidal nodular mass in the left main bronchus measuring 11 cm × 8 cm × 6 cm in size involving the lung 2 cm away from the pleural surface. The cut surface was grey and hard with focal areas of congestion. Lymph node measuring 2.5 cm × 1.3 cm × 1 cm was identified and the anterior mediastinal mass measured 7.5 cm x 7 cm x 5.5 cm. Cut surface of lymph node, lung and mediastinal mass was firm and greyish in colour. Microscopically, both the masses (lung and mediastinal) and resected lymph nodes had a similar histopathology; the tumour showed vaguely nodular architecture arranged in short fascicles, whorls and storiform patterns comprising of oval to spindle cells with dispersed nuclear chromatin and small nucleoli. Admixed, a few multinucleated and binucleated cells, lymphocytes, plasma cells and eosinophils were seen. Mitosis of 1-3/10 high-power field was seen. Immunohistochemical staining showed expression of CD21 (Figure 4A), D2-40 (Figure 4B) and SMA in the spindle tumour cells, which strongly supported the diagnosis of FDCS. CD34 (Figure 4D), CK, ALK, ERG, SS18, STAT6, HMB-45, claudin-4, TdT, CD45, CD30, Cd20, CD3, CD23, PAX5, EBV, CD15, CD1a, S-100, and desmin were negative. H3K27me3 was retained, thereby excluding the differential diagnosis of spindle cell neoplasms of vascular, neural, myogenic origin and Hodgkin's lymphoma. In addition, Ki-67 index was ~30% (Figure 4C) in the highest proliferating areas. Hence, a diagnosis of follicular dendritic cell sarcoma was made.

