

Received: 2021.10.04

Accepted: 2021.12.27

Available online: 2022.01.19

Published: 2022.02.25

# Rare Case of Hodgkin Lymphoma Transformation into Diffuse Large B-Cell Lymphoma with Atypical Spread Epidurally, Intradurally and Intramedullary: A Case Report

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

ABCDEFG 1,2

BCDEF 1,3

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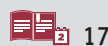
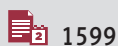
**Patient:** Female, 41-year-old  
**Final Diagnosis:** Large B-cell lymphoma  
**Symptoms:** Pain in right hip • paraparesis  
**Medication:** Intrathecal chemotherapy and radiation therapy  
**Clinical Procedure:** A vertebral body and lymph nodes biopsy  
**Specialty:** Oncology • Pathology • Radiology

**Objective:** Unusual clinical course

**Background:** Hodgkin lymphoma (HL) transformation into diffuse large B-cell lymphoma (DLBCL) is uncommon, and scant information has been published on transformed high-grade lymphomas. Therefore, it is important to present and discuss cases of lymphoma transformation to make new information on disease progression, diagnosis, and treatment more readily available. In this paper, we present a case of HL transformation into DLBCL with atypical dissemination.

**Case Report:** A 39-year-old woman presented with severe hip pain. A computed tomography (CT) scan was performed, which showed massive pathological retroperitoneal and pelvic lymphadenopathy. The lymph nodes were biopsied and revealed HL. The patient then underwent 7 cycles of ABVD therapy; however, clinical concern was raised for persistent disease due to the poor response to therapy. A vertebral body biopsy was performed to clarify the diagnosis, and histological analysis revealed DLBCL. Therefore, specific chemotherapy with the R-CHOP scheme was begun; the patient received 8 cycles of rituximab and residual lymphoma tissue irradiation. Two months later, magnetic resonance imaging later demonstrated radiological disease progression with multiple widespread metastases in the spinal vertebrae as well as prevertebral, epidural, intradural, and intramedullary metastatic spread. The patient underwent intrathecal chemotherapy and radiation therapy, after which, full metabolic remission was observed on PET/CT.

**Conclusions:** Vigilance should be maintained for patients with poor response to HL treatment owing to the possible transformation into DLBCL. However, even in such cases, full metabolic remission can be achieved with appropriate treatment.

**Keywords:** Hodgkin Disease • Multiparametric Magnetic Resonance Imaging • Spinal Cord CompressionFull-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/935014>

## Background

Hodgkin lymphoma (HL) is an uncommon lymphoid tumor that most commonly affects young adults, occurs in the lymph nodes of the neck (although not exclusively), and has a characteristic histological appearance. The prognosis for Hodgkin lymphoma is generally good, although it depends on a number of factors, including age and comorbidities [1-3]. HLs can be generally divided into classical HL (which have further subtypes) and nodular lymphocyte-predominant HL (NLPHL).

In some cases, HL has been observed to transform into non-HL (NHL), and most often into diffuse large B-cell lymphoma (DLBCL) [3]. The incidence of transformation in NLPHL is reported to be much higher than in classical HL [2]. In the past 20 years, previous observations suggest that there is a simultaneous or secondary transformation of NLPHL into DLBCL in up to 30% of cases [3-7]; however, the transformation rate of classical HL has been shown to be much lower, at around 1%. Therefore, very few cases have been observed, with most reports being case descriptions and case series, often from decades earlier [8]. Several studies have suggested that patients with NLPHL transformation have a favorable outcome [3,5,6,9], whereas in classical HL, with few cases that are temporally interspersed and reports that differ about impact on survivability, most authors emphasize transformation as a negative prognostic factor [8,10].

Because transformation of lymphoma is an uncommon phenomenon, its radiological appearance and development has been very rarely described, and visible involvement of the spinal cord is exceptional [11]. Because of this, we demonstrate a rare clinical case with a radiologically atypical finding of a transformed HL with epidural, intradural, and intramedullary metastatic spread with full metabolic remission on PET/CT after intrathecal chemotherapy and radiation therapy. A search of the literature yielded no similar published cases, with this being the first report of this kind.

