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A Rare Case Report of Histiocytic Sarcoma: Diagnostic Challenges and Management

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ABSTRACT

Histiocytic sarcoma (HS) constitutes a rare neoplasm with marked aggressiveness that often mimics Hodgkin's lymphoma or other neoplasms, creating significant diagnostic challenges. The diagnostic approach in this case included chest computed tomography, transthoracic biopsy, and video-assisted thoracoscopic surgery (VATS) for tissue sampling, followed by histopathology and immunohistochemistry. A 22-year-old female presented with persistent right back pain; imaging revealed a posterior lung mass, and initial biopsy suggested Hodgkin's lymphoma. This case illustrates the limitations of small biopsies, the critical role of VATS in securing adequate specimens, and the necessity of immunohistochemistry for diagnostic accuracy. Early and precise identification of HS is essential to guide management of this rare, aggressive tumor and to improve patient outcomes, underscoring the importance of multidisciplinary collaboration and advanced diagnostic tools.

Keywords: Histiocytic sarcoma; video-assisted thoracoscopic surgery; immunohistochemistry

Introduction

Histiocytic sarcoma (HS) is an unusual and aggressive tumor of histiocytic origin, with diagnosis often complicated by overlapping features with other malignancies.¹ In the 2016 revision of the World Health Organization (WHO) classification, HS is categorized as part of the macrophage-dendritic cell lineage, alongside other histiocytoses and dendritic cell tumors.³ The disease can manifest in several organs, with predilection for lymph nodes, skin, soft tissues, the gastrointestinal tract, and the central nervous system. However, its primary manifestation in the lungs is exceedingly rare.⁴

Due to its rarity and overlapping histopathological features with other malignancies, HS is often misdiagnosed, particularly as Hodgkin's lymphoma or other hematologic and non-hematologic malignancies.¹ Histologically, HS typically exhibits large, round or oval cells with abundant eosinophilic cytoplasm, oval or irregular nuclei, vesicular chromatin, and prominent nucleoli. Immunohistochemical analysis is essential to confirm the diagnosis, as HS expresses histiocytic markers such as CD68, CD163, and lysozyme while lacking markers for B cells, T cells, dendritic cells, epithelial cells, or myeloid lineage.⁴

Due to its aggressive course, the prognosis of HS is generally poor, with a median survival time of roughly six months.⁴ Standard therapeutic approaches combine surgical resection, chemotherapy, and radiotherapy, but outcomes remain unsatisfactory, with conventional chemotherapy regimens such as CHOP offering only modest efficacy.^{1,3} In cases where HS manifests as a localized thoracic mass, video-assisted thoracoscopic surgery (VATS) has emerged as a minimally invasive option that enables adequate tissue sampling, diagnostic confirmation, and in selected cases, therapeutic resection.^{2,5}

The aim of this report is to describe a case of thoracic HS in a young female patient that was initially misdiagnosed as Hodgkin's lymphoma, emphasizing the challenges in establishing a correct diagnosis and underscoring the pivotal role of VATS. This case contributes to the limited literature on pulmonary HS and highlights the value of advanced diagnostic and surgical approaches in managing this rare malignancy.^{2,5}

Case Presentation

A 22-year-old female presented with persistent right back pain for one month. She had no history of allergies, diabetes mellitus, hypertension, smoking, alcohol consumption, or family history of malignancy. Physical examination revealed no palpable masses.