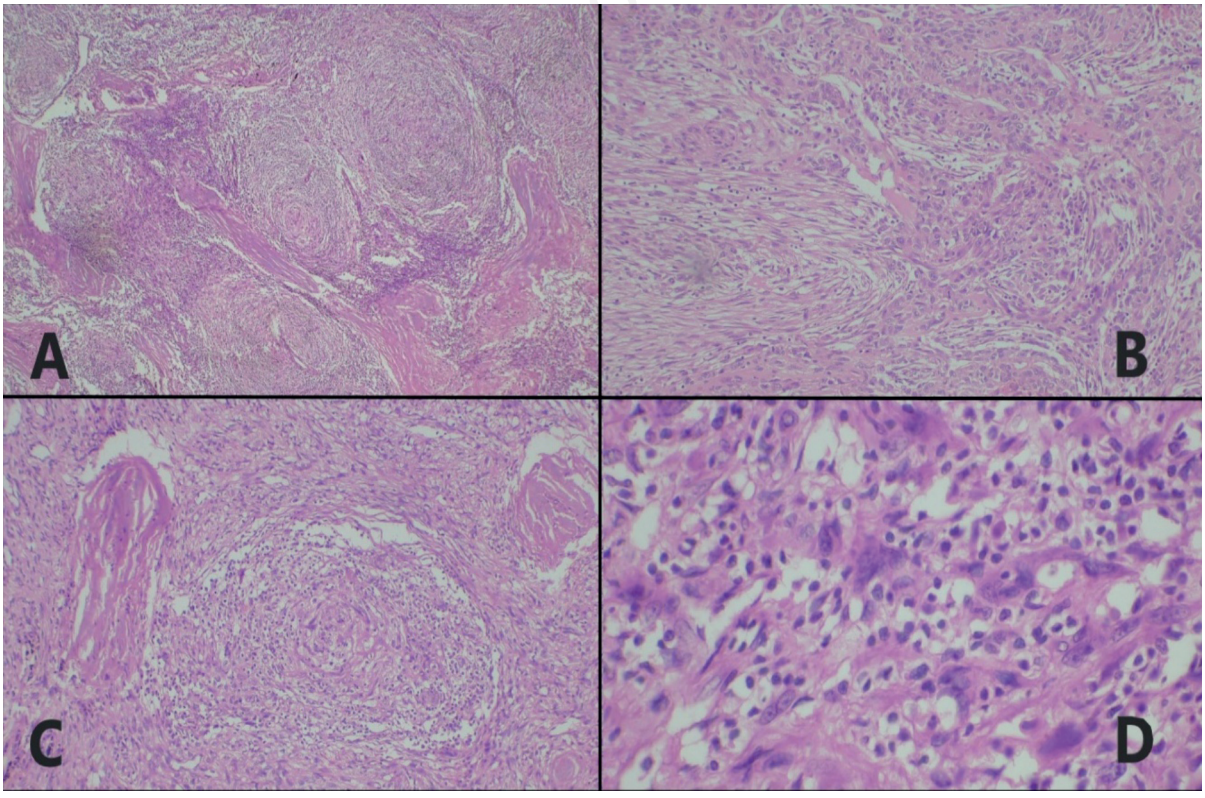

Figure 3. Histopathological examination of the specimen showing cells having a whorled architecture consisting elongated to spindle cells with eosinophilic nuclei admixed with lymphocytes, plasma cells and eosinophils; A) 4x; B) 10x; C) 40x. The spindle cells are arranged in disordered bundles and cytoplasm of spindle cells are pale or eosinophilic nuclei with moderate cytoplasmic cells arranged in fascicles; D) 100x.

Discussion

FDC are mesenchymal-derived cells found in the germinal centre of lymph nodes that are primarily involved in modulating the immune response via antigen presentation, and proliferation and differentiation of B-cells. Follicular dendritic cell sarcoma (FDCS), Indeterminate dendritic cell sarcoma (INDCS), Fibroblastic reticular cell tumour (FRCT), and Disseminated juvenile xanthogranuloma (DJX) are all histogenetically derived from cells of the stroma or mesenchyme. FDCS are low-grade malignancy derived from follicular dendritic cells that usually occurs sporadically [4]. It is typically seen in middle-aged adults presenting in fifth decade of life (median age=49 years; range=8-90) with no gender predilection. Most commonly, FDCS affects the extranodal lymph nodes sites (79.4%) such as liver, spleen and GI tract. Nodal involvement is seen around 15% of cases and 5.5% are with both nodal and extranodal involvement. It typically appears as a slow-growing mass, asymptomatic or painful, accompanied by systemic symptoms such as fever, malaise and weight loss. A variant of FDCS is seen with EBV infection of the tumour cells known as inflammatory pseudotumor (IPT) which is characterized by peculiar features like female predilection, with liver or spleen involvement, and frequent systemic symptoms. FDCS is also seen in association with few conditions like paraneoplastic pemphigus, myasthenia gravis, Castleman disease hyaline-vascular subtype (HV-CD), and epithelial or melanocytic malignant neoplasms [3].

Microscopically, a wide range of architectural patterns, such as whorled, storiform, fascicular and diffuse are seen in FDCS. FDC that are neoplastic usually look spindle shaped, oval or epithelioid, with mild to moderate atypia. Neoplastic FDC retains its normal nuclear structure; however, nuclear pseudo-inclusions can be seen, and its cytoplasm is highly eosinophilic. Tumours are densely cellular or may be dissociated by fibrovascular, myxoid, or hyaline stroma. In most of the cases, small lymphocytes are interspersed between tumour cells and are variably composed of B or T-cells that may express cognate CXCR5 receptor of CXCL13. The most reliable form of diagnosis for dendritic cell and histiocytic neoplasms remains immunohistochemistry. Tumour cells are variably positive for CD21, CD23, and CD35, while podoplanin, clusterin, and CXCL13 are more consistently expressed and show higher specificity in the differential diagnosis of tumours considered to mimic FDCS [5]. The wide distribution of FDCS and its morphological heterogeneity make it possibly difficult to differentiate it from various types of tumours. FDCS must be distinguished from interdigitated dendritic cell sarcoma, histiocytic sarcoma, spindle cell thymoma, metastatic melanoma, Inflammatory myofibroblastic tumour and pleomorphic sarcoma [6].

