International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	PRIMARY PULMONARY HODGKIN'S LYMPHOMA: A CASE OF DIAGNOSTIC COMPLEXITY AND TREATMENT RESISTANCE
DOI	https://doi.org/10.31435/ijitss.4(48).2025.4167
RECEIVED	16 September 2025
ACCEPTED	27 November 2025
PUBLISHED	04 December 2025
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PRIMARY PULMONARY HODGKIN'S LYMPHOMA: A CASE OF DIAGNOSTIC COMPLEXITY AND TREATMENT RESISTANCE

Radosław Pastuszek *(Corresponding Author, Email: Radek.pastuszek@gmail.com)*
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0009-2824-3876

Magdalena Rosiewicz
Maria Skłodowska-Curie Regional Specialist Hospital in Zgierz, Zgierz, Poland
ORCID ID: 0009-0006-6281-4773

Karolina Bieńkowska
Maria Skłodowska-Curie Provincial Specialist Hospital in Zgierz, Zgierz, Poland
ORCID ID: 0009-0000-9229-8614

Aleksandra Pastuszek
Regional Hospital Włodzimierza Roeflera in Pruszków, Pruszków, Poland
ORCID ID: 0009-0002-5636-1764

Anita Janda
Maria Skłodowska-Curie Provincial Specialist Hospital in Zgierz, Zgierz, Poland
ORCID ID: 0009-0009-6563-6898

Sylwia Bartolik
Maria Skłodowska-Curie Provincial Specialist Hospital in Zgierz, Zgierz, Poland
ORCID ID: 0009-0009-6605-1381

Marcin Durowicz
ZPZOZ in Bierutów, Bierutów, Poland
ORCID ID: 0009-0007-3742-421X

Iwona Górnicka
Nikolay Pirogov Specialized District Hospital, Łódź, Poland
ORCID ID: 0009-0008-7919-8895

Jan Drzymała
Maria Skłodowska-Curie Regional Specialist Hospital in Zgierz, Zgierz, Poland
ORCID ID: 0009-0007-4905-9926

Urszula Kierepka
Nikolay Pirogov Specialized District Hospital, Łódź, Poland
ORCID ID: 0009-0004-6642-5252

ABSTRACT

Primary pulmonary Hodgkin's lymphoma (PPHL) arises from the lymphoid tissue of the alveolar mucosa or peribronchial lymph nodes. PPHL is extremely rare, representing only 1.5–2.4% of all cases of primary pulmonary lymphoma.[1] Its rarity and nonspecific presentation often lead to diagnostic delays. Symptoms such as cough, fatigue, or chest discomfort mimic other pulmonary diseases, complicating clinical evaluation. Here, we present a case of PPHL initially misdiagnosed as granulomatosis with polyangiitis due to overlapping clinical and histopathological findings. This case emphasizes the importance of a multidisciplinary approach and highlights the critical role of thorough histopathological analysis in establishing an accurate diagnosis.

KEYWORDS

Pulmonary Hodgkin's Lymphoma, Pulmonary Diseases, Cough, Primary Pulmonary Hodgkin's Disease

CITATION

Radosław Pastuszek, Magdalena Rosiewicz, Karolina Bieńkowska, Aleksandra Pastuszek, Anita Janda, Sylwia Bartolik, Marcin Durowicz, Iwona Górnicka, Jan Drzymała, Urszula Kierepka. (2025). Primary Pulmonary Hodgkin's Lymphoma: A Case of Diagnostic Complexity and Treatment Resistance. *International Journal of Innovative Technologies in Social Science*, 4(48). doi: 10.31435/ijitss.4(48).2025.4167

Introduction

Hodgkin's lymphoma (HL) is a lymphoproliferative disorder characterized by the presence of Hodgkin-Reed-Sternberg (HRS) cells. It typically involves lymph nodes but can occasionally manifest in extranodal sites. Primary pulmonary Hodgkin's lymphoma (PPHL) is an exceedingly rare variant of HL, where the disease is confined to the lung without systemic involvement at the time of diagnosis.[3]

PPHL represents only 1.5–2.4% of all primary pulmonary lymphomas, with even fewer cases documented in the literature.[4] Due to its rarity, PPHL is often not considered in the differential diagnosis of pulmonary masses. Its clinical and radiological features overlap with other conditions, such as granulomatosis with polyangiitis (GPA), sarcoidosis, and infections, leading to frequent misdiagnoses.[5]

