Relapsed Primary Mediastinal Large B-Cell Lymphoma: The Crucial Role of PET-CT in Evaluating Disease Status and Treatment Response

Wienta Diarsvitri[1#*], Carlo Micelli[2#], Agnes Stephanie Harahap[3,4], Maria Francisca Ham[3,4]

[1]*Department of Community Medicine, Faculty of Medicine, Hang Tuah University, Indonesia*

[2]*Faculty of Medicine, Hang Tuah University, Indonesia*

[3]*Anatomical Pathology Department, Faculty of Medicine, Universitas Indonesia/Dr. Cipto Mangunkusumo National Central General Hospital, Indonesia*

[4]*Human Cancer Research Center-Indonesian Medical Education and Research Institute, Faculty of Medicine, Universitas Indonesia, Indonesia*

[#]*Equal Contribution*

***Correspondence:** Wienta Diarsvitri, Department of Community Medicine, Faculty of Medicine, Hang Tuah University, Surabaya 60244, Indonesia

wienta.diarsvitri@hangtuah.ac.id

Radiology Case. 2025 October; 19(10):1-11 :: DOI: 10.3941/jrcr.5850

ABSTRACT

Despite advances in treating primary mediastinal large B-cell lymphoma, 20–30% of patients experience relapse or refractory disease. We report a case of a patient initially presenting with a neck lump, later diagnosed as primary mediastinal large B-cell lymphoma via biopsy. Initial positron emission tomography/computed tomography imaging showed a large fluorodeoxyglucose-avid anterior mediastinal mass. Following first-line chemotherapy, the disease was found to be refractory, requiring second-line treatment. The positron emission tomography/computed tomography played a key role in evaluating disease extent, treatment response, and relapse, indicated by new hypermetabolic nodes or extranodal lesions. It remains essential in guiding further therapy, including stem cell transplantation and brentuximab vedotin maintenance.

CASE REPORT

BACKGROUND

Relapsed primary mediastinal large B-cell lymphoma (PMBCL) presents significant clinical challenges due to its aggressive nature and limited treatment options after initial therapy failure. Accurate assessment of disease status and treatment response is critical for guiding further management and improving outcomes. This case highlights the pivotal role of PET-CT imaging in detecting residual or recurrent disease, distinguishing between active lymphoma and post-treatment changes, and informing therapeutic decisions. By emphasizing PET-CT's utility in the relapsed setting, this report contributes to the growing body of literature supporting advanced imaging as an essential tool in the personalized management of PMBL.

CASE REPORT

The patient was a 29-year-old gentleman who initially presented with shortness of breath, cough, and palpable lymphadenopathy on the left side of his neck. This was biopsied, and haematoxylin and eosin stain demonstrated a diffuse and vaguely nodular growth pattern with areas of fibrosis. Tumor cells are arranged in sheets, appearing pale due to clear cytoplasm. The cells are large with pleomorphic nuclei, coarse chromatin, and a combination of clear and eosinophilic cytoplasm. Foci of tumor necrosis are also observed. The immunohistochemistry revealed tumor cells showing diffuse positivity for cluster of differentiation 20 (CD20). CD3 staining is negative. The antigen Ki-67 marker proliferation index is high, indicating a high proliferative activity. Tumor necrosis factor cluster differentiation CD30 and CD23 expression demonstrate heterogeneous positivity. CD10 staining is negative. Profile of primary mediastinal large B-cell lymphoma. Based on these findings, the main consideration was primary mediastinal large B-cell lymphoma (PMBL), a subtype of diffuse large B-cell lymphoma (DLBCL), which represented the most prevalent type of B-cell non-Hodgkin lymphoma (NHL), as shown in Figure 1. Moreover, the first positron emission tomography/computed tomography (PET-CT) indicated non-Hodgkin lymphoma (NHL) stage III (advanced lymphoma) as shown in Figure 2. He subsequently completed a six-cycle rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone (R-CHOP) regimen as the first-line chemotherapy, followed by two cycles of rituximab. He also received lenograstim, a granulocyte-colony stimulating factor (G-CSF), subcutaneous injections, for about three to five days post-chemotherapy to stimulate the bone marrow.