A thoracic CT scan performed on December 12, 2024, revealed a posterior right lung mass, with differential

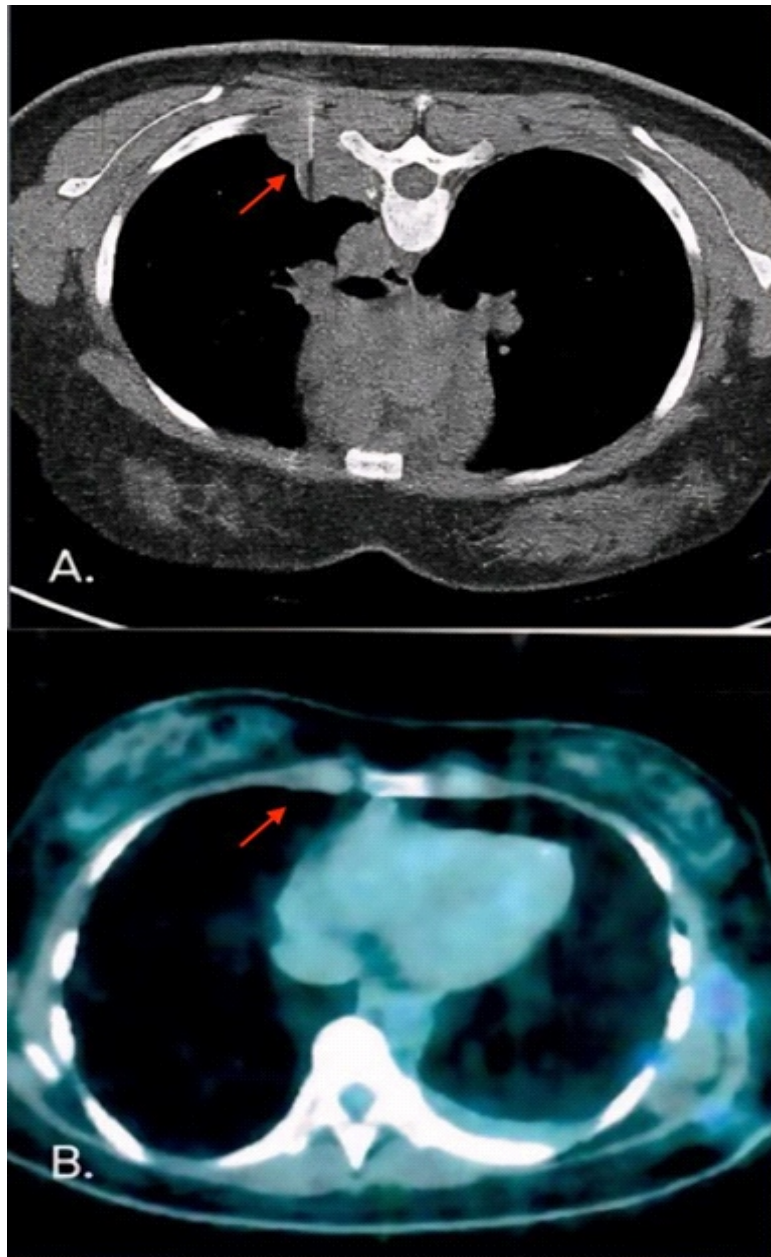
diagnoses including pulmonary Langerhans cell histiocytosis and posterior mediastinal tumor (Figure 1A). To establish a diagnosis, transthoracic needle aspiration (TTNA) using a 25G spinal needle and core biopsy with a 16G core needle were performed under local sedation. Histopathological examination of the core biopsy and TTNA specimens revealed large atypical cells in a reactive inflammatory background, initially raising suspicion of Hodgkin lymphoma (Figure 2A–B). However, immunohistochemistry (December 31, 2024) demonstrated positivity for CD68, CD163, and Ki-67 (30%), with negative staining for S100, LCA, CD34, ERG, CD1a, SALL4, and TTF-1, findings suggestive of histiocytic sarcoma (HS). For definitive diagnosis and surgical management, video-assisted thoracoscopic surgery (VATS) was subsequently performed, allowing complete resection of the mass. Histopathological evaluation of the mediastinal biopsy obtained through VATS showed similar morphology (Figure 2C), and postoperative immunohistochemistry (February 11, 2025) confirmed HS, with results demonstrating CD68+, CD163+, vimentin+, and a high Ki-67 proliferation index, while staining was negative for CD20, CD3, CD30, PAX5, MUM1, CD1a, S100, and cytokeratin (Figure 3). A postoperative PET/CT scan (January 18, 2025) revealed no hypermetabolic lesions (Figure 1B). The patient did not receive additional chemotherapy or radiotherapy, as she relocated abroad for academic purposes. This case report was conducted in accordance with the Helsinki Declaration (1975, as revised in 1983).

