GMR
The Original

HODGKIN'S LYMPHOMA MASQUERADING AS CRYPTOGENIC ORGANIZING PNEUMONIA: A DIAGNOSTIC CHALLENGE

Dr. Akshaya S[1], Dr. Ashwin Kailash[2*], Dr. Ghanshyam Verma[3], Dr. Elen Ann Abraham[4]

[1]Post graduate, Dept of Respiratory medicine, SBMCH, Email id: akshayasathish20@gmail.com, Orchid ID: 0009-0006-5539-6091
[2]Assistant professor, Dept of Respiratory Medicine, SBMCH, Orchid ID: 0000-0001-9987-4987, Email id: ashwinkailash93@gmail.com
[3]Professor & HOD, Dept of Respiratory medicine, SBMCH, Email id: drgsverma@gmail.com, Orchid ID- 0000-0001-7409-8133
[4]Associate professor, Dept of Respiratory medicine, SBMCH, Email id: drelenann153@gmail.com, Orchid ID: 0009-0007-1510-0935
*Corresponding Author: Email id: ashwinkailash93@gmail.com

ABSTRACT
A 27-year-old woman presented with persistent cough, intermittent fever, and dyspnea. Initial imaging revealed right lower lobe consolidation. Despite empirical antibiotics, symptoms persisted. Extensive infectious workup and bronchoscopy were non-contributory. A CT-guided lung biopsy suggested cryptogenic organizing pneumonia (COP), and corticosteroid therapy led to transient improvement. However, the recurrence of symptoms post tapering steroids due to steroid-related side effects prompted further investigation. A PET-CT scan revealed metabolically active hilar and mediastinal lymphadenopathy. EBUS-guided cryobiopsy of a right hilar node confirmed Hodgkin's lymphoma. The patient was started on CHOP chemotherapy and is currently improving. This case highlights how Hodgkin's lymphoma can mimic organizing pneumonia and underscores the importance of re-evaluating the diagnosis when clinical progression diverges from the expected course, even after initial tissue sampling.

KEYWORDS: Hodgkin's lymphoma, Cryptogenic organizing pneumonia, Non-resolving pneumonia, EBUS-guided cryobiopsy, PET-CT.

INTRODUCTION
Cryptogenic organizing pneumonia (COP) is a clinicopathologic entity characterized by intra-alveolar buds of granulation tissue composed of fibroblasts and myofibroblasts embedded within a loose connective matrix, forming the classic Masson bodies while preserving the underlying alveolar architecture. Although organizing pneumonia represents a nonspecific reparative response to lung injury, it is termed "cryptogenic" when no identifiable cause is found. Importantly, hematolymphoid malignancies are recognized causes of secondary organizing pneumonia, and accurate classification of such neoplasms requires correlation with standardized morphologic and immunophenotypic criteria as defined in the WHO Classification of Tumours of Haematolymphoid Tissues (1). This distinction is clinically critical because organizing pneumonia may mask an underlying malignant process.

From a global oncologic perspective, Hodgkin lymphoma constitutes a significant proportion of lymphoid malignancies worldwide. According to the most recent GLOBOCAN 2022 estimates, approximately 82,000 new cases of Hodgkin lymphoma and nearly 23,000 related deaths occurred globally in 2022, reflecting its continued public health relevance despite overall favorable survival in high-resource settings (2). Incidence rates are higher in very high Human Development Index regions, but mortality remains disproportionately elevated in low- and middle-income countries, where delayed diagnosis and limited access to specialized care contribute to adverse outcomes (2). These epidemiologic data underscore the importance of early and accurate identification of atypical presentations.

Standardized diagnostic pathways emphasize histologic confirmation and comprehensive staging. The National Cancer Grid of India recommends tissue biopsy with immunohistochemistry, radiologic staging including PET-CT where available, and risk-adapted therapy for Hodgkin lymphoma (3). In regions with high tuberculosis prevalence and infectious burden, pulmonary consolidations are often empirically treated as infection, which may delay recognition of malignant etiologies. Therefore, adherence to structured diagnostic algorithms is essential when radiologic findings and clinical course are discordant.