## Case Report

A 39-year-old woman presented to the Emergency Department with severe pain in her right hip. The pain radiated to the right leg, making it difficult to walk. No pathology was observed on a plain hip X-ray. Therefore, a non-contrast-enhanced computed tomography (CT) scan of the abdomen and pelvis, including the hip joints, was performed, which revealed massive retroperitoneal lymphadenopathy along the aorta, retrocrurally, and in the pelvis, with especially pronounced pathological conglomerate-type lymph nodes along the proximal abdominal aorta. Metastatic foci were observed in the liver, and the spleen was enlarged. Due to the overall radiological appearance, especially

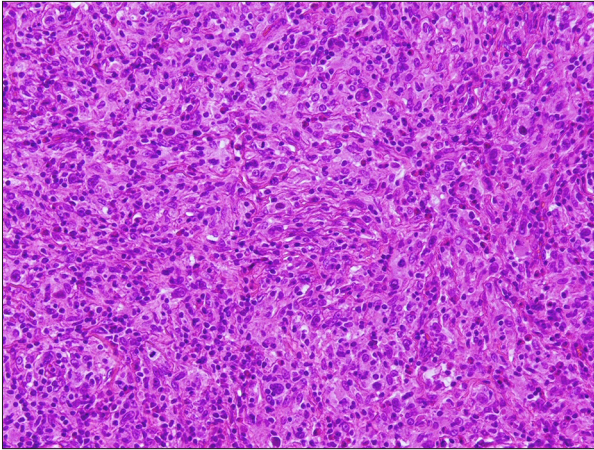
the enlarged lymph nodes, a diagnosis of malignant lymphoma was considered, and additional radiological examinations were done, including a contrast-enhanced thoracic CT scan, which demonstrated enlarged lymph nodes in the mediastinum and surrounding the thoracic aorta. Heterogeneous structure of the thoracic and lumbar spinal vertebral bodies was observed while examining the bone reconstruction algorithm of the thoracic CT, and a scintigraphy scan was recommended, which revealed hypermetabolic foci in the right femur sacroiliac joints and ala oisis ilii bilaterally and in the bodies of Th12 to L5 vertebrae.

Video-assisted thoracoscopic surgery-guided biopsy was performed from the enlarged mediastinal lymph nodes, but the obtained biopsy material was not informative. This was followed by a right-sided inguinal lymphadenectomy and biopsy from the paraaortic lymph nodes. Histological analysis of the resected and biopsied lymph nodes revealed nodular sclerosis with classical grade 2 HL (Figures 1-3), which prompted the medical team to prescribe a treatment regimen of 5 courses of ABVD treatment (doxorubicin 40 mg, vinblastin 10 mg, bleomycin 15 mg, dacarbazine 600 mg). After 2 months, a follow-up PET/CT scan showed good therapeutic effect with partial metabolic remission. Therefore, following the NCCN guidelines, it was decided to continue with 2 more courses of ABVD treatment and perform a subsequent control PET/CT scan.

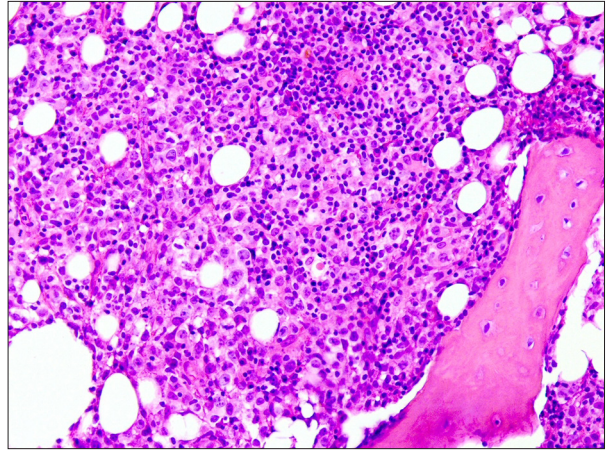
Despite earlier success, some of the patient's symptoms worsened, and the follow-up PET/CT scan showed signs of disease progression. The decision was made to perform a Th10 and L1 vertebral body biopsy with subsequent vertebroplasty to clarify the diagnosis. At this stage, the histological report showed lymphoproliferative infiltration, phenotypically and morphologically consistent with CD30+ and CD20++ diffuse large B-cell lymphoma, and transformation of HL could not be excluded (Figures 4-6).

