A CASE OF HODGKIN LYMPHOMA MIMICKING NON HODGKIN DIFFUSE LARGE B CELL LYMPHOMA

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Hodgkin lymphoma in elderly patients is rare. We present a case of Hodgkin Lymphoma manifesting in a 75-year-old man with clinical and pathologic characteristics suggestive of Diffuse Large B-Cell Lymphoma. This case illustrates the potential for diagnostic confusion.

Keywords: Hodgkin Lymphoma, minicking DLBCL

I. INTRODUCTION

Hodgkin Lymphoma is common in the second and third decades of life. After 65, Hodgkin disease is very rare. Hodgkin lymphoma is far different from non-Hodgkin Lymphoma in terms of clinical and pathologic characteristics. Patients usually present with cervical adenopathy in 60 - 80% of cases. Patients usually have clinical progression in the following pattern: unilateral cervical lymph nodes, then mediastinal lymph nodes, and then contralateral cervical lymph nodes followed by the lymph nodes present in the infra-diaphragmatic region (abdominal lymph nodes, inguinal nodes). The disease also has a different treatment strategy and a better prognosis than non-Hodgkin Lymphoma. Non - Hodgkin Lymphoma has a variety of clinical manifestations. Lymphadenopathy is the most common presentation and nodes can appear in many sites. The disease also manifests in the extra-nodal sites. About 20% of patients have constitutional symptoms. We report a case of Hodgkin Lymphoma characterized by demographic, clinical, and pathological features that were very similar to those of non-Hodgkin diffuse large B cell lymphoma.

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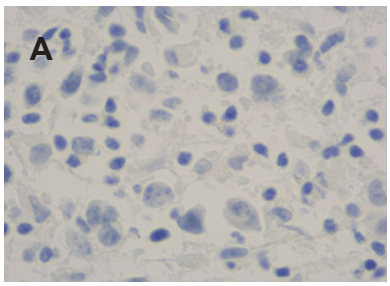
II. CASE PRESENTATION

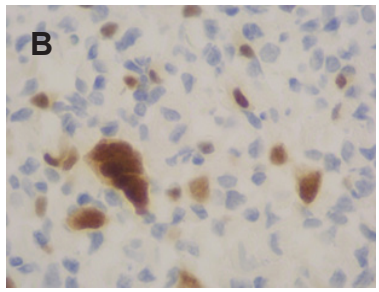
A 75 years old male patient presented with bilateral inguinal adenopathy with no B symptoms. On clinical examination, 2 - 3 cm inguinal lymph nodes were present, soft on palpation and are concentrated in clusters. The abdomen was soft, no hepato-splenomegaly, and no abnormal mass. In addition, there were no other peripheral lymph nodes in other sites. There was no mediastinal adenopathy on thoraco-abdominal CT scan, but there were multiple para-aortic and iliac lymph nodes, ranging from 1.0 to 3.0 cm.

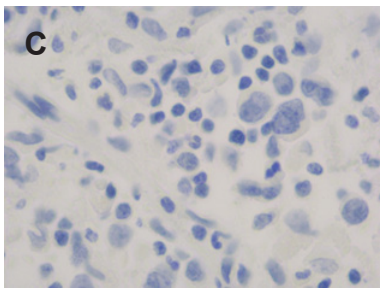
The patient had an open biopsy of the inguinal lymph nodes. The pathological result was reactive inflammatory lymph nodes, without malignant cells. Patient then had an abdominal laparoscopic lymph node biopsy. The histopathological results showed that there was presentations of numerous reactive lymphocytes admixed with non-classic popcorn-shaped RSC and immunohistochemical staining initially suggested a diagnosis of Hodgkin Lymphoma (Hanoi Medical University Hospital). Because of the patient's advanced age and infra-diaphragmatic presentation, we were initially skeptical of this diagnosis. We consulted other pathological

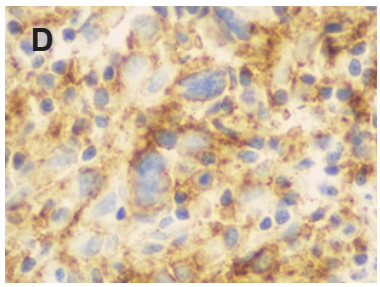
centers. Viet Duc Hospital suggested the diagnosis of Diffuse Large B-Cell Lymphoma. The Military Central Hospital 108 concluded Hodgkin Lymphoma, Nodular Lymphocyte Predominant subtype.