Discussion

Histiocytic sarcoma (HS) is an exceptionally rare non-Langerhans histiocytic malignancy, accounting for less than 1% of all hematolymphoid neoplasms. It most commonly arises in extranodal sites such as the gastrointestinal tract, superficial and deep soft tissues, lungs, and nasal cavity. In addition to its rarity, diagnosing HS is particularly challenging due to its potential overlap in both morphological and immunophenotypic features with other malignancies.^{1,3}

In this case, we report a 22-year-old female presenting with persistent right-sided back pain for one month. A similar clinical presentation was described by Matthew et al., involving a 51-year-old woman who experienced progressively worsening back pain.⁶ HS can occur across a broad age range, with a slight male predominance and a median age of diagnosis at 52 years.⁷

The clinical presentation of histiocytic sarcoma (HS) is highly variable, ranging from localized disease with a solitary mass to widespread, disseminated involvement.³ Patients commonly present with either localized masses or systemic symptoms, depending on the extent of disease.¹ In a study by Anuhya Kommalapati et al. involving 300 HS cases, the most common sites of

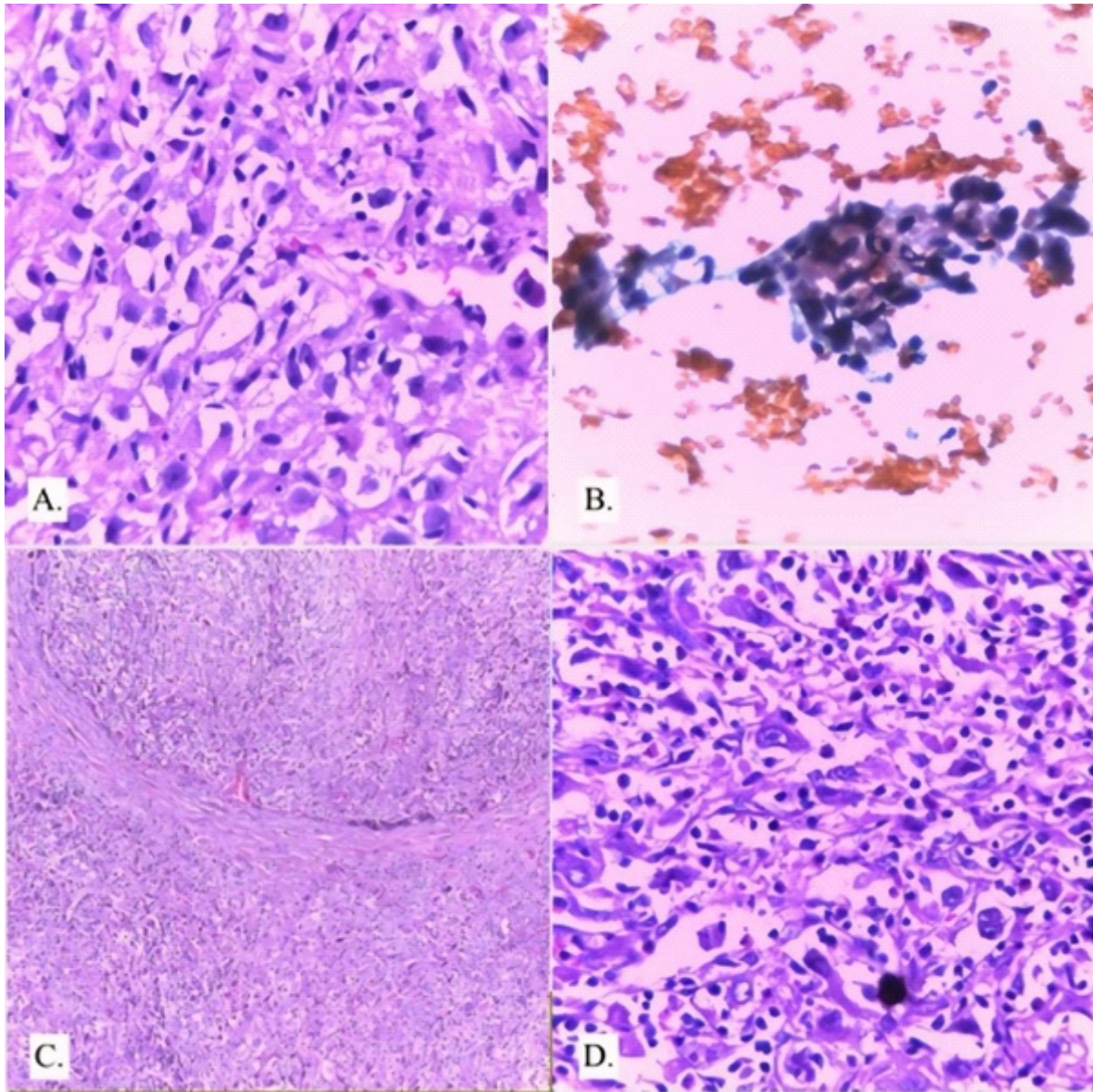


A) CT-guided transthoracic needle aspiration (TNA) and core biopsy was performed.
B) Postoperative PET/CT showed no residual hypermetabolic activity, consistent with effective disease control following VATS

Figure 1. CT scan showed a posterior right lung mass

presentation were the skin and connective tissue (41%), followed by lymph nodes (14%), the gastrointestinal tract (12%), and the hematopoietic system (9%).⁸ In our case, the patient experienced persistent right-sided back pain without associated radiation, palpable masses, or lymphadenopathy. HS involving the pulmonary system typically appears on

CT scans as a lung lesion or mass. In this case, thoracic CT imaging revealed a mass in the posterior segment of the right lower lobe. A similar finding was reported by Yuanjie Lin et al., who described a right lung lesion accompanied by multiple enlarged lymph nodes in the mediastinum, right supraclavicular region, and bilateral iliac wings.⁴



