International Research Journal of Pharmacy and Medical Sciences
ISSN (Online): 2581-3277

Nodular Lymphocyte-Predominant Hodgkin Lymphoma with Splenic and Multiple Bone Involvement: Case Report

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Abstract— *Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL), accounting only for 5% of all HL cases, presents as a diagnostic challenge due to its rare occurrence and diverse morphological features. The malignant lymphocyte predominant (LP) cells in NLPHL are positive for CD20 but lack CD30 and CD15, in contrast to the disease-defining Hodgkin and Reed-Sternberg (H-RS) cells in classical Hodgkin lymphoma (cHL). We report a rare instance of NLPHL stage IV B with spleen and multiple bone involvement in a young patient, diagnosed based on lymph node biopsy and PET/CECT. Furthermore, this case emphasizes the successful application of the R-CHOP regimen in the management of advanced NLPHL, highlighting its potential as a viable therapeutic strategy.*

Keywords— *CD20, Hodgkin Lymphoma, Nodular Lymphocyte-Predominant Hodgkin Lymphoma, NLPHL, R-CHOP, Rituximab.*

I. INTRODUCTION

Nodular lymphocyte-predominant Hodgkin Lymphoma (NLPHL), a unique subtype of Hodgkin lymphoma (HL), accounts for roughly 5% of all HL cases. Typically affecting men, it presents as a localized disease with an indolent clinical history. Due to its low prevalence and diverse morphological features, it is often misdiagnosed. The incidence rate is 0.1-0.2/100,000/year.[1]

Compared to the disease-defining Hodgkin and Reed-Sternberg (H-RS) cells in classical Hodgkin lymphoma (cHL), the malignant lymphocyte predominate (LP) cells in NLPHL are persistently positive for CD20 but devoid of CD30 and CD15. Epstein-Barr virus (EBV) is rarely found in NLPHL, but it has been significantly linked to cases of cHL.[2]

NLPHL has a nodular development pattern, with diffuse and nodular architectures coexisting under specific situations. It consists of small lymphocytes, histiocytes, eosinophils, dispersed LP cells, and plasma cells. LP cells have vesicular polylobulated nuclei and prominent, peripheral nucleoli surrounded by small lymphocytes.[3]

Most NLPHL patients are diagnosed with stage I or II, characterized by painless peripheral lymphadenopathy in the axilla or neck, often affecting a single lymph node station. Central lymph node involvement is uncommon. Constitutional B symptoms like fever, night sweats, and weight loss are rare due to the lack of pro-inflammatory cytokines in LP cells. Organ and bone marrow involvement is unusual. Stage III or IV patients often progress to diffuse large B-cell lymphoma (DLBCL).[4] The Ann Arbour staging system, with Cotswolds modifications, is utilized for NLPHL staging, which includes clinical evaluation, laboratory investigations, and positron emission tomography (PET) imaging.[5]

The current case report highlights the organ and multiple bone involvement in a young female patient with NLPHL, which is relatively rare, along with a review of the existing treatment options.

II. CASE REPORT

A 25-year-old female patient presented with a painless swelling in the right axillary region for the past 1 year, now associated with fever for 1 month. She also complained of a 5kg weight loss in the previous 2-3 months and loss of appetite. She denied any itching or bleeding symptoms. Physical examination revealed an enlarged lymph node located in the bilateral axillary region and a few lymph nodes were palpated below the diaphragm. The spleen was just palpable. The remaining physical examinations were normal.

A complete blood count disclosed a hemoglobin level of 8.4 g/dL, white blood cell count (WBC) of 7300/mm3, and platelet count of 441000/mm3. The results of the biochemical test showed raised levels of lactate dehydrogenase (LDH) at 504 IU/L, Alkaline phosphatase (ALP) at 193 IU/L, and globulin at 3.9 g/dl. Additionally, the ESR levels were also found to be significantly high at 98 mm/hr.

The patient then underwent an incisional biopsy of the right axillary lymph node. A microscopic examination revealed lymph nodes with effaced architecture due to nodules of small to medium-sized lymphoid cells. Admixed large mononuclear cells, few binucleated, and occasional multinucleated lymphoid cells with vesicular nuclei and prominent eosinophilic nucleoli cells were present. Few multilobulated popcorn-like cells were seen. Lacunar cells and sclerosis with nodularity absent.

Immunohistochemistry revealed that nodules were made up of CD20-positive small B lymphoid cells. Large cells are positive for CD20, EMA (some cells), LCA, and PAX5 but are negative for CD15 and STAT6. CD30 is occasionally positive in large cells. CD3 is expressed in T cells and forms rosettes around large cells.