Clinically, COP typically presents with subacute cough, progressive dyspnea, low-grade fever, and constitutional symptoms. High-resolution computed tomography commonly demonstrates patchy peripheral or peribronchial consolidations and ground-glass opacities. While corticosteroid therapy usually produces rapid symptomatic and radiologic improvement, transient response does not exclude secondary causes. Zeng et al. evaluated organizing pneumonia associated with hematologic malignancies and demonstrated that such cases often mimic cryptogenic disease at presentation, with similar imaging patterns and initial steroid responsiveness (4). Their cohort analysis emphasized that persistent or relapsing disease should prompt reconsideration of an underlying neoplastic etiology.

The relationship between lymphoma and pulmonary inflammatory patterns has become increasingly recognized in the era of immune-modulating therapies. Łyżwa et al. reported prolonged viral infection with organizing pneumonia in a patient with follicular lymphoma receiving B-cell–depleting therapy, highlighting how immune dysfunction can obscure

diagnostic interpretation of lung infiltrates (5). These findings illustrate the complex interplay between malignancy, immune status, and inflammatory lung injury.
Furthermore, novel cellular therapies such as CD19-directed CAR T-cell therapy have introduced additional layers of immune dysregulation in lymphoma patients. Zhao et al. described secondary hematologic neoplasms and immune-related complications following CAR T-cell therapy, reinforcing the broader concept that profound immune alterations may generate atypical clinical presentations (6). Although their focus was on secondary myeloid neoplasms, the principle extends to pulmonary manifestations in treated lymphoma populations.
Post-infectious organizing pneumonia has also been reported in immunocompromised hosts. Tiew et al. documented delayed organizing pneumonia following mild SARS-CoV-2 infection, demonstrating that inflammatory lung injury may persist or evolve despite apparent clinical recovery (7). Such scenarios are particularly relevant in lymphoma patients, where immune compromise may modify radiologic patterns and delay recognition of underlying malignancy.
In summary, while COP is often considered a benign, steroid-responsive condition, the global burden of Hodgkin lymphoma and the established association between organizing pneumonia and hematologic malignancies mandate careful evaluation. Persistent consolidation, relapse after steroid tapering, or concomitant lymphadenopathy should prompt comprehensive reassessment. Integration of clinical evolution, imaging findings, histopathology, and adherence to oncologic guidelines is essential to prevent delayed diagnosis and ensure timely institution of definitive therapy.

Case Report:
A 27-year-old previously healthy female presented with a 2-week history of cough with scanty mucoid expectoration, intermittent low-grade fever, and exertional dyspnea. She gave no history of weight loss, night sweats, or hemoptysis. Chest examination revealed reduced breath sounds in the right lower lung field.
A chest radiograph showed a non-homogeneous opacity in the right lower zone. High-resolution computed tomography (HRCT) of the chest revealed dense consolidation in the right lower lobe. Based on the working diagnosis of bacterial pneumonia, empirical broad-spectrum antibiotics were initiated. However, sputum AFB smear, CBNAAT, Gram stain, and bacterial culture were all negative. The patient's symptoms persisted despite two weeks of antibiotic therapy. Bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial lung biopsy was performed, which was negative for acid-fast bacilli, fungal elements, and malignancy. Histopathology showed no significant inflammation or granulomas. Given persistent symptoms and inconclusive findings, a CT-guided core biopsy of the pulmonary lesion was performed. Histopathological examination revealed fibroblastic plugs within alveolar ducts and spaces with no evidence of malignancy, suggestive of cryptogenic organizing pneumonia. The patient was started on oral corticosteroids (prednisolone), resulting in significant symptomatic improvement.
Over the following months, she developed Cushingoid features, prompting a gradual steroid taper. Azathioprine was introduced as a steroid-sparing agent. Soon after, her respiratory symptoms recurred with worsening cough and mild fatigue. A PET-CT was performed to rule out alternative diagnoses. It revealed metabolically active soft tissue nodules in the right lower lobe and FDG-avid mediastinal and right hilar lymphadenopathy, the largest being a 3.4 * 2 cm right hilar node.
Endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration followed by cryobiopsy of the right hilar lymph node was done. Histopathology demonstrated eosinophils, epithelioid histiocytes and scattered large cells with scant cytoplasm and hyperchromatic nuclei and adviced for immunohistochemistry. Immunohistochemistry was positive for CD15, CD30, PAX5, and CD20. Taking morphology and immunohistochemistry into consideration, patient was diagnosed with CLASSIC HODGKIN LYMPHOMA - MIXED CELLULARITY.
The patient was started on CHOP chemotherapy regimen (Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone). She is currently tolerating treatment well, with significant improvement in respiratory symptoms and overall functional status.