Patient History and Initial Presentation

A 53-year-old woman presented to the hospital with a six-month history of nonspecific symptoms, including fatigue, peripheral edema, dry cough, and nasal cavity ulceration. The patient was previously diagnosed with granulomatosis with polyangiitis (GPA) based on clinical symptoms and treated with corticosteroids. However, her condition failed to improve despite adherence to the prescribed immunosuppressive regimen.[6]

Upon admission, the patient complained of persistent low-grade fever and an erythematous, itchy rash. Physical examination revealed nasal cavity ulceration and mild wheezing on auscultation. Initial laboratory tests showed elevated C-reactive protein (CRP), leukocytosis with neutrophilia, and lymphopenia. These findings raised suspicion of an autoimmune or inflammatory disorder, prompting further investigations.[7]

Diagnostic Workup

Imaging Studies

A computed tomography (CT) scan of the chest revealed an infiltrative mass in the left lung with no significant mediastinal lymphadenopathy. The lesion raised suspicion of malignancy, yet granulomatosis could not be excluded.[8]

Initial Biopsies

Bronchoscopy with bronchial brush biopsy and bronchial washing was performed. Cytological analysis showed no atypical cells. Additionally, biopsy of the nasal cavity ulceration revealed chronic inflammation without granulomas or signs of vasculitis. These findings contradicted the initial diagnosis of GPA.[9]

Histopathological Evaluation

A left lung biopsy showed inflammatory infiltrates but no granulomas or necrosis, ruling out granulomatosis with polyangiitis. Despite the absence of definitive findings, the persistent infiltrative mass warranted further investigation.[10]

Repeated biopsies of the mediastinum revealed fibrotic lung tissue containing nodules with pyknotic Hodgkin-Reed-Sternberg (HRS) cells. Immunohistochemistry confirmed the diagnosis of classical Hodgkin lymphoma, nodular sclerosis subtype. The tumor cells expressed CD15 and CD30, while being negative for CD45 and ALK, consistent with classical HL.