Upon this result, a multidisciplinary tumor board decided to begin specific chemotherapy with the R-CHOP regimen. The patient received 6 courses of rituximab 700 mg, doxorubicin 95 mg, vincristin 2 mg, cyclophosphamid 1400 mg, and Solu-Medrol 250 mg and received radiotherapy of residual lymphoma tissues on the right side in the anterior part of the ala oisis ilii after finishing chemotherapy (1.8 Gy per fraction in photon mode, with a total dose of 45 Gy). After concluding the aforementioned therapy, the patient continued with additional cycles of rituximab 700 mg, making a total of 8 cycles.

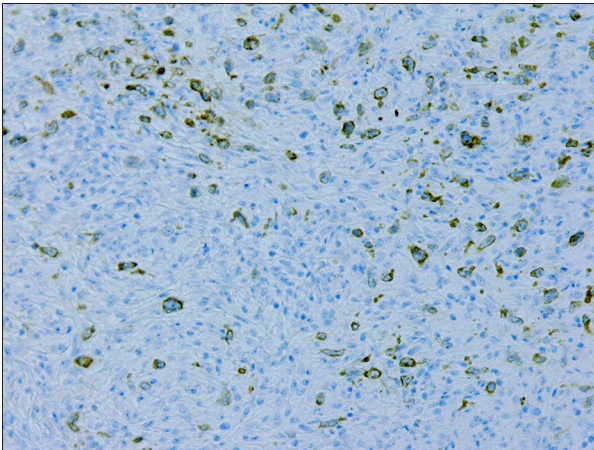
Two months later, a whole-spine MRI scan was performed because the patient had lower paraparesis and difficulty urinating, and the patient was hospitalized with spinal cord compression symptoms. MRI demonstrated multiple metastases in the thoracic and lumbar spine and abnormal prevertebral



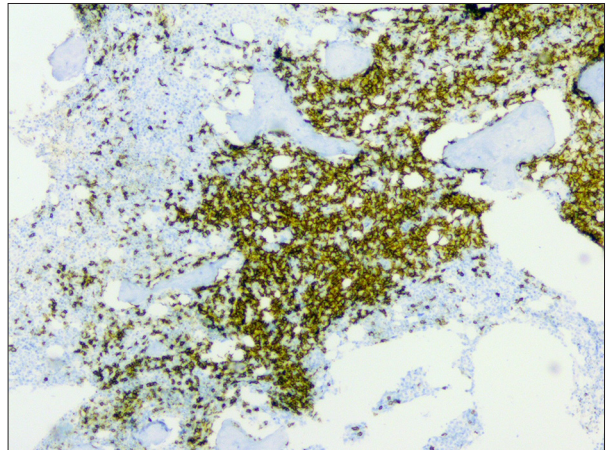
**Figure 1.** H&E staining, mixed heterogeneous infiltrate that contains pleomorphic large cells.



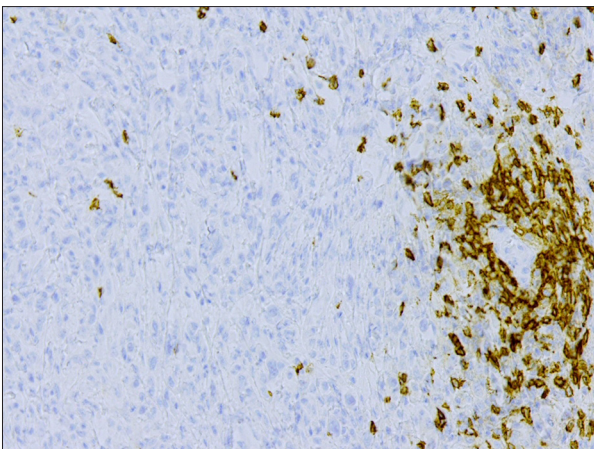
**Figure 4.** H&E staining, overview of the infiltrate and adjacent residual hemopoiesis.