Figures

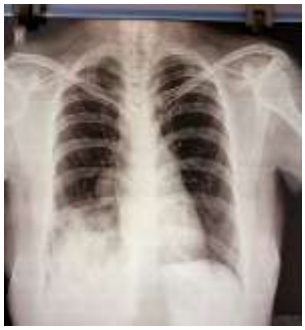

Figure 1: Pre-treatment/ presenting chest X-ray:

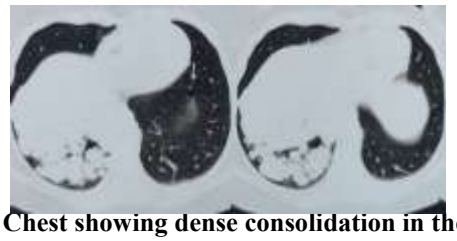

Figure 2: HRCT Chest showing dense consolidation in the right lower lobe

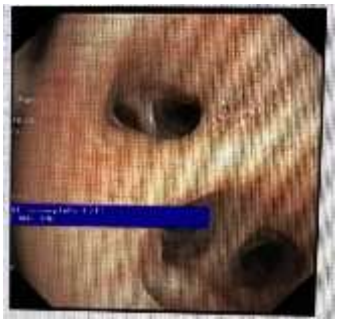

Figure 3: Bronchoscopy image (bronchus intermedius)

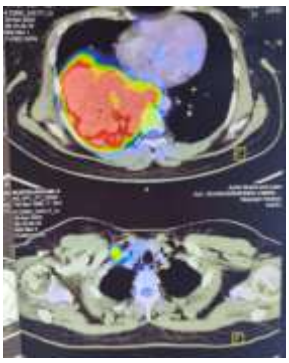

Figure 4: PET-CT (30 April 2024) showing FDG-avid nodules in right lower lobe.

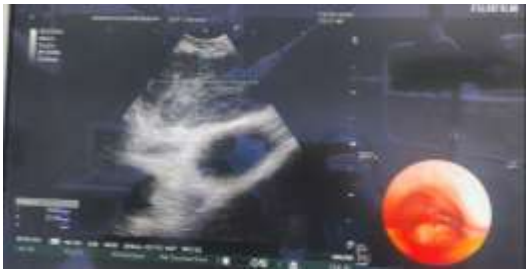

Figure 5: EBUS images showing right hilar and mediastinal lymph nodes

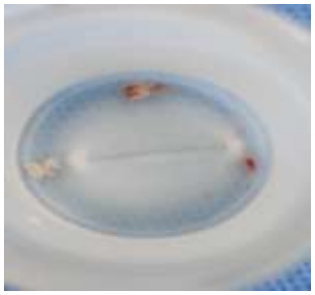

Figure 6: Gross image of EBUS cryobiopsy specimen suspended in formalin

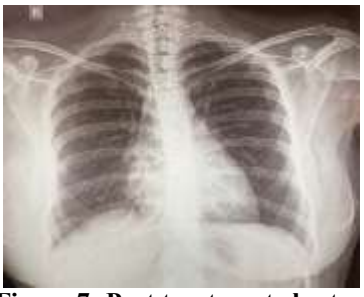

Figure 7: Post treatment chest xray

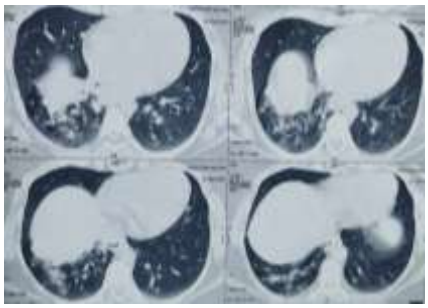

Figure 8: Repeat PET-CT (26 August 2024)