The second PET-CT evaluation revealed that the mediastinal mass had already disappeared. However, there were remaining lymph nodes with decreased metabolic activities in the gastrohepatic region and increased metabolic activities in the left posterior cervical region (maximum standardized uptake

value [SUVmax] = 7.74 vs 6.51) as shown in (Figure 3). Additionally, there were new lymph nodes in the paravertebral region at the T-V level, the aortocaval at the L-II level, and a new hypermetabolic irregular nodule in the inferior pole of the right kidney, as shown in Figure 3, indicating a possible relapse/refractory (R/R) of DLBCL.

The subsequent excisional biopsy on the lymph node in the left posterior cervical region showed an increased SUVmax on the last PET scan. The IHC report revealed that CD20 and CD45 were diffusely positive. CD10, B-cell lymphoma 6 (BCL-6), and multiple myeloma oncogene 1 (MUM-1) nuclear markers were weakly positive in a minority of cells. Ki-67 was positive in approximately 30% of cells. CD23 and CD30 were positive in some cells, whereas CD3, the pan cytokeratin AE1/AE3, and Cyclin-D1 were negative. The conclusion was consistent with the previous diagnosis: an NHL, DLBCL type, and PMBL subtype, as shown in Figure 1. Accordingly, the patient started a four-cycle second-line chemotherapy of rituximab, ifosfamide, carboplatin, and etoposide (R-ICE). An interim PET-CT evaluation revealed a Deauville score 1 (DS-1), consistent with a complete metabolic response, as shown in Figure 3. This finding indicated a significant improvement compared to the prior PET-CT results, although there were diffusely increased fluorodeoxyglucose (FDG) radiotracer uptakes in bone marrow, suggestive of reactive hyperplasia after chemotherapy. The PET-CT evaluation after the last R-ICE cycle showed no visible nodal or extra-nodal involvement in the supra or infra-diaphragm. The result was the same as the previous one, DS-1, as shown in Figure 2.

Afterward, the patient was evaluated before undergoing high-dose chemotherapy and autologous stem cell transplant (ASCT) with his stem cells. The laboratory tests revealed his Immunoglobulin G (IgG) for Cytomegalovirus (CMV), Epstein-Barr virus (EBV), and Toxoplasma were positive. In contrast, hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) antibody, and human immunodeficiency virus (HIV) antigen-antibody tests were non-reactive. Before harvesting the peripheral blood stem cells (PBSCs), the patient was given filgrastim, a recombinant human granulocyte colony-stimulating factor (rG-CSF) injection to produce more hematopoietic stem cells. He also received a plerixafor injection to address his low CD34+ cell count. Finally, the patient underwent high-dose chemotherapy with bis-chloroethyl-nitrosourea, etoposide, cytosine arabinoside, and melphalan (BEAM) regimen. The patient was also given preventive medications, including ursodeoxycholic acid, heparin, acyclovir, levofloxacin, and fluconazole, to reduce the risk of infection. During the ASTC, no allergic reaction was detected. Furthermore, he received two irradiated platelet concentrate transfusion units to treat his thrombocytopenia during the engraftment process. Before discharge from the hospital, the patient had nebulized pentamidine for fungal infection, pneumocystis jiroveci pneumonia prophylaxis. The patient repeated PET-CT after finishing ASCT, and the result was still DS-1.

The patient had maintenance chemotherapy with 16 cycles of brentuximab vedotin (BV) as targeted therapy (anti-CD30). Following chemotherapy, he experienced brentuximab vedotin-induced peripheral neurotoxicity (BVIN), which was addressed with physiotherapy and occupational therapy. The following PET-CT scan revealed the absence of FDG-avid nodal disease both above and below the diaphragm, and the absence of extranodal disease or focal lesions. The result was consistent with DS-1. Currently, the patient is in the second year of being cancer-free.