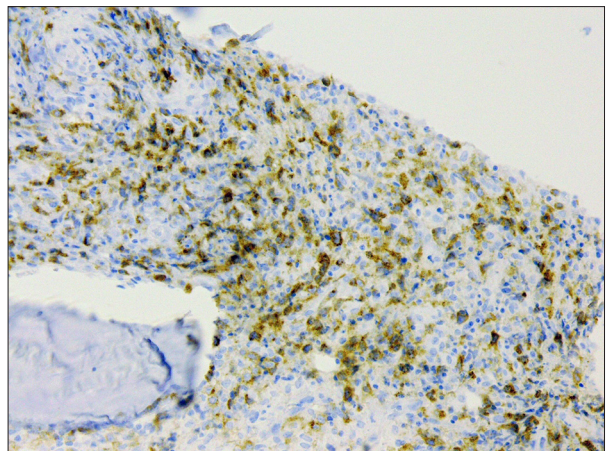
**Figure 2.** CD30, Hodgkin/Reed-Sternberg cells.



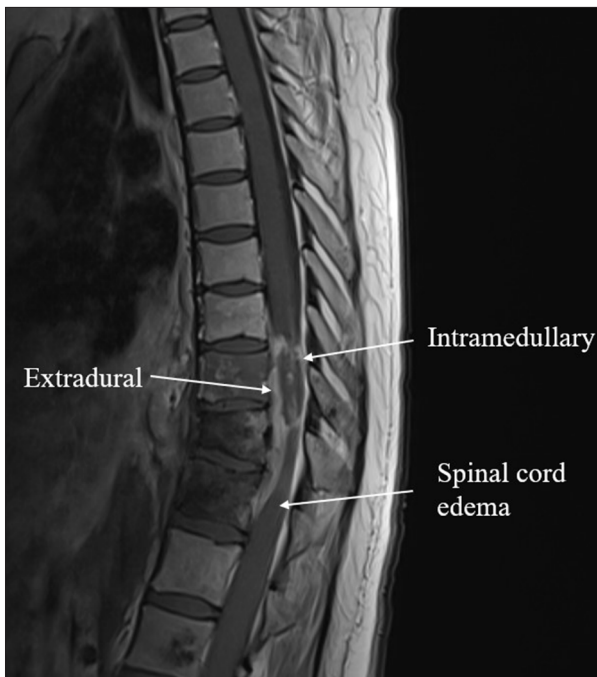
**Figure 5.** CD20, poorly demarcated tumor of strongly positive cells.



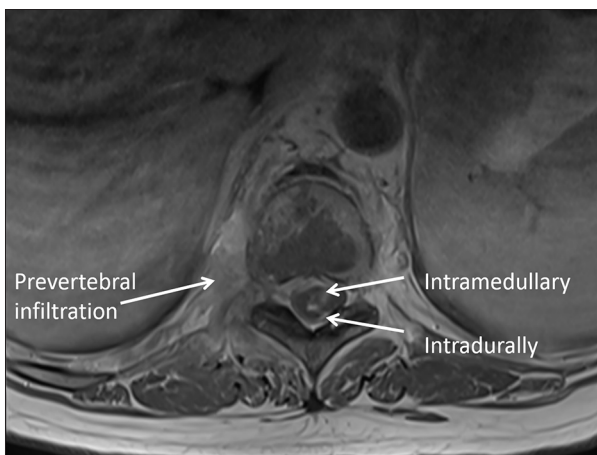
**Figure 3.** CD20, small residual clusters of B-cells, HRS cells negative.