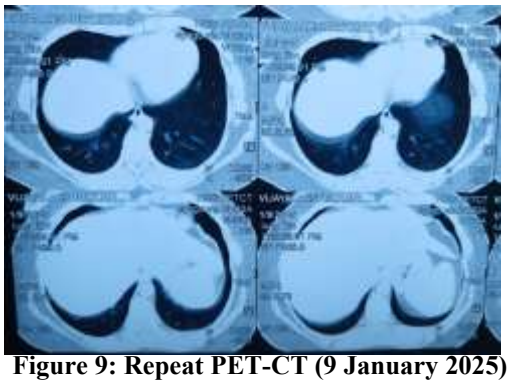

Figure 9: Repeat PET-CT (9 January 2025)

DISCUSSION

Delayed inflammatory pulmonary patterns in immunocompromised patients often obscure the underlying diagnosis. Tiew et al. described delayed organizing pneumonia in an immunocompromised host following mild COVID-19 infection, where persistent consolidation and steroid responsiveness initially suggested primary inflammatory lung disease (7). In contrast, our patient had no antecedent viral illness; however, she similarly demonstrated transient clinical improvement with corticosteroids before relapse. Unlike the post-infectious inflammatory mechanism described by Tiew et al., our patient's recurrence of symptoms after steroid tapering was ultimately attributable to an underlying lymphoproliferative disorder, highlighting that steroid responsiveness alone cannot distinguish cryptogenic from secondary pathology.

Pulmonary Hodgkin lymphoma can closely resemble inflammatory or vasculitic lung disease. Sławiński et al. reported primary pulmonary Hodgkin lymphoma mimicking granulomatosis with polyangiitis, presenting with pulmonary lesions that led to initial diagnostic confusion (8). Their case involved radiologic patterns suggestive of autoimmune disease, whereas our patient presented with a dense right lower lobe consolidation interpreted as organizing pneumonia. Both cases underscore a common theme: Hodgkin lymphoma may present with nonspecific pulmonary parenchymal abnormalities, leading to delayed oncologic diagnosis. However, in our case, the early CT-guided biopsy demonstrated organizing pneumonia without overt malignant cells, whereas in Sławiński et al., histologic evaluation eventually revealed primary pulmonary Hodgkin lymphoma without an intermediate organizing pneumonia diagnosis.

Accurate tissue acquisition is critical in such complex presentations. Botana-Rial et al., in a systematic review, demonstrated that mediastinal lymph node cryobiopsy (cryoEBUS) yields higher diagnostic adequacy compared with conventional EBUS-TBNA, particularly for lymphomas where architectural preservation is essential for immunophenotyping (9). In our case, initial lung biopsy sampling was insufficient to identify malignancy, capturing only reactive fibroblastic plugs. Definitive diagnosis was achieved only after EBUS-guided cryobiopsy of the FDG-avid hilar node, which provided preserved nodal architecture and enabled immunohistochemical confirmation of classic Hodgkin lymphoma. Thus, our experience directly aligns with the diagnostic advantage of cryoEBUS highlighted by Botana-Rial et al.

Agudile et al. described cavitary pulmonary Hodgkin lymphoma presenting with lung cavities mimicking infectious disease (10). Although cavitation was not observed in our patient, both cases share the feature of deceptive pulmonary imaging leading to initial misclassification as infection or inflammatory disease. Our patient's consolidation and FDG-avid nodules represent another radiologic phenotype of pulmonary Hodgkin lymphoma, reinforcing the heterogeneity of imaging findings described by Agudile et al.

