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Case Report

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A Case Report of Nodular Lymphocyte Predominant Hodgkin Lymphoma: A Rare Lymphoma in Myanmar

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ABSTRACT

Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is a germinal center–derived B-cell neoplasm. It is made up of scattered large neoplastic B cells with multilobulated nuclei (lymphocyte-predominant [LP] cells) located within nodules that are predominantly occupied by mantle zone B cells and follicular dendritic cells (FDCs). It manifests with lymph node involvement, and approximately 60% of all cases are attributed to early-stage disease.

We presented the case of a 23-year-old young man with left axillary lymph node enlargement for two weeks. He has no loss of appetite, no weight loss, and no fever during this period. Two days prior to consultation, he got tender sensation from these nodes along with a fever and consulted a surgeon. He had history of pulmonary tuberculosis infection and got complete anti-TB drugs at the age of 8 years old. The ultrasound examination of the left axilla shows multiple matted lymph node enlargement, and the largest one is 3.2 x 2.1 cm. The surgeon performed an excisional biopsy and sent it for histopathological examination. The histological section shows complete architectural effacement by a nodular proliferation with diffuse areas containing scattered large cells. Immunohistochemistry confirmed the diagnosis of NLPHL, with LP cells positive for CD20, BCL6, and EMA, and negative for CD30, CD15, CD3, CD4, MUM1, TIA1, and CD56. The true incidence of NLPHL in Myanmar is unknown due to a lack of reported cases. This case highlights the importance of early diagnosis and to give proper immediate management for the disease. A definite diagnosis was achieved through careful histopathological evaluation combined with immunohistochemical analysis.

Keywords: Rare Lymphoma, Lymphocyte Predominant (LP) Cells, Germinal Center-Derived B Cell Neoplasm, BCL6 Expression, B Cell Related Markers Expression

Introduction

Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is a germinal center–derived B-cell neoplasm. These neoplastic cells known as lymphocyte-predominant cells (LP cells) are found within the nodules primarily composed of mantle zone B cells and follicular dendritic cells (FDCs). LP cells have multilobated nuclei and scanty cytoplasm [1]. This lymphoma is characterized by the involvement of lymph nodes with approximately 60% of cases are diagnosed at early stages (stage I and II), and this prevalence being even higher in children, accounting for 80% [2]. Unlike Classic Hodgkin Lymphoma (CHL), the involvement of NLPHL tends to have a lower concentration in supradiaphragmatic lymph nodes. The cervical and axillary regions are affected in around 40% of cases, while the iliac and inguinal regions are involved in approximately 20%. Notably, Bulky disease (greater than 50 mm) is less commonly seen in NLPHL, with an occurrence of up to 40% of cases, compared CHL [3].

Case Report

A previously healthy 23-year-old man visited the surgical clinic with a fever lasting two days and left axillary lymph node enlargement. He noticed that this lymph node was enlarged since two weeks ago. However, he had no history of fever, cough, night sweat, or loss of appetite during this period. Two days before his consultation, he developed a fever with chills and rigors along

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with tenderness in the left axillary region. He had a history of pulmonary tuberculosis infection at the age of 8 years and got complete anti-tuberculosis regimen for 6 months. Ultrasound examination of the left axilla showed multiple matted lymph node enlargement with the largest measuring 3.2 x 2.1 cm. There was no palpable lymphadenopathy at other sites or organomegaly. Laboratory investigation showed a haemoglobin level of 12.1 mg/dl, a white blood cell counts of 10 x 10^9/L and a platelet count of 335 x 10^9/L. Renal and liver function tests were within normal limits. Serological screenings for HBs antigen, HCV antibody, and HIV antibody were negative. Furthermore, chest X-ray and abdominal ultrasound scans exhibited no noteworthy findings. An excisional lymph node biopsy was performed. The histological examination of lymph node showed complete architectural effacement of lymph node by a nodular proliferation with diffuse areas containing scattered large neoplastic cells (Figure 1a and 1b). These large neoplastic cells have multilobated nuclei with one or more nucleoli, and pale cytoplasm resembling popcorn cells (Figure 1c and 1d). The surrounding microenvironment is composed of numerous small lymphoid cells and histiocytes, with an absence of neutrophils and eosinophils.