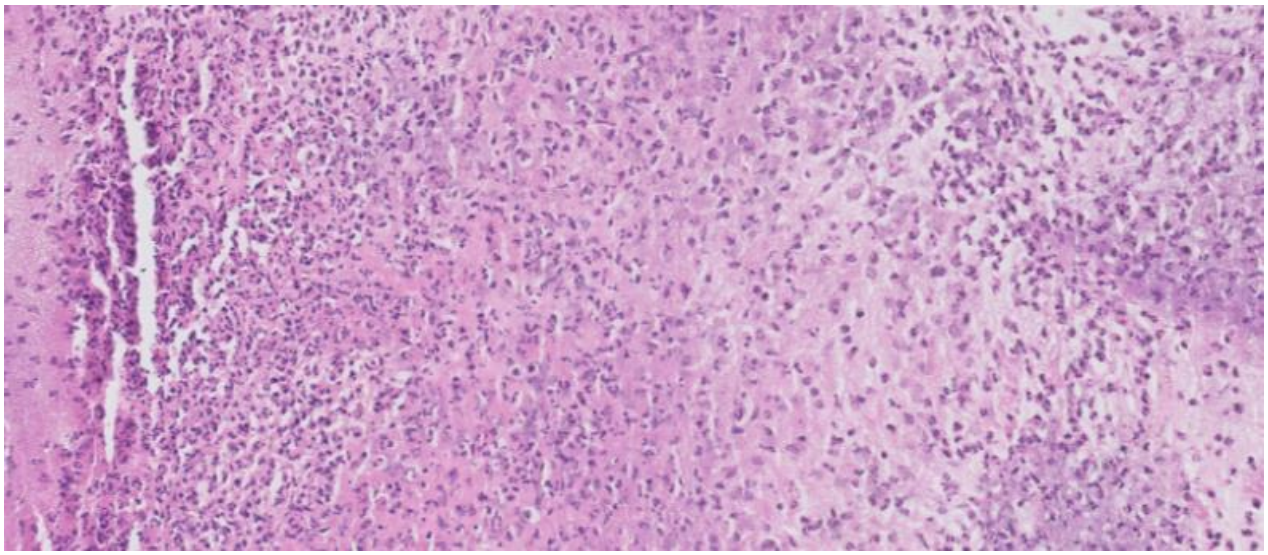

Fig. 1. *Mucosal ulceration of the nasal cavity*

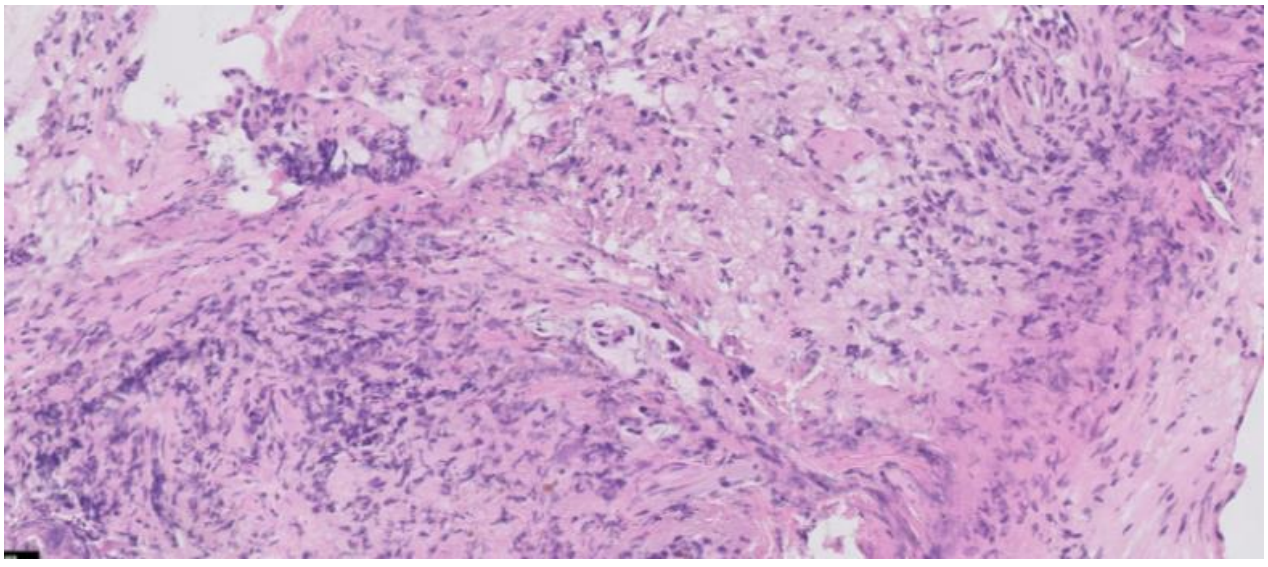

Fig. 2. *Left lung*

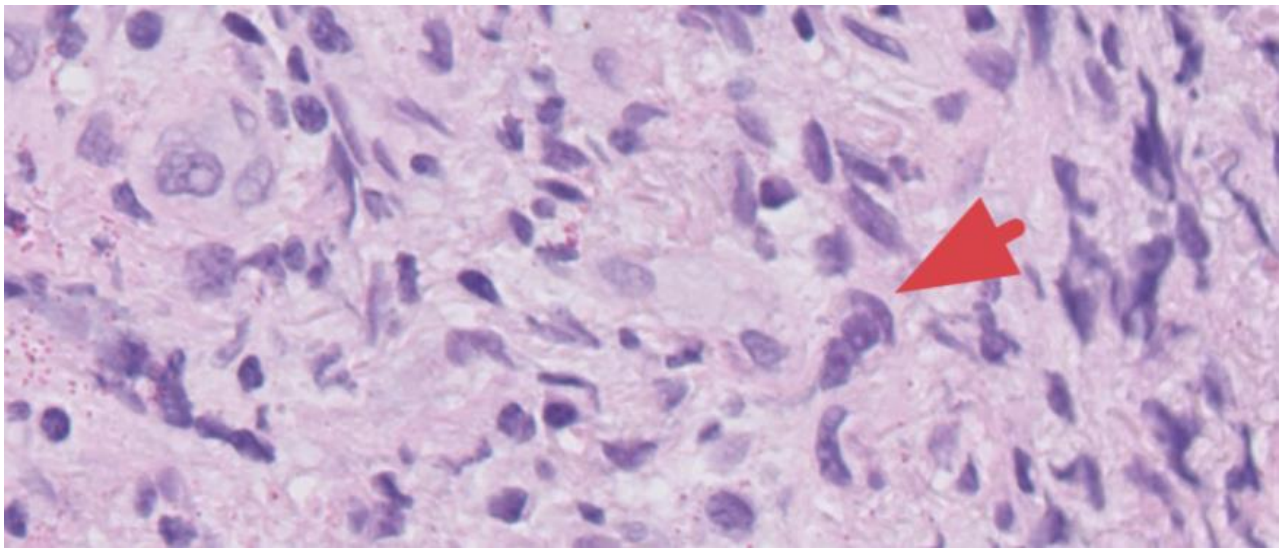

Fig. 3. *H&E. HR-S cells. Lots of eosinophils. Fibrosis*

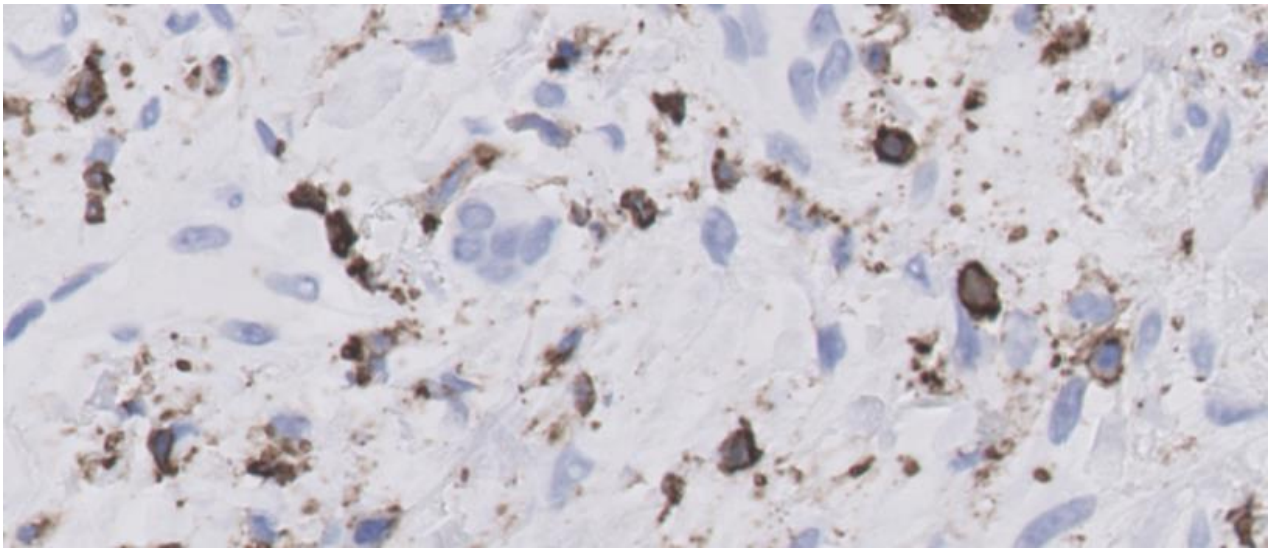

Fig. 4. *CD45 negative RS-H cells*

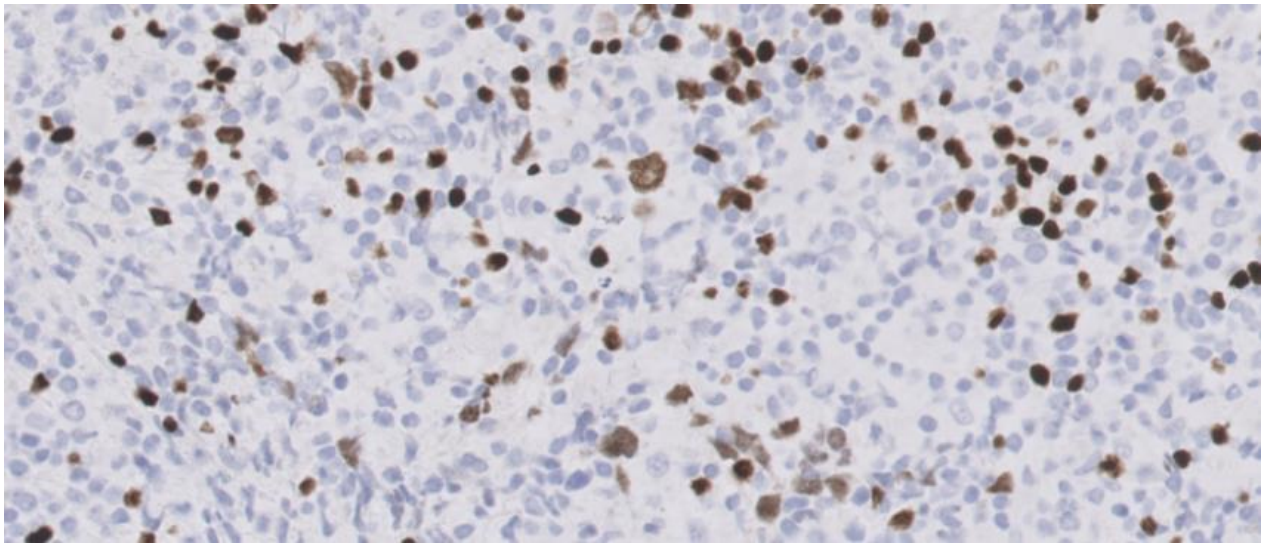

Fig. 5. *BSAP PAX positive RS-H cells*

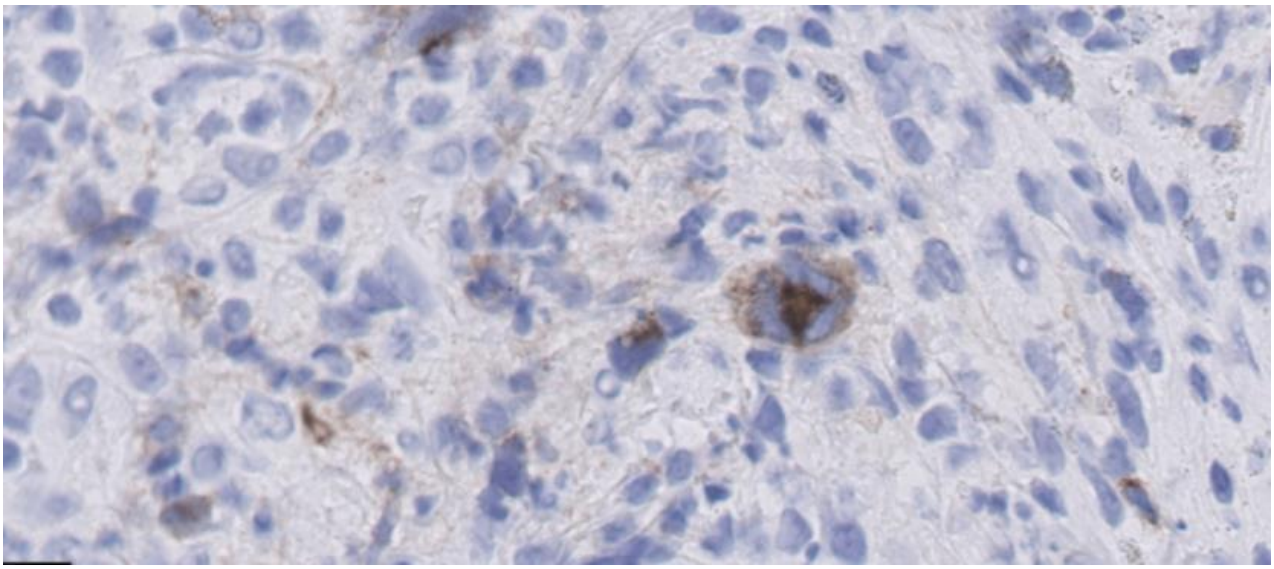

Fig. 6. *CD30 positive RS-H cells*

Staging and PET-CT

A PET-CT scan showed metabolic activity confined to the left lung with no evidence of nodal or systemic involvement. This confirmed the diagnosis of PPHL. [11]

Follow up

The patient was subsequently referred to the Department of Hematology for further management and specialized evaluation. Despite initial diagnostic efforts and targeted therapies, the disease exhibited progressive behavior. Follow-up PET scans demonstrated a significant escalation in metabolic activity, indicating disease involvement in multiple organ systems.

The high metabolic activity was first noted in the left lung and subsequently extended to the lymph nodes of the mediastinum and pulmonary hilum, signifying local disease progression. Further scans identified pathological uptake in the lymph nodes of the abdominal cavity, consistent with systemic dissemination. The disease also infiltrated the skeletal system, as evidenced by increased activity in multiple bones, raising concerns about extensive bone marrow involvement.

In addition to skeletal spread, there was clear evidence of disease affecting the spleen, a common site for lymphoproliferative disorders, which correlated with splenic enlargement observed in imaging studies. Furthermore, cutaneous involvement was confirmed by hypermetabolic activity localized to the skin of the abdomen, suggesting extranodal extension of the lymphoma.