DISCUSSION

Etiology and demographics

PMBL is a distinct subtype of DLBCL, accounting for approximately 2–4% of all NHLs and about 10% of all large B-cell lymphomas. It is a relatively rare lymphoma subtype affecting predominantly adolescents and young adults, with a median age at diagnosis around 30-35 years. There is a notable female predominance, with a female-to-male ratio of approximately 2:1 [1,2].

The underlying cause of PMBL remains poorly understood. However, general risk factors associated with NHL may also play a role in PMBL development. These include immunodeficiency states, autoimmune disorders like Sjögren's syndrome, systemic lupus erythematosus, celiac disease, and scleroderma, as well as certain viral infections (CMV, EBV), and family history [3-7]. Notably, a familial case of PMBL has been reported in Finland, potentially linked to the 5533C>A mutation in the mixed lineage leukemia (MLL) gene [8]. Modifiable risk factors have also been identified, particularly in DLBCL, which shares some characteristics with PMBL. These include exposure to radiation for the treatment of solid tumors [9,10], occupational chemical exposure among farm workers or painters [11,12], and tobacco use [13], which is primarily associated with an increased risk of central nervous system, testicular, and cutaneous DLBCL [14]. Exposure to sunlight has been associated with a lower incidence of DLBCL, potentially attributable to the enhanced synthesis of vitamin D3, a recognized modulator of immune function [15,16]. Despite these associations, no specific risk factors have been conclusively established for PMBL.

In this case, the patient had no family history of malignancy, and there was no history of smoking or alcohol consumption. However, serological tests revealed positive IgG for CMV and EBV, both of which have been implicated in the pathogenesis of NHL [6,7]. Given the patient's profession as a physician, occupational exposure may have increased his susceptibility to these viral infections.

Clinical and imaging findings

Clinically, PMBL typically presents as a rapidly enlarging anterior mediastinal mass, causing local compressive symptoms such as cough, dyspnea, chest pain, and, in some cases, superior vena cava syndrome. B symptoms, such as fever, night sweats,

and weight loss may occur in one-third of patients. Symptoms generally progress rapidly, with approximately 80% of cases diagnosed at stage I or II [17]. However, up to a quarter of patients present with advanced-stage disease, as seen in this case, where the patient was diagnosed at stage III [18].

The patient initially experienced neck discomfort along with shortness of breath, cough, and fatigue. Given its feasibility and non-invasive nature, ultrasound was chosen as the initial imaging modality for evaluating the cervico-supraclavicular region. This examination revealed multiple lymphadenopathies, prompting an incisional biopsy of the left subclavian lymph nodes to confirm the initial diagnosis of lymphoma. Although studies specifically highlighting the value of ultrasound in lymphoma are limited, it has demonstrated higher sensitivity in detecting cervical lymph nodes (96.8%) compared to palpation (73.3%). Moreover, ultrasound is more sensitive in identifying small lymph nodes, capable of detecting nodes as small as 2 mm, whereas CT may have difficulty detecting those smaller than 5 mm [19].

In cases of PMBL, CT typically demonstrates a bulky anterior mediastinal mass, often exceeding 10 cm and displaying low attenuation due to necrosis, cystic degeneration, or hemorrhage. Infiltration of adjacent structures, including the lungs, chest wall, pleura, and pericardium, occurs in 70–80% of cases [18,20]. Although CT plays a crucial role in staging, its utility in assessing residual lesions and monitoring treatment response is limited, as it cannot reliably distinguish between persistent disease and post-treatment fibrotic changes [20].