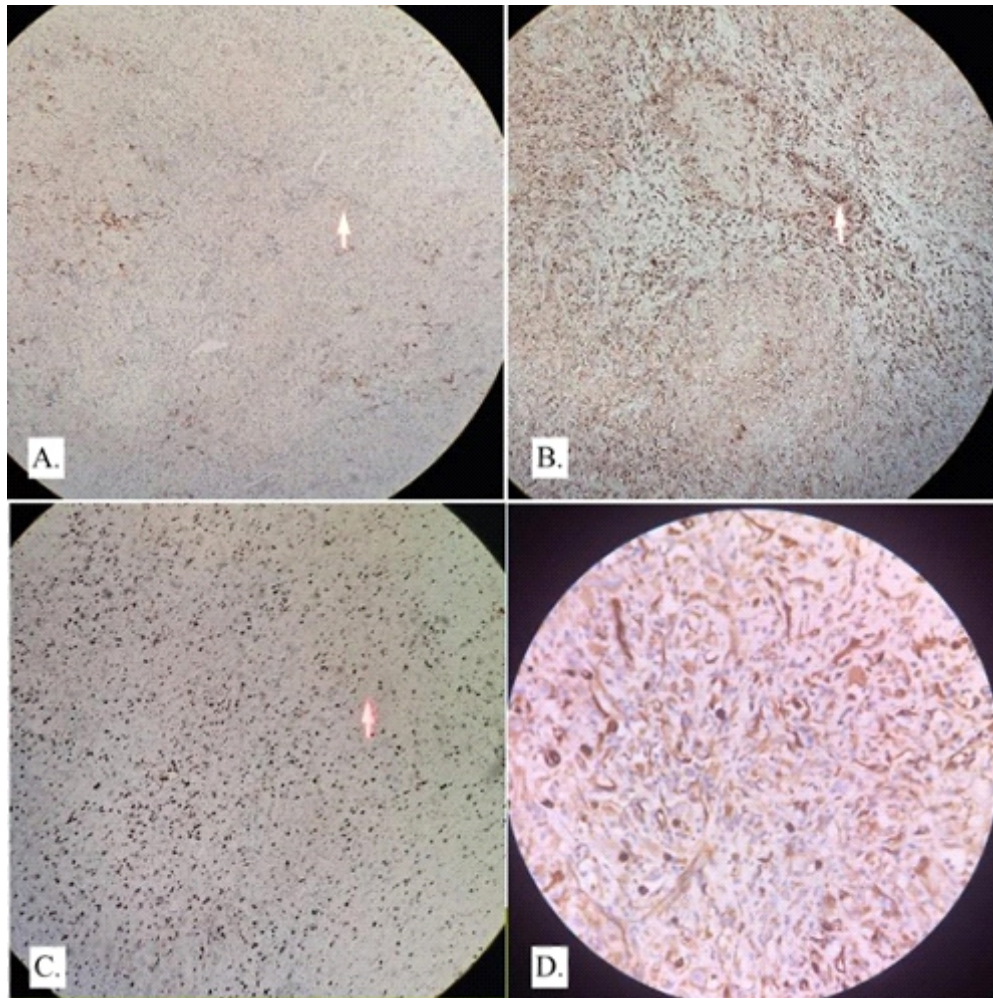
A) Core biopsy sample,
B) Transthoracic needle aspiration (TNA) sample,

Figure 2. Histopathological evaluation initially demonstrated large atypical cells in a reactive inflammatory background, raising suspicion for Hodgkin lymphoma

Histiocytic sarcoma has a wide range of differential diagnoses, since its morphology can mimic other tumors composed of large epithelioid or pleomorphic cells. These include lymphomas (particularly anaplastic large cell lymphoma and Hodgkin lymphoma), undifferentiated carcinomas, malignant melanoma, certain sarcomas such as epithelioid sarcoma and epithelioid angiosarcoma, dendritic cell neoplasms like follicular dendritic cell sarcoma, as well as histiocytic conditions such as

Langerhans cell histiocytosis.¹ In this case, the primary differential diagnoses included malignant posterior mediastinal tumor or pulmonary Langerhans cell histiocytosis suspected.

To confirm the diagnosis or rule out malignancy, a biopsy followed by pathological and immunohistochemical analysis of the lesion is essential. Decision analysis with TTNA suggest that minimally invasive tissue acquisition methods are more cost-effective than PET imaging or



A) CD1a negative;
 B) CD68 positive;
 C) Ki-67 positive with high proliferative index;
 D) Vimentin positive.

Figure 3. Immunohistochemical staining results

VATS, especially when the likelihood of cancer exceeds 65%.^{9,10} The diagnostic accuracy of CT-guided percutaneous TTNA ranges between 82% and 98%, making it particularly suitable for peripheral lesions—although it is now increasingly used for central lesions as well. Drew Willey et al. reported that image-guided needle aspiration of pulmonary nodules yielded diagnostic results in most patients, with malignancy confirmed in 70% and benign pathology identified in 9%.^{10,11}

Biopsy procedures were carried out with the patient in either a supine or prone position, depending on the location of the lesion. CT guidance helped determine a safe needle trajectory while avoiding critical thoracic structures. Ideally, the needle path was positioned as perpendicular to the pleura as possible and kept as short

as feasible through the lung parenchyma. After standard skin disinfection, 5 mL of 1% lidocaine was injected subcutaneously for local anesthesia. In this case, transthoracic needle aspiration (TTNA) was performed using a 25G spinal needle, followed by a core biopsy with a 16G core needle under local sedation. A 20 mL syringe was used to apply negative pressure for aspiration. Sample adequacy was evaluated by the operator. The obtained specimens were sent for cytopathological and histopathological analysis, and in cases with suspected infection, microbiological evaluation was also conducted.