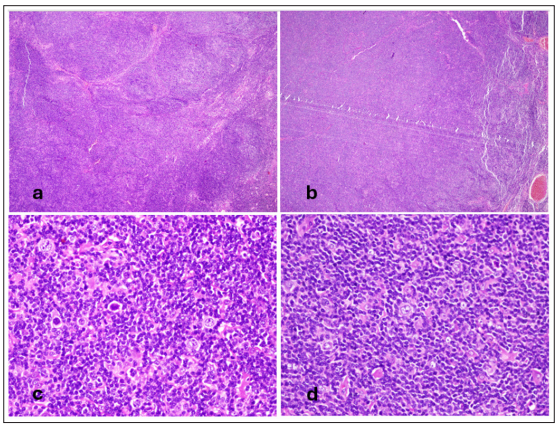

Figure 1: The lymph node architecture is completely effaced by a nodular proliferation with diffuse areas (a and b). Scattered large neoplastic cells, known as popcorn cells, are observed; these cells exhibit multilobated nuclei with one or more nucleoli and pale cytoplasm (c and d).

Immunohistochemical staining showed that the large neoplastic LP cells were positive for CD4, D20, CD30, BCL6, EMA and MUM1 (Figure 2a-f) and negative for CD3, CD15, TIA1 and CD56. These findings match the diagnosis of NLPHL.

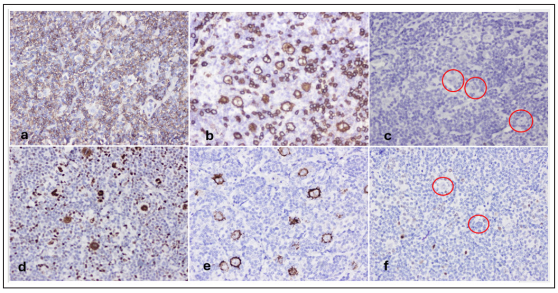

Figure 2(a-f): Immunohistochemistry of tumor. (a) large neoplastic cells are surrounded by CD4+ T cells. (b) Neoplastic cells, LP cells are positive for CD20. (c) CD30-negative cells are highlighted by red circles. (d) Neoplastic cells show positivity for BCL6, and (e) EMA positivity is observed. (f) MUM1 negative tumor cells are indicated by red circles.

The patient underwent six cycles of R-CHOP chemotherapy (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone) over six months. His clinical condition remained stable, with no recurrence to date.

Discussion

According to the German Hodgkin lymphoma study group, approximately 40% of NLPHL cases occur in the cervical or axillary regions, while around 20% are found in the iliac and inguinal areas [3]. In our case, the patient presented with isolated left axillary lymph node enlargement, with no evidence of involvement at other sites.

Most NLPHL patients initially present with painless, localized lymphadenopathy, sometimes persisting for years. Approximately 40% of patients are diagnosed at an advanced stage (stage III or IV) [4,5]. Here, the patient reported noticing lymph node enlargement two weeks before consultation. During this period, he reported no history of fever, cough, night sweats, or loss of appetite. After that, two days before consulting a clinician, the patient developed a fever accompanied by chills and rigors, along with tenderness in the left axillary region, prompting him to consult a surgeon. According to Thomas A. Ollila et al., approximately 15-20% of patients with NLPHL experience B symptoms, such as night sweats, fever, and significant weight loss; however, these symptoms are not associated with specific laboratory findings [5].

During his consultation with the surgeon, the patient had been doing the basic medical investigations, but all results were unremarkable.

NLPHL predominantly affects males, with a male-to-female ratio of 2.5 to 3:1. It spans a wide age range, from childhood to over 80 years old with most cases diagnosed between the ages of 30 and 60 [6,7]. Our patient, a young adult male, was diagnosed at 23 years old.