Concurrent organizing pneumonia in association with lymphoma has been documented in other B-cell malignancies. Lu et al. reported pulmonary diffuse large B-cell lymphoma with coexistent organizing pneumonia, where reactive fibroblastic proliferation obscured the malignant process (11). This observation closely parallels our case: the initial CT-guided biopsy demonstrated organizing pneumonia without detectable malignancy, likely reflecting a secondary reactive process adjacent to lymphomatous involvement. Both cases illustrate that organizing pneumonia may represent a paraneoplastic or obstructive inflammatory response rather than a primary idiopathic disorder.

Jose et al. described primary pulmonary lymphoma presenting as persistent consolidation initially treated as pneumonia, emphasizing delayed diagnosis due to overlapping clinical and radiologic features (12). Our patient similarly underwent empirical antibiotic therapy and extensive infectious evaluation before alternative diagnoses were considered. However, unlike the primary pulmonary lymphoma described by Jose et al., our case demonstrated significant mediastinal and hilar lymphadenopathy on PET-CT, indicating nodal Hodgkin lymphoma with pulmonary extension rather than isolated pulmonary origin.

Jain et al. reported Hodgkin lymphoma presenting as multiple cavitary lung lesions, highlighting that pulmonary involvement may precede classic nodal symptoms (13). While our patient did not exhibit cavitary lesions, she lacked constitutional “B symptoms” such as weight loss or night sweats at presentation, similar to the atypical systemic profile described by Jain et al. In both cases, absence of classic lymphoma features contributed to initial diagnostic delay.

Chowdhary et al. described primary pulmonary Hodgkin lymphoma with coexisting pulmonary histoplasmosis, illustrating the potential coexistence of infection and malignancy in pulmonary presentations (14). Although no fungal infection was identified in our patient, the study underscores the diagnostic complexity in regions where infectious diseases are prevalent. Our case reinforces that even in the absence of confirmed infection, persistent consolidation with nodal metabolic activity warrants reevaluation for malignancy.

Collectively, comparison with these contemporary reports demonstrates that our patient’s presentation—isolated consolidation, transient steroid response, relapse after tapering, and subsequent identification of FDG-avid nodal disease—fits within the expanding spectrum of deceptive pulmonary manifestations of Hodgkin lymphoma. The key distinguishing feature in our case was the initial histologic diagnosis of organizing pneumonia preceding lymphoma confirmation, emphasizing that reactive inflammatory patterns may mask underlying malignancy.

CONCLUSION

This case demonstrates how classic Hodgkin lymphoma can masquerade as cryptogenic organizing pneumonia, leading to diagnostic delay. In our patient, right lower lobe consolidation with histologic features of organizing pneumonia and transient steroid response initially supported a benign inflammatory diagnosis. However, relapse after steroid tapering and detection of FDG-avid mediastinal lymphadenopathy prompted repeat evaluation. EBUS-guided cryobiopsy established the diagnosis of mixed cellularity Hodgkin lymphoma. This case emphasizes that organizing pneumonia is a reactive pattern rather than a definitive diagnosis and highlights the need for re-evaluation in persistent or atypical cases to ensure timely identification of underlying malignancy.