¹² The initial histopathological assessment suggested Hodgkin lymphoma, highlighting the diagnostic complexity due to overlapping morphologic features. Therefore, immunohistochemistry (IHC) was essential to

confirm the diagnosis and exclude other mimickers. Introduced in the early 1990s, VATS provided a minimally invasive alternative for the surgical management of lung cancer. Since then, it has become the preferred technique for surgical resection in early-stage lung cancer. To minimize surgical trauma, VATS uses small access ports into the thoracic cavity, thereby eliminating the need for large incisions or rib-spreading. The term “VATS segmentectomy” refers to the resection of one or more lung segments under thoracoscopic visualization. This procedure can be performed with varying numbers of thoracic ports but usually involves an access window without rib-spreading.¹³ Segmentectomy can be categorized as typical or atypical, with the former—including basilar segmentectomy—more commonly performed via VATS. In our case, the patient underwent a typical posterior basal segmentectomy (S10) of the right lower lobe using a standardized three-port VATS technique. For lower lobe resections, the procedure typically involves sequential division of the segmental artery, bronchus, and intersegmental plane. Accurate delineation of this plane is essential to achieve clear resection margins while preserving lung function, which can be facilitated by selective segmental inflation or dye-assisted methods.¹³ According to the meta-analysis conducted by Wenqi Wu and colleagues, patients undergoing single-port VATS experienced fewer surgical site infections than those treated with the multi-port approach. The main advantage of single-port VATS lies in the reduction of incisions. However, proper drain placement is also crucial. Drains that are not positioned directly at the incision site may prolong drainage duration, which can negatively impact wound healing.¹⁴

Immunohistochemistry (IHC) played a pivotal role in establishing the diagnosis in this case. The tumor cells expressed CD68 and CD163, which are hallmark markers for histiocytic differentiation. These findings strongly support the diagnosis of histiocytic sarcoma, particularly in the absence of lineage-specific markers from other malignancies. The tumor was negative for CD3 and CD20, ruling out T- and B-cell lymphomas, respectively. Additionally, the lack of expression of CD30, PAX5, and MUM1 helped exclude Hodgkin's lymphoma, especially the syncytial variant. CD1a and S100 were also negative, making Langerhans cell histiocytosis unlikely. High Ki-67 proliferation index and vimentin positivity further supported the aggressive nature and mesenchymal origin of the tumor. The combination of positive histiocytic markers and absence of markers for lymphoid, epithelial, or dendritic lineages confirmed the diagnosis of histiocytic sarcoma and excluded other hematologic malignancies considered in the initial differential diagnosis.³

S has a wide spectrum of clinical features due to its potential to involve different organs, often appearing on 18F-FDG PET/CT as multiple hypermetabolic extranodal

sites.¹⁵ In this case, the patient underwent a postoperative 18F-FDG PET/CT scan. No hypermetabolic activity was observed in the posterior segment of the right lung.

Conclusion

We highlight the role of video-assisted thoracic surgery (VATS) in achieving a definitive diagnosis when less invasive methods prove inconclusive. This is supported by the postoperative PET scan showing no hypermetabolic activity, indicating effective disease control. However, due to the poor prognosis and high recurrence rate associated with histiocytic sarcoma, close monitoring and a multidisciplinary approach remain essential in long-term management. Considering the diagnostic challenges—particularly its potential to mimic other malignancies such as Hodgkin lymphoma—timely and accurate identification is critical, especially given the aggressive course and a median overall survival of approximately six months.⁴