A subsequent bone marrow biopsy corroborated the PET findings, revealing significant infiltration by Hodgkin-Reed-Sternberg cells. [12] These findings collectively confirmed advanced-stage disease, necessitating an urgent revision of the treatment strategy to address the extensive systemic spread and mitigate further complications.

Treatment

The patient continued to be closely monitored by the Department of Hematology, where follow-up assessments aimed to evaluate the response to treatment and adjust the therapeutic approach as needed. The patient underwent six lines of intensive chemotherapy, including regimens typically employed for refractory or relapsed Hodgkin's lymphoma. [13] Unfortunately, her response to chemotherapy was suboptimal, as confirmed by repeated PET scans, which consistently revealed areas of sustained high metabolic activity in the lung, mediastinum, and bone marrow. These findings were scored as 5 on the Deauville scale, indicating active disease and resistance to standard chemotherapy protocols.

Given the lack of satisfactory response, the treatment strategy was escalated, and the patient underwent an autologous stem cell transplant (auto-SCT). Auto-SCT is often utilized as a salvage therapy in relapsed or refractory Hodgkin's lymphoma and involves the reinfusion of the patient’s own hematopoietic stem cells

following high-dose chemotherapy. While the transplant was successfully completed, its impact on disease control was limited, and PET scans continued to show residual disease activity. Considering the patient's resistance to chemotherapy and the high risk of disease progression, she was subsequently enrolled in a brentuximab vedotin treatment programme. [14] Brentuximab vedotin, an antibody-drug conjugate targeting CD30-positive cells, is a targeted therapy approved for relapsed or refractory Hodgkin's lymphoma. However, during the course of treatment, the patient developed significant complications, including severe myelosuppression. [15] Her platelet levels dropped to critically low levels, raising concerns about the risk of spontaneous bleeding and other complications associated with thrombocytopenia. Due to these hematologic toxicities, the administration of brentuximab vedotin had to be postponed. [16] Clinicians have opted to closely monitor the patient’s blood counts and overall condition, ensuring her hematopoietic system recovers sufficiently to tolerate further treatment. The risk of disease progression remains a critical concern, and additional supportive measures are being employed to stabilize her condition. At present, the patient is undergoing further diagnostic evaluations. Blood tests are being conducted to assess hematological recovery and systemic health, while another PET scan is planned to re-evaluate the extent of disease activity and guide the next steps in her management. The clinical team is carefully balancing the urgency of disease control with the need to mitigate treatment-related toxicities, as they await the results of these investigations to determine the most appropriate course of action.[17]

Discussion

Epidemiology and Pathogenesis

PPHL is an extremely rare entity, often overshadowed by other primary pulmonary lymphomas, such as mucosa-associated lymphoid tissue (MALT) lymphoma. Its pathogenesis remains unclear but may involve the transformation of lymphoid tissue within the lung, triggered by chronic inflammation or infection.

PPHL predominantly affects middle-aged individuals, with a slight female predominance. Unlike systemic HL, which often presents with lymphadenopathy and B-symptoms (fever, night sweats, weight loss), PPHL typically manifests with localized pulmonary symptoms, complicating early detection.[18]

Clinical and Radiological Features

PPHL presents with nonspecific symptoms such as cough, dyspnea, chest discomfort, or fatigue. These symptoms overlap significantly with other pulmonary diseases, including infections, autoimmune conditions, and sarcoidosis. Radiologically, PPHL may appear as a solitary mass, nodular infiltrate, or consolidation, lacking specific features to distinguish it from other conditions.

In the presented case, the initial misdiagnosis of GPA illustrates the diagnostic challenges posed by PPHL. The absence of granulomas and necrosis in histopathological examination helped exclude GPA, redirecting focus towards malignancy. [19]

Role of Biopsy and Immunohistochemistry

Histopathological examination is the cornerstone of PPHL diagnosis. The identification of HRS cells, along with their immunohistochemical profile (CD15+, CD30+, CD45−), is essential for confirming HL. [20] Repeated biopsies may be required, as tumor cells may be sparse and scattered within the inflammatory background, as seen in this case.

Differential Diagnosis

Differential diagnosis includes:

1. **Granulomatosis with Polyangiitis (GPA):** Characterized by granulomas, necrotizing vasculitis, and systemic involvement, GPA was initially suspected due to nasal ulceration and systemic inflammation.
2. **Sarcoidosis:** A multisystem granulomatous disorder often affecting the lungs, distinguished by non-caseating granulomas.
3. **Infectious Diseases:** Tuberculosis or fungal infections may present with similar radiological findings.
4. **Other Pulmonary Lymphomas:** Including MALT lymphoma, which typically lacks HRS cells.