Fluorine-18 FDG PET/CT is an essential imaging modality for evaluating FDG-avid lymphomas, including PMBL. In this case, following the confirmation of lymphoma through tissue biopsy and IHC staining, FDG PET/CT was utilized to assess metastatic spread and detect extra-mediastinal involvement (such as bone marrow infiltration) for pre-treatment staging. It was also employed for mid-treatment and end-of-treatment evaluations, facilitating the monitoring of therapeutic outcomes [21]. Furthermore, the modality was chosen in this patient for its ability to distinguish residual disease from post-treatment changes, reliably differentiating active tumor tissue from non-viable tissue, such as fibrosis or necrosis, making it invaluable for detecting relapse or recurrent disease [22].

In this patient, relapse was confirmed by end-of-treatment FDG PET/CT, which demonstrated the resolution of the mediastinal mass but revealed new pathological findings. Specifically, new lymph nodes were detected in the paravertebral region at the T-V level and the aortocaval region at the L-II level, along with a hypermetabolic irregular nodule in the inferior pole of the right kidney. These findings highlighted the critical role of FDG PET/CT in assessing treatment response and detecting recurrent disease. While other imaging modalities, such as ultrasound, CT, and MRI are also valuable for lymphoma evaluation, PET/CT remains superior for detecting metabolic activity. In certain scenarios, chest X-ray can be useful for initial assessment of mediastinal masses, tracheal deviation, or pleural effusions [23].

In conclusion, the accurate diagnosis and staging of PMBL require a comprehensive approach, including patient history, physical examination, imaging modalities, laboratory tests, and tissue biopsy with immunohistochemistry. Bone marrow aspiration may also be indicated in specific cases to assess marrow involvement [24].

Treatment and Prognosis

The first-line treatment of PMBL typically involves the R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), with the option of consolidative radiotherapy. In some cases, especially where resources are available, the more intensive dose-adjusted R-EPOCH regimen (rituximab, etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone), which has demonstrated high efficacy, may be preferred [25]. In this case, the patient received R-CHOP as first-line therapy due to its availability and inclusion under the Indonesian national health insurance scheme, whereas EPOCH-based regimens are not currently covered.

For medically fit patients with late-**relapse PMBL,** second-line chemotherapy followed by **ASCT** remains a standard therapeutic approach, especially in those who achieve a complete response to salvage therapy. However, chimeric antigen receptor T-cell (CAR-T) therapy has replaced ASCT as the standard care, particularly in the group of patients with refractory disease or early relapse (less than 12 months after therapy). CAR-T therapy demonstrated significant survival benefits compared to the previous standard of care [26].

Following re-biopsy to confirm histopathological consistency, the patient proceeded with second-line chemotherapy using the R-ICE regimen (rituximab, ifosfamide, carboplatin, and etoposide). R-ICE was selected due to its widespread use and established efficacy in mobilizing peripheral blood stem cells for subsequent ASCT [27]. In certain scenarios, such as patients with the germinal center B-cell subtype or central nervous system involvement, alternative regimens like R-DHAP (rituximab, dexamethasone, high-dose cytarabine/Ara-C, cisplatin/platinum) may be more appropriate due to the enhanced central nervous system penetration provided by high-dose cytarabine [28]. Although this patient met the criteria for CAR-T therapy due to early relapse, access to this treatment was not available in the country. Consequently, salvage chemotherapy followed by ASCT was selected as the preferred therapeutic approach. Nevertheless, this case illustrates that for patients who respond well to salvage chemotherapy, regardless of the timing of relapse, ASCT remains a viable option, particularly for those achieving complete remission.

Interestingly, the patient in this case exhibited CD30 expression. While the CD30 antigen is mainly linked with

systemic anaplastic large cell lymphoma and Hodgkin lymphoma (HL), it has also been identified in several subtypes of NHL, making it a viable target for therapeutic intervention. Brentuximab vedotin (BV), a CD30-directed antibody-drug conjugate, has generated favorable outcomes in various cases of relapsed or refractory CD30-positive NHL. When used as an early consolidation targeted therapy following ASCT, it enhances the duration of prolonged progression-free survival in this patient population [29].