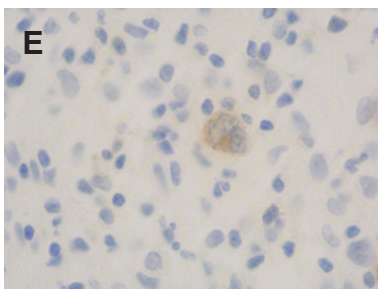
Immunohistochemistry results were as follows: CD45 (+); CD3, CD5, CD20 and CD43 (+) with similar intensity; CD15 (-), CD30 (-) with small lymphocytes but positive in large, double, or popcorn lymphocytes; PAX-5 and BOB-1 (+) were scattered cells; EMA, ALK, Fascin, and MUM-1 negative.

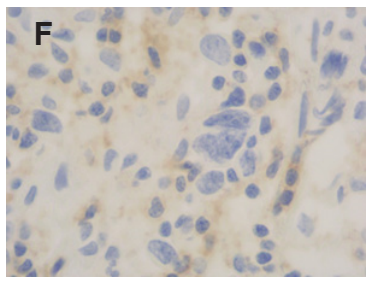


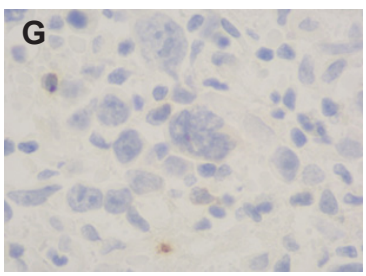


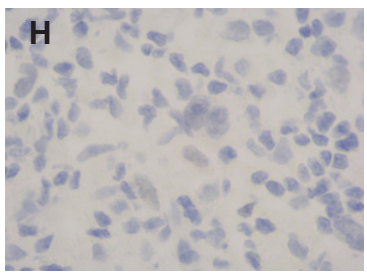












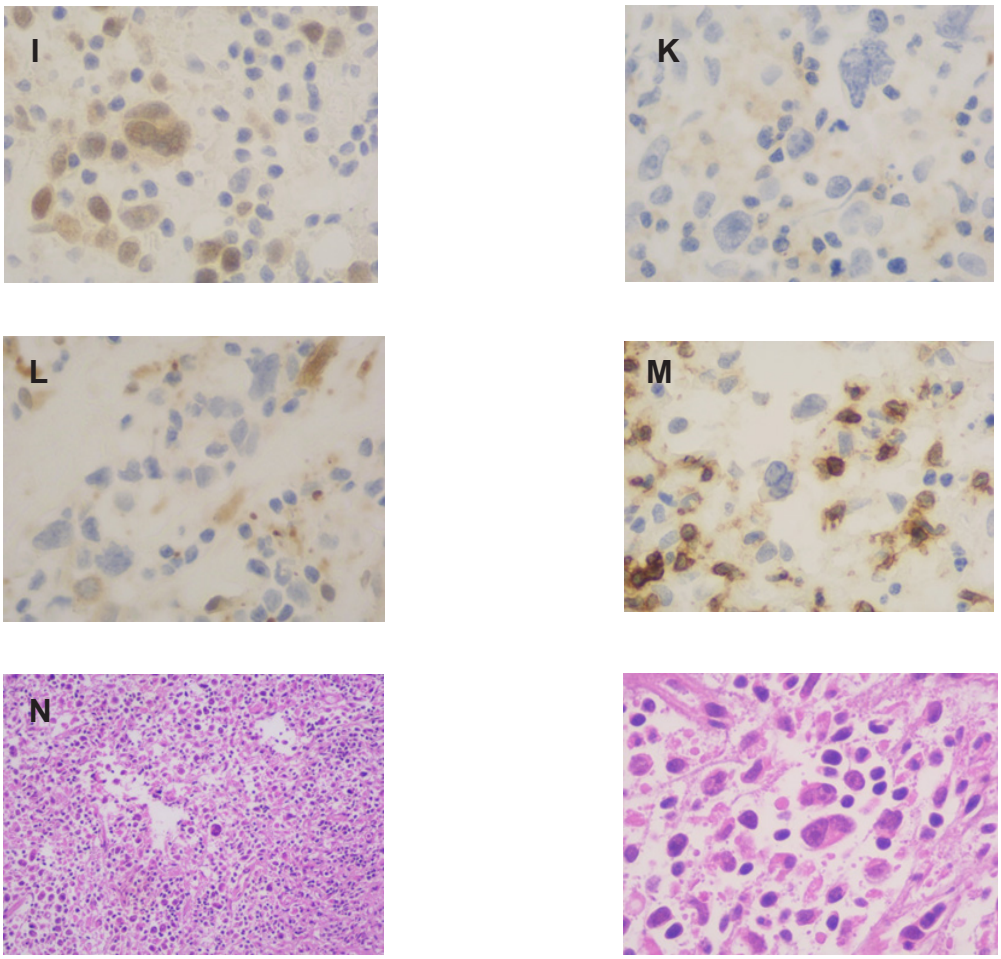


Figure 1. HE and Immunohistochemical staining

A. ALK (-)

B. BOB-1 (+) scattered with some cells

C. CD15(-)

D. CD20 (+)

E. CD30 (-) with small lymphocytes but positive in large, double, or popcorn lymphocytes

F. CD43 (+)

G. EMA(-)

H. MUM-1 (-)

I. PAX-5 (+) scattered with some cells

K. CD5 (+)

L. Fascin (-)

M. CD3 (+)

N. HE staining

On literature review, we found that Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL) accounts for about 5% of Hodgkin Lymphoma and has some pathological features that mimic Diffused Large B-Cell Lymphoma. When advanced, the treatment of these two diseases is similar. We decided to use R-CHOP chemotherapy. After 6 cycles of R-CHOP, the inguinal lymph nodes were neither palpable nor detectable on ultrasound.

Pre-treatment abdominal CT scan (Figure 2) and after 6 cycles of R-CHOP (Figure 3):

