



Very Late Relapse of Nodular Lymphocytic-Predominant Hodgkin Lymphoma in a Young Adult

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Abstract

Background: Our study describe a case of very late relapse in a patient treated for Nodular Lymphocytic-Predominant Hodgkin Lymphoma (NLPHL). NLPHL is the rarest subtype of Hodgkin Lymphoma (HL), accounting for up to 10% of these neoplasms with an annual incidence of 0.1 to 0.2/100,000. The characteristic cells of this type of lymphoma are multilobulated, surrounded by a tumor micro-environment composed mostly of lymphocytes, histiocytes, and follicular dendritic cells. Unlike classic HL, LNHL typically expresses pan-B markers (CD19, CD20, CD79a, CD22) and germinal center markers (BCL-6), and is negative for CD15 and CD30. In addition to having a distinct morphology and Immunophenotype (IF) from classic Hodgkin Lymphoma (HL). NLPHL usually has an indolent course, favorable prognosis, and absence of B symptoms. The most conservative treatment includes surgery, active surveillance, radiotherapy alone, anti-CD20 antibody therapy, and low-intensity chemotherapy. Very Late Relapse (VLR), which occurs after 10 years from the initial diagnosis, is a rare event.

Case report: A 29-year-old male patient presented in October 2024 with a late recurrence of NLPHL in the right axillary region, 14 years after his initial Stage IIIA diagnosis at age 14. While the primary treatment in 2009 involved ABVD and radiotherapy, the localized relapse (Stage IA Bulky) was managed with two cycles of R-CVP and consolidative radiation. The patient achieved a complete remission by February 2025 and currently remains in follow-up with no evidence of a second recurrence.

Conclusion: While late relapses are more frequent in NLPHL than in other lymphomas, patients typically maintain high second remission rates. However, vigilant monitoring of cumulative treatment-related late effects is essential to minimize long-term morbidity and mortality.

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Introduction

Representing approximately 5-10% of all Hodgkin lymphoma cases, Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL) remains a rare entity with an incidence of 0.1 to 0.2 per

100,000 person-years. Although management has historically mirrored that of Classical Hodgkin Lymphoma (cHL), its distinct pathological and clinical profile has sparked an ongoing debate regarding the suitability of cHL-standardized protocols for this specific subtype [1-4].



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NLPHL exhibits a bimodal age distribution, peaking in childhood and again in the third to fourth decades of life. The disease shows a notable male predominance, with approximately 75% of patients presenting with localized peripheral lymphadenopathy and early-stage disease. Unlike Classical Hodgkin Lymphoma (cHL), clinical features such as bulky disease, mediastinal involvement, and B symptoms are infrequent. While Positron Emission Tomography (PET) remains a valuable tool for staging and response assessment, Standardized Uptake Values (SUVs) in NLPHL are typically lower than those observed in cHL [1,3,5].

The diagnosis of NLPHL necessitates the identification of Lymphocyte-Predominant (LP) cells, typically situated within large nodules of B lymphocytes. While typical growth patterns (Patterns A and B) are common, variant patterns including T-cell-rich nodular or diffuse B/T-cell-rich arrangements (Patterns C–F) are frequently associated with advanced disease and higher recurrence rates. Architecturally and immunophenotypically, LP cells are distinct from the Hodgkin and Reed-Sternberg (H-RS) cells seen in classical Hodgkin lymphoma. Specifically, LP cells consistently express the B-cell marker CD20 but lack CD30, whereas H-RS cells are characteristically CD30-positive and only rarely express CD20 [1-3].

Through modern risk-stratified and response-adapted modalities, NLPHL has become a highly curable malignancy, with 80–90% of newly diagnosed patients becoming long-term survivors. Despite this success, 20–30% of patients experience a relapse following first-line therapy. While the majority of these events occur within three years of achieving complete remission, Very Late Relapses (VLR)—defined as those occurring ten or more years after the initial diagnosis—represent rare but clinically significant events.⁴⁻⁷ This report aims to describe a successful therapeutic intervention for VLR using Rituximab and chemotherapy, providing a detailed account of the patient's clinical outcome and recovery.

Case report

A male patient was admitted to the service at 14 years of age presenting with a 4-month history of cervical, supraclavicular, and inguinal lymphadenopathy, in the absence of B symptoms. Following a biopsy and staging workup with CT scans (confirming involvement of cervical, supraclavicular, and inguinal nodes), he was diagnosed with Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL), Stage IIIA. The patient completed three cycles of ABVD on December 30, 2009, followed by radiotherapy, which concluded on March, 2010. In October 2024, at age 29, the patient presented with progressive right axillary lymphadenopathy of two weeks' duration, without B symptoms. A Computed Tomography (CT) scan revealed globose, post-contrast enhancing right axillary lymph nodes (Figure 1), measuring up to 4.3 x 3.7 cm. **A repeat biopsy confirmed recurrent NLPHL.** Following staging with Positron Emission Tomography (PET-CT) (Figures 2), the disease was classified as Stage IA with Bulky disease. Treatment consisted of two cycles of R-CVP (Rituximab, Vinblastine, cyclophosphamide and Prednisone) followed by radiotherapy, resulting in an excellent therapeutic response. Complete remission was achieved in February 2025.