Peripheral neuropathy is the most common and clinically significant adverse effect of BV, often referred to as BVIN. It primarily affects sensory nerves but may also involve motor and autonomic functions. Although often reversible, symptoms can persist for months or even years, negatively impacting patients' quality of life, including work and social functioning. Pharmacologic treatments such as gabapentin/pregabalin, duloxetine, and tricyclic antidepressants can help relieve symptoms, while non-pharmacologic strategies like physical therapy, acupuncture, and keeping extremities warm may offer additional benefit [30]. Healthcare providers should be aware of these potential effects as major issues for lymphoma survivors. In general, the prognosis is very favorable, with a 5-year survival rate exceeding 80% in most reports [25,31].

Differential diagnosis

Previously classified as a subtype of DLBCL, PMBL has been reclassified as a distinct type in the WHO classification since 2016, based on its unique clinical presentation, histopathological features, and molecular profile [32]. PMBL should be carefully differentiated from other types with overlapping features, including classic Hodgkin lymphoma (cHL), mediastinal grey zone lymphoma (MGZL), and DLBCL. Although these entities differ in origin, epidemiology, and clinical course, all can present with mediastinal involvement, ranging from 20% in DLBCL to nearly 100% in PMBL, making clinical manifestation alone insufficient for accurate diagnosis [33]. Distant metastasis is uncommon in PMBL, cHL, and MGZL; however, recurrence of PMBL frequently involves extranodal sites [34]. Therefore, a definitive diagnosis requires a comprehensive evaluation of morphological features, immunohistochemical profiles, and imaging findings. For instance, overexpression of CD79a, B-cell-specific octamer binding protein-1 (BOB1), and cyclins (D2, A, B1) supports the diagnosis of cHL, whereas CD23 positivity is a useful marker in distinguishing PMBL from DLBCL [35].

Classic Hodgkin lymphoma (cHL)

cHL is typically found in bimodal age groups: young adults (20-30s) and the elderly (50-60s). It is often asymptomatic, and B-symptoms appear in advanced stages. Mediastinal involvement is common, especially in the nodular sclerosis subtype, whereas extranodal involvement is rare. cHL shows indolent to moderate aggressiveness [36, 37].

In CT findings, cHL appears as an anterior mediastinal mass or lymphadenopathy. It shows high FDG uptake in PET-CT. Lymph node morphology is usually symmetric enlargement with discrete nodes. Mediastinal mass appearance is homogenous, but may have fibrosis in the nodular sclerosis subtype [38,39].

Mediastinal grey zone lymphoma (MGZL)

MGZL is primarily found in young adults (20-40s) with a male predominance. B-symptoms are common, and they may present with fever, weight loss, and night sweats. Mediastinal involvement is prominent, such as a bulky anterior mediastinal mass. Extranodal involvement is sometimes seen and may involve adjacent structures. MGZL shows an intermediate/aggressive course [40].

A bulky anterior mediastinal mass or heterogenous is often seen in CT findings. In PET-CT, it shows high FDG uptake or a heterogeneous appearance. Lymph node morphology appears as a confluent, bulky mass or is more heterogeneous. Mediastinal mass appearance is typically irregular, heterogeneous, and may invade surrounding structures [38].

Diffuse large B-cell lymphoma (DLBCL)

DLBCL is commonly found in older adults, with a median age of 64, and a slight male predominance. Around 30% of cases show B-symptoms, mediastinal involvement is possible but less often dominant, extranodal involvement is common, and it is aggressive [41].

Masses in nodal or extranodal sites with rapid growth. High FDG uptake is common in CT findings, and is often more widespread. Lymph node morphology is often asymmetric, with mass-like nodes. Mediastinal mass appearance is more variable, not typically central mediastinal [42-46].