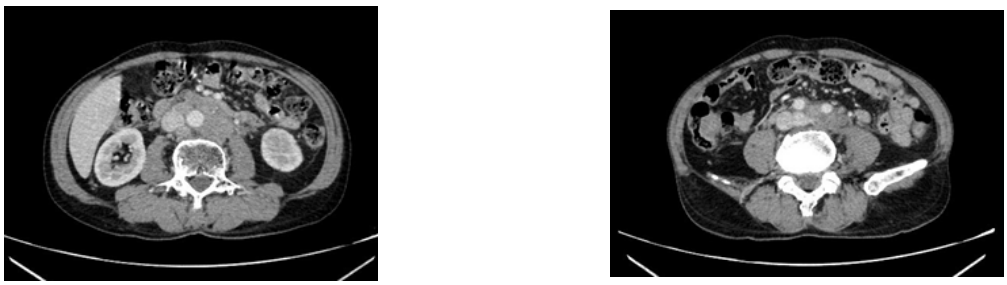


Figure 2. Pre-treatment abdominal CT scan show that there was multiple peritoneal lymph nodes along the abdominal aorta and bilateral iliac artery

Post-treatment CT scans show the disappearance of the nodes along the aorta, and the bilateral iliac arteries.

The patient completed treatment and has 2 years regular follow-up without evidence of recurrence.

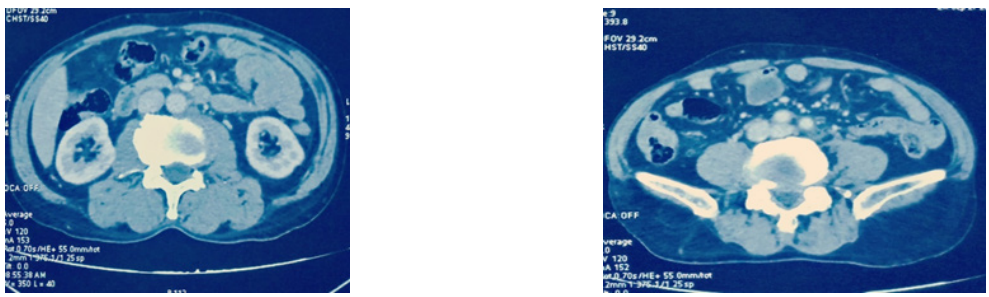


Figure 3. Post-treatment abdominal CT scan show that there was disappearance of abnormal large peritoneal lymph nodes along the abdominal aorta and bilateral iliac artery

III. DISCUSSION

Nodular lymphocyte predominant Hodgkin's lymphoma (NLPHL) is an indolent CD20(+) form of lymphoma.[1,2] The disease is no longer classified as a form of classic Hodgkin Lymphoma.[3] The main reason is that the Reed-Sternberg cell variants in this subtype of Hodgkin Lymphoma invariably express B lymphocyte markers such as CD20, unlike classic Hodgkin disease. Twelve percent of NLPHL cases may transform to Diffuse Large B-Cell Lymphoma. Therefore repeat biopsy is required at relapse.[13] One study found a transformation rate of 7.6%, and suggested that prior exposure to chemotherapy and a presentation with splenic involvement were associated with increased risks of transformation.[20]