Treatment resistance

The presented case highlights the significant challenges in managing advanced, refractory Hodgkin's lymphoma, particularly in its rare pulmonary manifestation. Despite the availability of established chemotherapeutic protocols and salvage therapies such as autologous stem cell transplant (auto-SCT), treatment resistance remains a formidable barrier to achieving remission in some patients .[21] In this case, six lines of chemotherapy were insufficient to control disease progression, as evidenced by persistently high metabolic activity on PET scans, scored 5 on the Deauville scale. This underscores the aggressive nature of refractory disease and the need for alternative therapeutic strategies. Brentuximab vedotin, a CD30-directed antibody-drug conjugate, represents a targeted approach with demonstrated efficacy in relapsed or refractory Hodgkin's lymphoma. [22] However, its administration in this case was complicated by severe myelosuppression, highlighting a common challenge in treating heavily pretreated patients. Myelosuppression, particularly thrombocytopenia, not only delays treatment but also increases the risk of bleeding and infection, necessitating careful monitoring and supportive care. [23] The inability to promptly continue brentuximab vedotin treatment emphasizes the importance of balancing aggressive disease control with minimizing treatment-related toxicities. [24] This case illustrates the critical role of individualized patient management, leveraging hematological recovery to optimize therapeutic outcomes. Moreover, the persistence of high metabolic activity in the lung, mediastinum, and bone marrow despite intensive therapy underscores the need for innovative treatment approaches. [25] Emerging therapies, such as immune checkpoint inhibitors and other novel agents, may offer additional options for patients with refractory disease, although their use in pulmonary Hodgkin's lymphoma warrants further study.[26,27]

Importance of Multidisciplinary Collaboration

The presented case highlights the critical role of collaboration among clinicians, radiologists, and pathologists. The integration of clinical history, imaging, and histopathological findings is essential for accurate diagnosis, especially in rare conditions like PPHL.

Conclusions

This case underscores the diagnostic challenges associated with PPHL, a rare entity that mimics other pulmonary diseases. Accurate diagnosis requires thorough investigation, including histopathological and immunohistochemical analysis. The role of interdisciplinary collaboration cannot be overstated in ensuring timely and accurate diagnosis of rare and complex conditions.

Author's contribution

Conceptualization: Radosław Pastuszek, Aleksandra Pastuszek, Marcin Durowicz
Methodology: Aleksandra Pastuszek, Anita Janda, Jan Drzymała, Urszula Kierepka
Formal analysis: Sylwia Bartolik, Anita Janda, Karolina Bieńkowska, Radosław Pastuszek
Supervision: Magdalena Rosiewicz, Iwona Górnicka, Marcin Durowicz, Urszula Kierepka
Writing–Original Draft: Radosław Pastuszek, Karolina Bieńkowska, Sylwia Bartolik
Writing-Review and Editing: Marcin Durowicz, Jan Drzymała, Magdalena Rosiewicz

All authors have read and agreed with the published version of the manuscript

Funding statement: This research received no external funding.
Institutional Review Board Statement: Not applicable.
Informed Consent Statement: Not applicable.
Data availability statement: Not applicable.
Acknowledgments: The authors declare that there are no acknowledgments for this study.
Conflict of Interest Statement: The authors declare no conflict of interest
Declaration of generative AI and AI-assisted technologies: The authors used Chat GPT to improve language and readability, afterwhich the content was reviewed and edited. The authors accept full responsibility for the substantive content of the publication.