CONCLUSION

This case highlights the complexity of diagnosing and managing PMBL, a rare and distinct type of NHL. Accurate diagnosis requires a multidisciplinary approach that integrates clinical presentation, imaging, histopathology, and immunohistochemical markers, especially when differentiating PMBL from overlapping entities such as cHL, MGZL, and DLBCL. In this patient, the disease showed a partial response to first-line R-CHOP therapy but relapsed shortly thereafter. Due to the unavailability of CAR-T therapy in the country, the patient was successfully treated with salvage chemotherapy (R-ICE), followed by ASCT and maintenance targeted therapy with BV. This case also underscores the relevance of CD30 expression as a therapeutic target and the importance of monitoring and managing BVIN as a long-term survivorship concern. Overall, the patient achieved complete remission and continues to do well four years after diagnosis, emphasizing the potential for durable outcomes with timely diagnosis and individualized treatment strategies in resource-constrained settings.

TEACHING POINT

PMBL appears as FDG-avid anterior mediastinal mass on PET/CT, with relapse often presenting as new hypermetabolic lymph nodes or extranodal lesions. PET/CT plays a central role in evaluating treatment response to second-line therapy and autologous stem cell transplantation, especially in CD30-positive cases where brentuximab vedotin may be indicated as maintenance therapy.

ETHICAL STATEMENT

The authors declare that they have obtained written informed consent from the patient for images and other clinical information to be reported in the journal for this case report voluntarily. This study was approved by the Research Ethics Committee, Faculty of Medicine, Hang Tuah University, with certificate number I/024/UHT.KEPK.03/VI/2024.

QUESTIONS

1. Which imaging findings are typical for relapsed primary mediastinal large B-cell lymphoma (PMBL) on PET/CT scan?

Please select all that apply.

A. High FDG uptake in the anterior mediastinal mass
B. Decreased SUV in all regions of the lymph nodes
C. Increased SUV in newly appearing lymph nodes
D. Normal uptake in all regions indicates relapse
E. Diffuse bone marrow uptake due to reactive hyperplasia

Correct Answers: A, C, E

Explanation: PET/CT in relapse may show high FDG avidity in new lymph nodes (e.g., paravertebral, aortocaval) and residual nodal activity. Diffuse bone marrow FDG uptake may suggest reactive hyperplasia rather than active disease

[Case report section; Figure 3].

2. Which of the following are components of the BEAM regimen used for high-dose chemotherapy in PMBL?

Please select all that apply.

A. Bendamustine
B. Etoposide
C. Ara-C (Cytarabine)
D. Melphalan
E. Carmustine

Correct Answers: B, C, D, E

Explanation: The BEAM regimen includes carmustine, etoposide, cytarabine (Ara-C), and melphalan. Bendamustine is not part of the BEAM protocol

3. What role does PET/CT imaging play in evaluating response to second-line therapy in PMBL?

Please choose the single best answer.

A. Detects calcifications in mediastinal masses
B. Determines eligibility for radiation therapy
C. Assesses metabolic response via Deauville scoring
D. Evaluates cardiac function post-chemotherapy
E. Detects bone fractures due to chemotherapy

Correct Answer: C

Explanation: PET/CT with Deauville scoring is key in assessing metabolic response to therapy, with DS-1 indicating a complete metabolic response.

4. Which statements about CD30 expression in lymphoma and targeted therapy are true?

Please select all that apply.

A. CD30 is exclusively expressed in Hodgkin lymphoma
B. CD30 expression is associated with poor prognosis
C. CD30 can be targeted using brentuximab vedotin
D. CD30 levels correlate with disease stage and tumor burden
E. CD30-positive PMBL may benefit from CD30-targeted maintenance therapy post-ASCT

Correct Answers: B, C, D, E

Explanation: CD30 is not exclusive to Hodgkin lymphoma and is seen in PMBL and other NHL subtypes. It is associated with advanced disease and poor prognosis. Brentuximab vedotin targets CD30 and may be used in maintenance therapy.

5. What are the most common side effects of brentuximab vedotin therapy in PMBL patients?

Please select all that apply.

A. Nephrotoxicity
B. Peripheral neuropathy
C. Muscle atrophy
D. Diarrhea
E. Sensory and motor deficits

Correct Answers: B, C, E

Explanation: Brentuximab vedotin-induced peripheral neurotoxicity (BVIN) commonly results in sensory and motor impairments, as well as muscle atrophy due to disuse.