NLPHL is an uncommon sub-type that is composed of numerous reactive lymphocytes

mixed with large popcorn-shaped Reed-Sternberg cells. These cells exhibit B-cell markers, including CD20, CD19, CD79, immunoglobulin gene rearrangements, and epithelial membrane antigen, but lack expression of CD30 and CD15, in contrast to classical HL, where RS cells typically express CD15, CD30 and lack expression of B-cell markers.[4]

The NCCN treatment guideline for this form of the disease includes.[13]:

Watch and Wait

The asymptomatic patient is observed without immediate treatment. The patient should be evaluated at least every 3 months.[16]

Surgical Excision

In children and at early stage, surgical lymph node excision may be indicated at the time of diagnosis.[13] Biasoli et al found that nearly 50% of patients had sustained complete remission after surgical lymph node excision at the time of diagnosis.[13]

Radiation Therapy

In the study of Solanki et al, stage I-II patients treated with radiation therapy had 10-year overall survival rate of 98%. The rate of radiotherapy-related secondary malignancies was not increased by the treatment (1% after 10 years).[17] Chen et al published in 2013 their study's result on a large group of patients with early-stage NLPHL showing that limited-field radiation therapy may be a potential sole treatment for early-stage disease.[9]

Immunotherapy

Rituximab, an anti-CD20 agent, has been shown significant benefit in treatment of NLPHL, especially in advanced stages.[16,19,13] Maintenance treatment with Rituximab every 6 months for 2 years is suggested to reduce the relapse rate.[12] Rituximab has been also shown to improve the treatment outcomes after histological transformation.[20]

Chemotherapy

The anthracycline-based regimens, like ABVD, BEACOPP and CHOP, are recommended to treat this form of disease.[16] The standard chemotherapy is controversial. There is evidence to support treatment with R-CHOP instead of ABVD, as there appears to be a higher rate of relapse after 10 years with ABVD.[12] BEACOPP has a worse toxicity profile.[22] Results of the Appel's trial showed that children with NLPHL treated by COPP/ABV alone, without radiation, had positive results.[21]

Combined Treatment

R-CHOP followed by radiation therapy is recommended in front-line to advanced-stage disease, while for early-stage disease radiation therapy alone (stage IA without risk factors) or brief ABVD-based chemotherapy followed by radiation therapy (early stages other than stage IA without risk factors) was suggested.[22]

Because of an overall response rate of 100% after single-agent anti-CD20 antibody treatment with rituximab and the clinical similarity to indolent B-NHL, R-CHOP was considered to be a promising alternative to ABVD.

The present analysis by Fanale and colleagues included a larger series of NLPHL patients receiving first-line treatment with R-CHOP. The reported 5-year PFS rates with this protocol were excellent. No patient developed histologic transformation into aggressive B-NHL. However, PFS and transformation rates have to be interpreted with caution because the median follow-up of 6.6 years is not sufficient for definitive conclusions. According to an analysis by the German Hodgkin Study Group evaluating characteristics and outcome of relapsed NLPHL, the median time from initial diagnosis to disease recurrence was 6.2 years.[10] Similarly, a Canadian report on histologic transformation in NLPHL patients revealed a median time

to transformation of 8.1 years.

Nonetheless, the use of R-CHOP optionally followed by RT in newly diagnosed advanced NLPHL is supported by the results from the present study despite all limitations associated with retrospective analyses and indirect comparisons. The R-CHOP protocol appears to be more effective than ABVD and less toxic than BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone) and thus has a more favorable risk-benefit ratio than these regimens. In contrast, patients with early-stage NLPHL are usually not candidates for R-CHOP treatment because they have an excellent outcome after RT alone (stage IA without risk factors) or a brief ABVD-based chemotherapy followed by RT (early stages other than stage IA without risk factors).[22]

Prognosis is favorable as compared to classic HL.[18,13,12] Relapse can occur when diagnosed in advanced stage in comparison to classic HL.[12] There is limited information regarding the outcome for patients with advanced-stage progression.[12]

IV. CONCLUSION

The 75-year-old patient's clinical case with a diagnosis of NLPHL has shown an example of a rare subgroup of lymphomas characterized by demographic, clinical, and pathological features that were very similar to those of non-Hodgkin diffuse large B cell lymphoma. Unlike classic Reed-Sternberg (RS) cells, the non-classic RS cells of NLPHL are CD15 and CD30 negative while positive for the B cell marker CD20. A careful review of the morphology, particularly the histologic appearance at low magnification, is of paramount importance. Immunohistochemical stains and clinical information can be of great assistance in confirming the initial histologic impression and appropriately classifying this type of Hodgkin lymphoma. The anti-CD20 monoclonal antibody Rituximab is indicated in NLPHL.

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