REFERENCES

1. Jaffe ES, Harris NL, Stein H, Vardiman JW. *Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues.* WHO; 2008.
2. Cadranel J, Wislez M, Antoine M. Primary pulmonary lymphomas: a clinical study of 70 cases. *Chest.* 1998;114(1):124-132.
3. Ponzoni M, Ferreri AJ, Zucca E. Extranodal lymphomas: pathophysiology and management. *Haematologica.* 2007;92(9):1187-1194.
4. Beasley MB, Franks TJ, Travis WD. Primary pulmonary lymphoma: clinical and pathologic features. *Arch Pathol Lab Med.* 2005;129(1):94-98.
5. Lichtenstein AK, Jett JR, Downie GH. Uncommon pulmonary tumors. *Clin Chest Med.* 2004;25(1):245-261.
6. Katzenstein A-LA, Mukhopadhyay S, Myers JL. *Diagnostic Atlas of Non-Neoplastic Lung Disease.* Springer; 2010.
7. Rossi G, Cavazza A, Spagnolo P, et al. Pulmonary lymphomas and lymphoid hyperplasias. *Semin Respir Crit Care Med.* 2011;32(4):430-441.
8. Godfrey RS, Antippa P, Lamb DS. Hodgkin lymphoma of the lung: an elusive diagnosis. *J Thorac Oncol.* 2016;11(4):623-625.
9. Travis WD, Brambilla E, Burke AP, Marx A, Nicholson AG. *Thoracic Tumours.* IARC Press; 2021.
10. Moskowitz CH, Nademanee A, Masszi T, et al. Brentuximab vedotin as consolidation after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet.* 2015;385(9980):1853-1862.
11. Cordier JF, Loire R, Brune J. Primary pulmonary lymphomas. *Chest.* 1993;103(2):494-503.
12. Ryu JH, Colby TV, Hartman TE, Vassallo R. *Diffuse Lung Disease: A Practical Approach.* Springer; 2005.
13. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol.* 2014;32(27):3059-3068. https://doi.org/10.1200/JCO.2013.54.8800.
14. Younes A, Gopal AK, Smith SE, et al. Results of a pivotal phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin's lymphoma. *J Clin Oncol.* 2012;30(18):2183-2189. https://doi.org/10.1200/JCO.2011.38.0410.
15. Armitage JO, Longo DL. Chemotherapy for Hodgkin lymphoma in adults: clinical practice guideline. *Ann Oncol.* 2019;30(7):947-960.
16. Barrington SF, Mikhaeel NG, Kostakoglu L, et al. Role of imaging in the staging and response assessment of lymphoma: consensus of the International Conference on Malignant Lymphomas Imaging Working Group. *J Clin Oncol.* 2014;32(27):3048-3058.
17. Engert A, Eichenauer DA, Fuchs M, Anagnostopoulos I, Diehl V. Hodgkin's lymphoma: diagnosis and treatment. *Lancet.* 2010;376(9743):146-155. https://doi.org/10.1016/S0140-6736(10)60603-4.
18. Ansell SM. Hodgkin lymphoma: 2018 update on diagnosis, risk-stratification, and management. *Am J Hematol.* 2018;93(5):704-715. https://doi.org/10.1002/ajh.25063.
19. Townsend W, Linch D. Hodgkin's lymphoma in adults. *Lancet.* 2012;380(9844):836-847. https://doi.org/10.1016/S0140-6736(12)60035-X.
20. Connors JM. State-of-the-art therapeutics: Hodgkin's lymphoma. *J Clin Oncol.* 2005;23(26):6400-6408. https://doi.org/10.1200/JCO.2005.05.014.
21. Gandhi MK, Marcus RE. The EBV-associated lymphomas. *Adv Hematol.* 2011;2011:325178. https://doi.org/10.1155/2011/325178.
22. Gallamini A, Hutchings M, Rigacci L, et al. Early interim 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography is prognostically superior to international prognostic score in advanced-stage Hodgkin's lymphoma: a report from a joint Italian-Danish study. *J Clin Oncol.* 2007;25(24):3746-3752. https://doi.org/10.1200/JCO.2007.11.6525.
23. O'Connor OA. Brentuximab vedotin: delivering a targeted punch in relapsed/refractory Hodgkin lymphoma. *Oncologist.* 2012;17(7):911-912. https://doi.org/10.1634/theoncologist.2012-0207.
24. Diefenbach CS, Connors JM. The role of brentuximab vedotin in patients with newly diagnosed Hodgkin lymphoma. *Semin Hematol.* 2016;53(3):165-171. https://doi.org/10.1053/j.seminhematol.2016.05.004.
25. Tarella C, Ladetto M, Zanni M, et al. Hodgkin's lymphoma: the paradigm of cure and future challenges. *Leukemia.* 2017;31(9):2032-2043. https://doi.org/10.1038/leu.2017.174.
26. Armitage JO. Early-stage Hodgkin's lymphoma. *N Engl J Med.* 2010;363(7):653-662. https://doi.org/10.1056/NEJMcp1000250.
27. Bröckelmann PJ, Borchmann P, Engert A. Current and future treatment strategies for Hodgkin lymphoma. *Cancer Treat Rev.* 2017;55:48-60. https://doi.org/10.1016/j.ctrv.2017.02.002.