REFERENCES

[1] Savage KJ. Primary mediastinal large B-cell lymphoma. *Blood.* 2022; 140: 955–970.

[2] Alhejazi A, Motabi I, Sagheir A, et al. Primary mediastinal large B-Cell lymphoma: Saudi Lymphoma Group's clinical practice guidelines for diagnosis, management and follow-up. *Saudi J Med Med Sci.* 2019; 7(3): 231-233. PMID: 31543751.

[3] Ruan JS, Xu S, Shan NN. Inextricable association of connective tissue disease with B-cell lymphoma (Review). *Mol Clin Oncol.* 2025; 22(6): 48. PMID: 40236836.

[4] Chiu BCH, Hou N. Epidemiology and etiology of non-Hodgkin lymphoma. *Cancer Treat Res.* 2015; 165: 1–25. PMID: 25655604.

[5] Mafra A, Laversanne M, Gospodarowicz M, et al. Epidemiology of Non-Hodgkin Lymphoma: Global Patterns of Incidence, Mortality, and Trends. *Blood*. 2022; 151(9): 1474-1481. PMID: 35695282.

[6] Mehravaran H, Makvandi M, Samarbaf Zade A, et al. Association of Human Cytomegalovirus with Hodgkin's Disease and Non-Hodgkin's lymphomas. *Asian Pac J Cancer Prev.* 2017; 18(3): 593-597. PMID: 28440608.

[7] Malpica L, Marques-Piubelli ML, Beltran BE, Chavez JC, Miranda RN, Castillo JJ. EBV-positive diffuse large B-cell lymphoma, not otherwise specified: 2022 update on diagnosis, risk-stratification, and management. *Am J Hematol.* 2022; 97(7): 951–965. PMID: 35472248.

[8] Juskevicius D, Lundberg P, Tzankov A, Dirnhofer S, Stenner F. Genetic Factors in Familial Manifestation of Primary Mediastinal Large B-Cell Lymphoma over Two Generations. *Pathobiology.* 2023; 90(6): 422-428. PMID: 37490879.

[9] Joelsson J, Wästerlid T, Rosenquist R, et al. Incidence and time trends of second primary malignancies after non-Hodgkin lymphoma: a Swedish population-based study. *Blood Adv.* 2022; 6(8): 2657–2666. PMID: 35042239.

[10] Parsons MW, Rock C, Chipman JJ, et al. Secondary malignancies in non-Hodgkin lymphoma survivors: 40 years of follow-up assessed by treatment modality. *Cancer Med* .2023; 12(3): 2624–2636. PMID: 36812123.

[11] Chihara D, Nastoupil LJ, Williams JN, Lee P, Koff JL, Flowers CR. New insights into the epidemiology of non-Hodgkin lymphoma and implications for therapy. *Expert Rev Anticancer Ther.* 2015; 15(5): 531-544. PMID: 25864967.

[12] Francisco LFV, da Silva RN, Oliveira MA, et al. Occupational Exposures and Risks of Non-Hodgkin Lymphoma: A Meta-Analysis. *Cancers (Basel).* 2023; 15(9): 2600. PMID: 37174074.

[13] Taborelli M, Montella M, Libra M, et al. The dose-response relationship between tobacco smoking and the risk of lymphomas: A case-control study. *BMC Cancer.* 2017; 17(1): 421. PMID: 28622762.

[14] American Association for Cancer Research. *AACR Cancer Progress Report. [*https://cancerprogressreport.aacr.org/progress/get-a-copy/ (2024, accessed 9 June 2025)].

[15] Berhan A, Almaw A, Damtie S, et al. Diffuse large B cell lymphoma (DLBCL): epidemiology, pathophysiology, risk stratification, advancement in diagnostic approaches and prospects: narrative review. *Discover Oncology. 2025;* 16: 2025; 16: 1–15.