**Figure 6.** CD30, partial positivity, mostly in large cells.

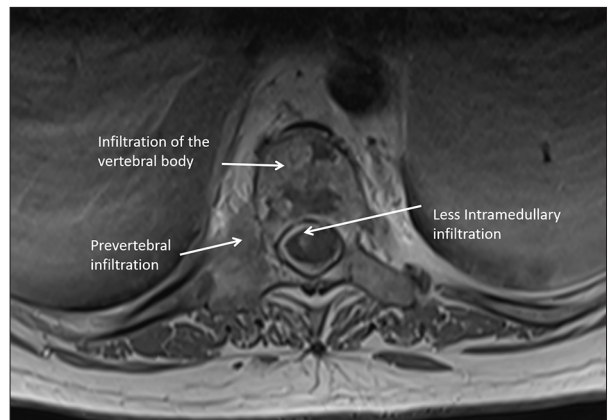


**Figure 7.** First spine MRI with contrast, T1 sequence sagittal. Distribution of metastases in a length of approximately 3.7 cm extradurally, intradurally, and intramedullary, causing spinal cord edema and compression.

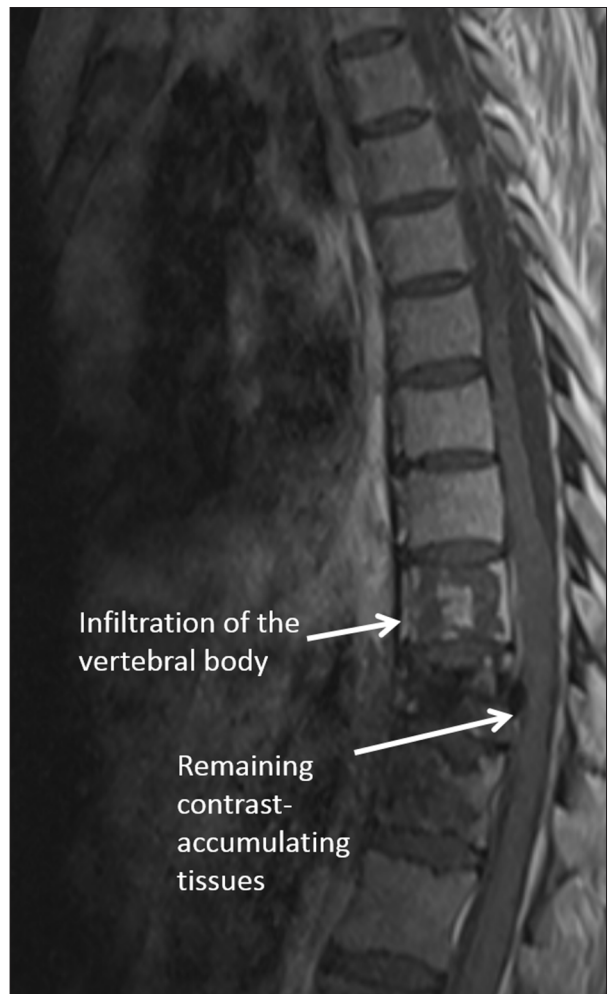


**Figure 8.** First spine MRI with contrast, T1 sequence axial. Prevertebral pathological tissues and abnormal infiltration in the spinal canal at the same level were observed, localizing more in the anterior parts and laterally to the left, with visible compression of the spinal cord.

tissues and epidural spinal canal infiltration between Th9 and Th11 vertebrae, which caused observable spinal cord compression from the anterolateral right side. MRI showed spinal cord edema and a diffuse volume increase with a hyperintense signal on T2 and FLAIR sequences that were most likely due to spinal cord compression and the spread of intradural



**Figure 9.** Second spine MRI with contrast, T1 sequence axial. Positive variability is observed, pathological tissues in the spinal canal are no longer differentiated intradurally, as well as epidurally.