A whole-body PET/CECT scan demonstrated tracer uptake in bilateral supraclavicular lymph nodes (SUVmax 5.63),

Sneha Mavis M, "Nodular Lymphocyte-Predominant Hodgkin Lymphoma with Splenic and Multiple Bone Involvement: Case Report," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 2, pp. 74-76, 2024.

bilateral axillary and deep pectoral lymph nodes (SUVmax 28.92), and hypodense lesion in the spleen (SUVmax 8.56). The tracer uptake was also seen in abdominal and bilateral pelvic lymph nodes. Mild uptake was seen in the left scapula, multiple vertebrae (T4, T5, T1l, LS vertebrae), sacrum and bilateral pelvic bones (SUVmax in T11 vertebra 16.61), soft tissue component extending into the sacral spinal canal, sacral foramen, and right sacroiliac joint (SUVmax 25.97). The microscopic examination and immunohistochemistry confirmed the diagnosis of NLPHL. Based on the PET/CT findings and a history of B symptoms, NLPHL stage IV B was diagnosed.

Six cycles of chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab (R-CHOP) were administered to the patient. During each cycle, the patient received rituximab 600mg, cyclophosphamide 1000mg, doxorubicin 70mg, vincristine 2mg, and prednisone 100mg for all six cycles. The patient handled chemotherapy well, requiring no hospitalizations for fever or neutropenia and exhibiting no major toxicities. The patient is currently being followed up.

III. Discussion

NLPHL is a slow-growing CD20-positive variant of Hodgkin lymphoma. The variable growth patterns in NLPHL are associated with relapse and progression to DLBCL. Determining the diagnostic border between DLBCL and NLPHL is challenging, due to variable histologies present. Similarities between the two diagnoses, established by morphology and immunophenotype include the rare presence of big tumor B-cells and the milieu rich in lymphocytes and histiocytes. NLPHL shares similarities with cHL and T-cell lymphomas, and non-neoplastic conditions like germinal center transformation make it difficult to diagnose.[6]

Early-stage NLPHL has an excellent prognosis, with progression-free survival and a rate of overall survival exceeding 90% following involved-field radiotherapy (IF-RT) alone (stage IA) or combined modality treatment which includes brief chemotherapy followed by two cycles of ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) chemotherapy accompanied by IF-RT (early stages other than stage IA). However, despite more intensive first-line treatment with 6–8 cycles of multiagent chemotherapy, individuals with advanced condition at diagnosis are likely to relapse.[7]

Patients with advanced NLPHL have also been treated using standard therapy for advanced cHL. However, the most employed chemotherapies in advanced cHL, namely ABVD and escalating BEACOPP, may not be optimum for treating advanced NLPHL. A retrospective analysis of 42 patients with advanced NLPHL who received first-line treatment with ABVD or ABVD-like protocols found that 40% of patients experienced lymphoma recurrence, indicating that ABVD is not the optimal regimen for newly diagnosed advanced NLPHL due to its high recurrence rate.[8] The aggressive BEACOPP protocol, which includes bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone, has been evaluated in advanced NLPHL patients, with 8-year overall survival (OS) and progression-free survival (PFS) rates of 76.2% and 87.4%, respectively.[9]

A few retrospective studies have investigated the use of rituximab in conjunction with conventional chemotherapy. A total of 308 patients who had stage II-IV disease treated at 20 centers in Italy, received chemotherapy alone or chemotherapy plus rituximab. The chemotherapy-alone group received ABVD, while the chemotherapy plus rituximab group received either ABVD or CHOP. The 5-year PFS rate for rituximab-containing patients was 89.6%, significantly better than the group treated without rituximab.[10] The B-NHL-directed R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) regimen produced encouraging results. 85.7% was the estimated 10-year PFS in a retrospective single-center analysis involving 14 patients with stage III/IV NLPHL.[11]

IV. Conclusion

NLPHL is still a very rare condition with an adequate overall prognosis in both children and adults. Here, we report a case of a 25-year-old female patient who was newly diagnosed with NLPHL stage IV B, with splenic and multiple bone involvement. She has been successfully treated with the R-CHOP regimen. However, there is a lack of randomized controlled trials focused on NLPHL treatment results. The case supports the use of rituximab in combination with conventional chemotherapy regimens as first-line therapy, but prospective studies are needed to verify the additional advantage of this combined treatment strategy.

Acknowledgment

I express gratitude to Dr. C.N. Nalini, M.Pharm., Ph.D., Principal, C L Baid Metha College of Pharmacy for providing all the essential facilities in bringing out this paper. I thank my beloved parents for trusting and supporting. Above all, I thank and praise the Almighty God for the grace and blessing throughout the entire work.

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