Discussion

NLPHL is a rare clinical entity, accounting for approximately 5% of all Hodgkin lymphoma cases. As emphasized [1,3] NLPHL is biologically distinct from Classical Hodgkin Lymphoma (cHL). While cHL is defined by CD30-positive Reed-Sternberg cells, NL-



Figure 1: Computed Tomography scan revealed globose, post-contrast enhancing right axillary lymph nodes.



Figure 2: PET-CT reveals lymph node marking in the right axillary region with high SUV.

PHL is characterized by “popcorn cells” or Lymphocyte Predominant (LP) cells. These cells consistently express B-cell markers such as CD20 and are typically negative for CD30.

In this case, the immunophenotype was essential to confirm the lineage during the 2024 recurrence, allowing for a therapeutic shift from a cHL-standardized protocol (ABVD) to a B-cell-targeted approach with Rituximab.

The patient presented with a recurrence 14 years after the initial treatment. Population-based studies [5,6], demonstrate that patients diagnosed as children or young adults face a life-long risk of late relapses (defined as events occurring after a 5-year disease-free interval). Unlike cHL, where the majority of relapses occur within the first 2 to 3 years, NLPHL exhibits an indolent but persistent behavior with a higher propensity for late events. El-Galaly et al [4] describe these events as “needles in a haystack” due to their rarity, yet they underscore that such relapses significantly impact long-term survivorship and necessitate lifelong surveillance.

Historically, NLPHL was managed using cHL protocols, as seen in this patient's initial treatment in 2009. However, Gorde-Grosjean et al² and Spinner et al³ highlight a shift toward risk-adapted and biology-driven approaches.

Literature suggests that patients with Late Relapse (LR) have a significantly better prognosis and Overall Survival (OS) compared to those with early relapse [6,7]. The patient's excellent response and complete remission by February 2025 corroborate the highly chemosensitive nature of NLPHL, even after long intervals.

However, as highlighted by the Danish and Hungarian registry studies, long-term morbidity remains a primary concern. Repeated exposure to radiotherapy and chemotherapy necessitates rigorous monitoring for late effects, such as secondary malignancies and cardiovascular toxicity.

Conclusion

In conclusion, the characteristics of Very Late Relapse (VLR) in NLPHL closely mirror those of the primary disease. Patients with VLR benefit from conventional-dose chemotherapy, though regimens must be meticulously tailored to prior therapies with specific attention to cumulative toxicity. With the implementation of modern risk-adapted strategies and lifelong surveillance, late recurrences demonstrate a favorable prognosis and superior Overall Survival (OS) compared to early relapses.

References

1. Binkley MS, Advani RH. SOHO state of the art updates and next questions treatment approaches for nodular lymphocyte-predominant Hodgkin lymphoma. *Clin Lymphoma Myeloma Leuk*. 2023; 23: 471-476.
2. Gorde-Grosjean S, Guimard G, Lambilliotte A, Coulomb-Lhermine A, Montravers F, Landman-Parker J. Nodular lymphocyte-predominant Hodgkin lymphoma in children: clinical course, biology, and management. *Bull Cancer*. 2014; 101: 881-890.
3. Spinner MA, Varma G, Advani RH. Modern principles in the management of nodular lymphocyte-predominant Hodgkin lymphoma. *Br J Haematol*. 2019; 184: 17-29.
4. El-Galaly TC, Glimelius I. Late relapses in Hodgkin lymphoma - should we search for the needle in the haystack? *Br J Haematol*. 2022; 198: 11-13.
5. Andersen MD, Hamilton-Dutoit S, Modvig L, Vase M, Christiansen I, Christensen JH, Dahl-Sørensen RB, Stoltenberg D, Kamper P, d'Amore F. Late recurrence of lymphoid malignancies after initial treatment for Hodgkin lymphoma - a study from the Danish Lymphoma Registry. *Br J Haematol*. 2022; 198: 50-61.
6. Pinczés L, Miltényi Z, Illés Á. Young adults diagnosed with Hodgkin lymphoma are at risk of relapsing late: a comprehensive analysis of late relapse in Hodgkin lymphoma. *J Cancer Res Clin Oncol*. 2018; 144: 935-943.
7. Andersen MD, Hamilton-Dutoit S, Modvig L, Vase M, Christiansen I, Christensen JH, Dahl-Sørensen RB, Stoltenberg D, Kamper P, d'Amore F. Late recurrence of lymphoid malignancies after initial treatment for Hodgkin lymphoma - a study from the Danish Lymphoma Registry. *Br J Haematol*. 2022; 198: 50-61.