The neoplastic origin of FDCS is supported by the alterations on genes belonging to the NF-κB regulatory pathway, including loss or missense mutations of NFKBIA, CYLD, TRAF3, SOCS3 and TNFAIP3 and five different translocations leading to fusion proteins were also identified that includes TYK2-ATPAF2, MAP3K1- GCOM1, NTRK1-PDIA3, BPTF-WDR72 and HDGRFP3-SHC4 [7]. Mutations in cell-cycle regulators have been observed in studies suggesting a tumour suppressor-driven biology seen in oncosuppressor genes *CDKN2A* (most commonly affected gene), RB1, TP53, MDM2 and CDK4. PDGFRB N666S mutation is notably seen in HV-CD. FDCS lacks mutations of genes such as KRAS, NRAS and MAP2K1. However,

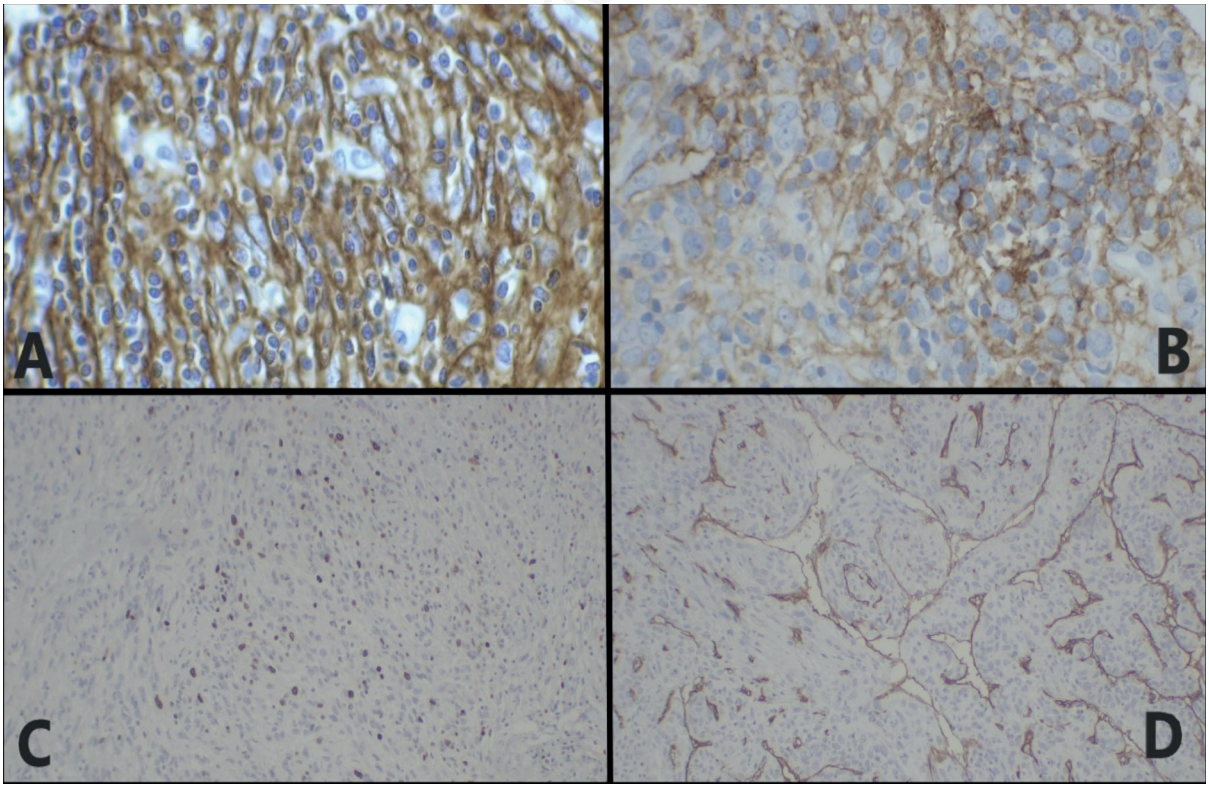

Figure 4. Immunohistochemistry showing positivity to CD21 (A), D2-40 (B), Ki-67 (C), and negative for CD-34 (D).