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References

1. Susan D, Philip J, Sherief A, Narayanan G, Nair SG, Av J. Histiocytic Sarcoma: Clinical Features and Outcomes of Patients Treated at a Tertiary Cancer Care Center. *Cureus*. 2022;14(6):e25814. DOI:10.7759/cureus.25814.
2. Salfity H, Tong BC. VATS and Minimally Invasive Resection in Early-Stage NSCLC. *Semin Respir Crit Care Med*. 2020;41(3):335-45.
3. Hung YP, Qian X. Histiocytic Sarcoma. *Arch Pathol Lab Med*. 2020 May;144(5):650-654. doi: 10.5858/arpa.2018-0349-RS.
4. Lin Y, Cao Q, Hong A, Liang X. Primary pulmonary histiocytic sarcoma with high PD-L1 expression benefited from immunotherapy: A case report and bioinformatic analysis. *Clin Respir J*. 2024;18(3). DOI:10.1111/crj.13741.
5. Yang L, Guo C, Zhang Y, Jiang H, Ma L, Liu H, et al. Simultaneous bilateral video-assisted thoracic surgery is safe and feasible for multiple primary lung cancers. *J Cardiothorac Surg*. 2024;19(1):1–9. DOI: 10.1186/s13019-024-02941-2.

6. Harwood M, Craig FE, Yang M. Rare Multisystem Histiocytic Sarcoma on 18 F-FDG PET/CT. *J Nucl Med Technol.* 2021;49:358–9. DOI:10.2967/jnmt.121.262247.
7. SEER Hematopoietic and Lymphoid Neoplasm Database. 2025. Available from URL: <https://seer.cancer.gov/seertools/hemelymph/51f6cf59e3e27c3994bd5477/>.
8. Kommalapati A, Tella SH, Go RS, Goyal G. Predictors of survival, treatment patterns, and outcomes in histiocytic sarcoma. *Leuk Lymphoma.* 2015;60(2):553–5. DOI:10.1080/10428194.2018.1492128.
9. Nam H, Min GJ, Kim TY, Jeon Y, Cho SG. Case Report: A case series on histiocytic sarcoma – various clinical features and patient outcomes. *Front Oncol.* 2025;15:1505737. DOI:10.3389/fonc.2025.1505737.
10. Willey D, Garcia-Saucedo J, Stancampiano F, Heckman MG, Klopman Z, Koralewski A, et al. Safety and Diagnostic Yield of Transthoracic Needle Aspiration of the Lung in Elderly Patients. *Lung.* 2021;199(2):171–6. DOI: 10.1007/s00408-021-00429-7.
11. Polat G, Özdemir Ö, Serçe Unat D, Karadeniz G, Ayrancı A, Unat ÖS, et al. Pneumothoraxes after CT-guided percutaneous transthoracic needle aspiration biopsy of the lung: A single-center experience with 3426 patients. *Tuberk Toraks.* 2023;71(1):67–74. DOI:10.5578/tt.20239909.
12. Huang ZG, Sun HL, Wang CL, Gao BX, Chen H, Yang MX, et al. CT-guided transthoracic needle biopsy of pulmonary lesions: comparison between the cutting needle and aspiration needle. *Br J Radiol.* 2020;94(1118):20190930. DOI:10.1259/bjr.20190930.
13. Nakazawa S, Shimizu K, Mogi A, Kuwano H. VATS segmentectomy: past, present, and future. *Gen Thorac Cardiovasc Surg.* 2018;66(2):81–90. DOI:10.1007/s11748-017-0878-6.
14. Wu W, Zhao Y, Zhang Z, Jiang J, Feng C, Qin D, et al. Effect of single-port video-assisted thoracoscopy on surgical site wound infection and healing in patients with lung cancer: A meta-analysis. *Int Wound.* 2023;20(9):3483. DOI:10.1111/iwj.14220.
15. Harwood M, Craig FE, Yang M. Rare Multisystem Histiocytic Sarcoma on 18 F-FDG PET/CT. *J Nucl Med Technol.* 2021;49:358–9. DOI:10.2967/jnmt.121.262247.