NLPHL can be associated with autoimmune lymphoproliferative syndrome (ALPS) and other primary immunodeficiency syndromes as reported in studies by Van den Berg et al. and Lorenzi, L et al. [8,9]. Unlike classical Hodgkin lymphoma (CHL), Epstein-Barr virus (EBV) is not significantly involved in the development of NLPHL and EBV positivity is extremely rare in these cases [10]. The tumor cells in NLPHL are clonal germinal center B cells with ongoing somatic hypermutation and intraclonal diversity in their rearranged immunoglobulin genes [11].

According to the study of Bharat N. Nathwani et al., lymph nodes affected by NLPHL exhibit partial or complete architectural disruption due to a nodular proliferation, which may include diffuse areas. The neoplastic LP cells are large and characterized by multilobated nuclei containing one or more nucleoli. These cells have pale cytoplasm often resembling popcorn; and account for 1–5% of the overall mass. While LP cells typically found singly, occasional clusters or increased numbers may be observed within the nodules. The immune microenvironment consists of numerous non-neoplastic B and T cells, which frequently displayed activated morphological characteristics, such as clear cytoplasm and a more open chromatin structure [12].

In our case, the axillary lymph node excisional biopsy showed complete architectural effacement by a nodular proliferation with diffuse areas. Scattered large neoplastic cells characterized by multilobated nuclei with one or more nucleoli, and pale cytoplasm resembling popcorn cells were observed. The surrounding microenvironment is composed of numerous small lymphoid cells and histiocytes. Notably, neutrophils and eosinophils were absent.

The majority of NLPHL cases express a wide range of B-cell markers, including CD20, CD79a, OCT2, BOB1, and PU.1. Germinal center B-cell markers, such as BCL6, LMO2, and HGAL, are also positive in most cases, whereas CD10 is typically negative. LP cells are usually negative for CD30 and only rarely express CD15 [1]. In our case, the large neoplastic popcorn-like cells were positive for CD20, BCL6 and EMA but negative for CD4, CD30 and MUM1. They are also negative for CD3, CD15, TIA1 and CD56. Here the neoplastic cells have aberrant expression of EMA on immunostaining.

Regarding clinical course, relapses are more common in NLPHL compared to CHL according to study of European Task Force on Lymphoma project on lymphocyte predominance Hodgkin disease [13]. We need to do closed clinical follow up for this young adult man.

Treatment options depend on risk stratification and disease staging, ranging from active surveillance for asymptomatic patients without organ involvement or bulky disease to intensive chemotherapy for advanced diseases. In our case, the patient underwent six cycles of R-CHOP, achieving a good clinical response. A post-treatment PET scan shows no evidence of disease. No further treatment was required, and the patient is being monitored through regular follow-up.

Treatment for disease recurrence should be determined based on several factors, including the histology at the time of relapse, the interval until relapse, the extent of disease upon recurrence, and previous treatments received [14].

Patients with NLPHL have a better prognosis than those with CHL, even when considering stage and baseline characteristics. Although there is a noted association between radiation therapy and improved disease-specific survival (DSS) and overall survival (OS) in this cohort, the use of radiation among NLPHL patients is decreasing. Therefore, distinct treatment strategies for NLPHL are necessary for both early and advanced stages of the disease as emphasized by Gerber, N. K et al. [15].

Here, the proper morphological examination and appropriate immunohistochemical staining are essential for the definite diagnosis of NLPHL. This case highlights the importance of early diagnosis and timely management to achieve favorable outcomes.

Statement of Ethics

The authors have no ethical conflicts to disclose. Informed consent was obtained from the patient.

Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Win Myat Oo was responsible for the concept designing, laboratory diagnosis through histologic morphology, immunohistochemical study and confirmation of the case diagnosis. Sein Win conducted case investigation, case review and clinical management. Nyein Chan Aung performed the literature search and prepared the manuscript. The case was conducted in Department of Clinical Haematology, North Okkalarpa General and Teaching Hospital, Yangon, Myanmar.

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