Programmed Cell Death Ligand-1 (PD-L1) has been detected in the majority of cases with a low mutational burden (<6 mutations/megabase) [3].

No specific Guidelines are currently available for FDCS but different approaches like surgery, radiotherapy, chemotherapy, and tyrosine kinase inhibitors have been tried. FDCS is mainly treated with surgery which remains to be gold standard, and systemic therapy plays an uncertain role. Kinase inhibitors have been tried in few cases that includes mTOR inhibitor (sirolimus and ridaforolimus), pazopanib, sorafenib and sunitinib [3] FDCS is associated with a poor prognosis when it has prominent nuclear atypia or pleomorphism, a size ≥6 cm, ≥5 mitoses/10 high-power fields or presence of coagulative necrosis [8]. The main sites of metastases are lung, liver, lymph nodes and bones [3].

A 2-year survival rate of 82% and 80% is reported for early localized and locally advanced tumours respectively, while a 42% survival rate is reported for metastatic diseases [9]. One-third of cases will have local recurrence or distant metastasis. Thoracic FDCS was found to have a median and 5-year recurrence-free survival post-surgery of about 4.41 years and 47% respectively. The 5-year overall survival rate for patients with localized disease was 55%, compared with 38% for those with metastatic disease [10].

In our case, pneumonectomy was performed with anterior mediastinal mass resection and mediastinal lymph node dissection. Post-surgery, patient was referred for radiotherapy and advised to follow-up every 3 monthly for 2 years.

Conclusions

FDCS is an extremely rare tumour with an indolent course. Due to its similar histopathology to other dendritic cell-derived tumors, it is difficult to diagnose. It mandates IHC for an appropriate diagnosis. Early surgical intervention is essential to achieve a complete clearance of the tumour that might preserve the remaining lung. FDCS should be kept as a differential diagnosis in a spindle cell tumour of the lung.

References

1. 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;122:562–72.
2. Kranich J, Krautler NJ. How follicular dendritic cells shape the B-cell antigenome. Front Immunol 2016;7:225.
3. Facchetti F, Simbeni M, Lorenzi L. Follicular dendritic cell sarcoma. Pathologica 2021;113:316–29.
4. Dalia S, Shao H, Sagatys E, et al. Dendritic cell and histiocytic neoplasms: Biology, diagnosis, and treatment. Cancer Control 2014;21:290–300.
5. Facchetti F, Lorenzi L. Follicular dendritic cells and related sarcoma. Semin Diagno Pathol 2016;33:262–76.
6. Pathology Outlines [Internet]. Follicular dendritic cell sarcoma (FDCS). Accessed: 2022 Feb 18. Available from: https://www.pathologyoutlines.com/topic/lymphnodesFDCsarcoma.html
7. Massoth LR, Hung YP, Ferry JA, et al. Histiocytic and dendritic cell sarcomas of hematopoietic origin share targetable genomic alterations distinct from follicular dendritic cell sarcoma. Oncologist 2021;26:e1263–72.
8. Chen T, Gopal P. Follicular dendritic cell sarcoma. Arch Pathol Lab Med 2017;141:596–9.
9. Saygin C, Uzunaslan D, Ozguroglu M, et al. Dendritic cell sarcoma: A pooled analysis including 462 cases with presentation of our case series. Crit Rev Oncol Hematol 2013;88:253-71.
10. Gounder M, Desai V, Kuk D, et al. 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.