REFERENCES

1. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Vardiman JW, editors. WHO Classification of Tumours of Haematolymphoid Tissues. 4th ed. Lyon: IARC; 2017.
2. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024 May-Jun;74(3):229-263. doi: 10.3322/caac.21834. Epub 2024 Apr 4. PMID: 38572751.
3. National Cancer Grid (India) — NCG adult hematolymphoid management guidelines (NCG, guideline portal; Adult hematolymphoid 2019/2021 manual pages for Hodgkin lymphoma workup & staging
4. Zeng H, Ma Y, He X, Cai S, Chen P, Chen Y, Luo H. Characteristics and Follow-Up of Organizing Pneumonia Associated with Haematological Malignancies. Int J Gen Med. 2022 Jan 7;15:301-310. doi: 10.2147/IJGM.S337321. PMID: 35027840; PMCID: PMC8752074.
5. Łyżwa, E., M. Sobiecka, K. Lewandowska, I. Siemion-Szcześniak, I. Barańska, M. Klatt, R. Langfort, M. Szturmowicz, and W. Tomkowski. 2023. "Prolonged SARS-CoV-2 Infection and Organizing Pneumonia in a Patient with Follicular Lymphoma, Treated with Obinutuzumab—Challenging Recognition and Treatment" Viruses 15, no. 3: 693. https://doi.org/10.3390/v15030693
6. Zhao A, Zhao M, Qian W, Liang A, Li P, Liu H. Secondary myeloid neoplasms after CD19 CAR T therapy in patients with refractory/relapsed B-cell lymphoma: Case series and review of literature. Front Immunol. 2023 Jan 13;13:1063986. doi: 10.3389/fimmu.2022.1063986. PMID: 36713414; PMCID: PMC9880439.
7. Tiew HW, Tan JWP, Teo CHY. Delayed organising pneumonia in an immunocompromised host after a mild COVID-19 infection. BMJ Case Rep. 2023 May 16;16(5):e254737. doi: 10.1136/bcr-2023-254737. PMID: 37192779; PMCID: PMC10193096.
8. Sławiński L, Sołek JM, Miłkowska-Dymanowska J, Jesionek-Kupnicka D, Góra-Tybor J, Mikulski D, Braun M. Primary pulmonary Hodgkin's lymphoma mimicking granulomatosis with polyangiitis - a case report of diagnostic and therapeutic dilemmas. Contemp Oncol (Pozn). 2023;27(2):113-117. doi: 10.5114/wo.2023.131034. Epub 2023 Aug 20. PMID: 37794994; PMCID: PMC10546969.
9. Botana-Rial M, Lojo-Rodríguez I, Leiro-Fernández V, Ramos-Hernández C, González-Montaos A, Pazos-Area L, Núñez-Delgado M, Fernández-Villar A. Is the diagnostic yield of mediastinal lymph node cryobiopsy (cryoEBUS) better for diagnosing mediastinal node involvement compared to endobronchial ultrasound-guided transbronchial needle

aspiration (EBUS-TBNA)? A systematic review. Respir Med. 2023 Nov;218:107389. doi: 10.1016/j.rmed.2023.107389. Epub 2023 Aug 12. PMID: 37579981.
10. Agudile EP, Elkhawas I, Solangi Z, Schembri F, Manzoor K. Cavitary Hodgkin Lymphoma of the Lung. Cureus. 2024 Apr 12;16(4):e58152. doi: 10.7759/cureus.58152. PMID: 38741830; PMCID: PMC11089491.
11. Lu X, Zhou D, Zou L, Zhou G. Pulmonary diffuse large B-cell lymphoma with concurrent organizing pneumonia: a case report. Front Med (Lausanne). 2025 Aug 6;12:1599268. doi: 10.3389/fmed.2025.1599268. PMID: 40842531; PMCID: PMC12364685.
12. Jose M, Jayanthi N, P H, P S. Unveiling the Unseen: A Rare Case of Primary Pulmonary Lymphoma. Cureus. 2024 Oct 6;16(10):e70959. doi: 10.7759/cureus.70959. PMID: 39507165; PMCID: PMC11540108.
13. Jain E, Al-Tarbsheh AH, Oweis J, Jacobson E, Shkolnik B. Hodgkin's Lymphoma Presenting as Multiple Cavitary Lung Lesions. Eur J Case Rep Intern Med. 2021 Dec 1;8(12):003024. doi: 10.12890/2021_003024. PMID: 35059335; PMCID: PMC8765687.
14. Chowdhary GS, Mehta R, Tyagi R. Primary pulmonary Hodgkin's lymphoma with pulmonary histoplasmosis. Med J Armed Forces India. 2020 Oct;76(4):462-465. doi: 10.1016/j.mjafi.2018.11.009. Epub 2019 Apr 2. PMID: 33162658; PMCID: PMC7606111.