**Figure 10.** Second spine MRI with contrast, T1 sequence sagittal. It is seen that pathological tissues remain and do not cause cerebral edema and spinal cord compression.

and intramedullary metastases (Figures 7, 8). Following these grim findings, the patient underwent intrathecal salvage chemotherapy (DHAP regimen 3 cycles: doxorubicin 45 mg, vinblastin 10 mg, bleomycin 15 mg, dacarbazine 660 mg) and irradiation of the spinal metastases.

The follow-up spine MRI scan after 2 months revealed a pathological Th10 vertebral body wedge fracture with vaulting of the dorsal contour of the vertebral body in the spinal canal with relative spinal canal stenosis at this level, and abnormal contrast-accumulating tissues remained up to the level of Th9. Prevertebral infiltration decreased with remaining tissues on the right-side foramina at the levels of Th9-10 and Th10-11 (Figures 9, 10).

One month later, a subsequent PET/CT scan was performed, showing a marked improvement over the previous scans, and no pathologic metabolic activity in the bone marrow could be observed. There were some residual tissues retroperitoneally without hypermetabolism: all pointing toward full metabolic remission. Although it cannot be said that complete recovery was achieved, in a consecutive MRI, spinal metastases had disappeared, leaving residual changes indicative of spinal atrophy with ischemic sequelae.

## Discussion

Although the first cases of lymphoma transformation were described as early as 1942 by Gall and 1956 by Rappaport, still little is known about the way HL morphs into DLBCL. Most reports on the topic are either case descriptions or case series, often from decades earlier, with more recent literature paying closer attention to NLPHL instead of classical HL, which was the case in our patient. What is currently known is that every year, 2 to 19 out of 100 people with low-differentiated (low-grade) lymphoma undergo transformation into highly differentiated lymphoma [12]. This is more common in NLPHL than in classical HL; nonetheless, the reason for the transformation and the mechanism of histological transformation is not completely understood [13,14].

The age of our patient at 39 years roughly corresponds to the reported median ages of patients with HL transformation into DLBCL, which range from 37 to 46 years, as reported by Al-Mansour et al and Huang et al, respectively [4,5]. The transformation of lymphoma confirmed by histological analysis is a common diagnostic standard worldwide [15]. Despite lymphadenopathy being a common radiological sign

of a lymphoproliferative disease, because of the limited number of cases, no specific radiological signs of possible imminent transformation have been described, and the appearance and signs of lymphomas, whether classical HL or transformed, can be variable. Patients with splenic involvement in HL have a higher risk of lymphoma transformation [5]. Splenic involvement in the form of splenomegaly was also seen in our patient and can easily be assessed by many radiological methods. Other factors that possibly improved the outcome for our patient were successful detection of spinal metastases, which could then be biopsied for a definitive diagnosis of transformation. Radiological examinations also are invaluable when assessing response to treatment, as was seen in our patient.

Several studies have suggested that patients with lymphoma transformation have a favorable outcome [3,5,6,9] in the case of NLPHL transformation; however, information about classical HL is contradictory, although authors seem to point toward any transformation being a risk factor of adverse outcomes because of the need to change therapy and other factors. However, this variability could reflect the accuracy of the original diagnosis of NLPHL, particularly in older studies before diagnoses were based on the REAL/WHO classification, as well as limited follow-up, because this event can occur years later [16]. Even so, although the number of described cases with HL to DLBCL transformation is limited, it is known that there are other forms of transformation that are not yet clearly classified [17].

## Conclusions

There has been relatively little study of transformation of HL into DLBCL, and publications are scant. Our case report demonstrates a unique case of such a transformation with epidural, intradural, and intramedullar proliferation and subsequent remission following intrathecal chemotherapy, which adds value to this clinical case. All physicians treating patients with HL, especially patients with NLPHL, should be aware of the possibility of transformation, and radiological tools are indispensable in a multifaceted and multidisciplinary treatment of transformed HL, such as assessing for possible transformation risk factors (splenomegaly) or evaluating dissemination and treatment response.

## Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

## References:

1. Wang HW, Balakrishna JP, Pittaluga S, Jaffe ES. Diagnosis of Hodgkin lymphoma in the modern era. *Br J Haematol.* 2019;184(1):45-59
2. Kenderian SS, Habermann TM, Macon WR, et al. Large B-cell transformation in nodular lymphocyte-predominant Hodgkin lymphoma: 40-year experience from a single institution. *Blood.* 2016;127(16):1960-66
3. Hansmann ML, Stein H, Fellbaum C, et al. Nodular paraganuloma can transform into high-grade malignant lymphoma of B type. *Hum Pathol.* 1989;20(12):1169-75
4. Huang JZ, Weisenburger DD, Vose JM, et al. Diffuse large B-cell lymphoma arising in nodular lymphocyte predominant Hodgkin lymphoma: A report of 21 cases from the Nebraska Lymphoma Study Group. *Leuk Lymphoma.* 2004;45(8):1551-57
5. Al-Mansour M, Connors JM, Gascoyne RD, et al. Transformation to aggressive lymphoma in nodular lymphocyte-predominant Hodgkin's lymphoma. *J Clin Oncol.* 2010;28(5):793-99
6. Biasoli I, Stamatoullas A, Meignin V, et al. Nodular, lymphocyte-predominant Hodgkin lymphoma: A long-term study and analysis of transformation to diffuse large B-cell lymphoma in a cohort of 164 patients from the Adult Lymphoma Study Group. *Cancer.* 2010;116(3):631-39
7. Jackson C, Sirohi B, Cunningham D, et al. Lymphocyte-predominant Hodgkin lymphoma – clinical features and treatment outcomes from a 30-year experience. *Ann Oncol.* 2010;21(10):2061-68
8. Bennett MH, MacLennan KA, Vaughan Hudson G, Vaughan Hudson B. Non-Hodgkin's lymphoma arising in patients treated for Hodgkin's disease in the BNLI: A 20-year experience. *British National Lymphoma Investigation. Ann Oncol.* 1991;2 (Suppl. 2):83-92
9. Cotta CV, Coleman JF, Li S, Hsi ED. Nodular lymphocyte predominant Hodgkin lymphoma and diffuse large B-cell lymphoma: A study of six cases concurrently involving the same site. *Histopathology.* 2011;59(6):1194-203
10. Makita S, Maeshima AM, Taniguchi H, et al. Classical Hodgkin lymphoma primary refractory to brentuximab vedotin, with transformation to CD30-positive diffuse large B-cell lymphoma. *Int J Hematol.* 2016;104(3):396-99
11. Al-Tourah AJ, Gill KK, Chhanabhai M, et al. Population-based analysis of incidence and outcome of transformed non-Hodgkin's lymphoma. *J Clin Oncol.* 2008;26:5165-69
12. Hubbard SM, Chabner BA, DeVita VTJ, et al. Histologic progression in non-Hodgkin's lymphoma. *Blood.* 1982;59:258-64
13. Acker B, Hoppe RT, Colby TV, et al. Histologic conversion in the non-Hodgkin's lymphomas. *J Clin Oncol.* 1983;1:11-16
14. Bastion Y, Sebban C, Berger F, et al. Incidence, predictive factors, and outcome of lymphoma transformation in follicular lymphoma patients. *J Clin Oncol.* 1997;15:1587-94
15. Wang HW, Balakrishna JP, Pittaluga S, Jaffe ES. Diagnosis of Hodgkin lymphoma in the modern era. *Br J Haematol.* 2018;184(1):45-49
16. K Hell, ML Hansmann, JH Pringle, et al. Combination of Hodgkin's disease and diffuse large cell lymphoma: An in situ hybridization study for immunoglobulin light chain messenger RNA *Histopathology.* 1995;27:491-99
17. Bernstein SH, Burack WR. The incidence, natural history, biology, and treatment of transformed lymphomas. *Am Soc Hematol Educ Program.* 2009;2009(1):532-41