[16] Kim HB, Kim JH. Sunlight exposure in association with risk of lymphoid malignancy: a meta-analysis of observational studies. *Cancer Causes and Control.* 2021; 32(5): 441–457. PMID: 33606147.

[17] Martelli M, Ferreri A, Di Rocco A, et al. Primary mediastinal large B-cell lymphoma. *Crit Rev Oncol Hematol* . 2017; 113: 318–327.

[18] Yu Y, Dong X, Tu M, et al. Primary mediastinal large B cell lymphoma. *Thorac Cancer.* 2021; 12: 2837.

[19] Tavarozzi R, Manzato E, Lombardi A. Lymph Node Ultrasound in Lymphoproliferative Disorders: Where Are We Now? *J Clin Imaging Sci.* 2021; 11: 22.

[20] Pfau D, Smith DA, Beck R, et al. Primary mediastinal large B-cell lymphoma: A review for radiologists. *AJR Am J Roentgenol.* 2019; 213(5): W194-W210. PMID: 31414888.

[21] Melani C, Advani R, Roschewski M, et al. End-of-treatment and serial PET imaging in primary mediastinal B-cell lymphoma following dose-adjusted EPOCH-R: a paradigm shift in clinical decision making. *Haematologica.* 2018; 103(8): 1337-1344. PMID: 29748435.

[22] Sabri YY, Ewis NM, Zawam HEH, et al. Role of diffusion MRI in diagnosis of mediastinal lymphoma: initial assessment and response to therapy. *Egyptian Journal of Radiology and Nuclear Medicine* 2021; 52: 1–11.

[23] Nappi AG, Dondi F, Lazzarato A, et al. Primary Mediastinal B-Cell Lymphoma and [18F]FDG PET/CT: What We Learned and What Is New. *Hematol Rep.* 2025; 17(3): 23. PMID: 40407633.

[24] Olawaiye AB, Baker TP, Washington MK, Mutch DG. The new (Version 9) American Joint Committee on Cancer tumor, node, metastasis staging for cervical cancer. *CA Cancer J Clin.* 2021; 71(4): 287-298. PMID: 33784415.

[25] Camus V, Rossi C, Sesques P, et al. Outcomes after first-line immunochemotherapy for primary mediastinal B-cell lymphoma: a LYSA study. *Blood Adv.* 2021; 5(19): 3862-3872. PMID: 34461634.

[26] Strüßmann T, Marks R, Wäsch R. Relapsed/Refractory Diffuse Large B-Cell Lymphoma: Is There Still a Role for Autologous Stem Cell Transplantation in the CAR T-Cell Era? *Cancers (Basel).* 2024; 16(11): 1987. PMID: 38893108.

[27] Holmberg LA, Linenberger M, Connelly-Smith L. Mobilization of Autologous Peripheral Blood Stem Cells (PBSC) in CD20+ Lymphoma Patients Using RICE, Granulocyte-Colony Stimulating Factor (G-CSF) and Plerixafor. *OBM Transplant.* 2023; 7: 1–15.

[28] Doorduijn JK, van Imhoff GW, van der Holt B, et al. Treatment of secondary central nervous system lymphoma with intrathecal rituximab, high-dose methotrexate, and R-DHAP followed by autologous stem cell transplantation: results of the HOVON 80 phase 2 study. *Hematol Oncol.* 2017; 35(4): 497–503. PMID: 27530779.

[29] Jagadeesh D, Horwitz S, Bartlett NL, et al. Response to Brentuximab Vedotin by CD30 Expression in Non-Hodgkin Lymphoma. *Oncologist.* 2022; 27(10): 864-873. PMID: 35948003.

[30] Clifford K, Copeland A, Knutzen G, Samuelson E, Grove L, Schiavo K. Brentuximab vedotin: A nursing perspective on best practices and management of associated adverse events. *Clin J Oncol Nurs.* 2018; 22(4): E103-E114. PMID: 30035778.

[31] Polgarova K, Janíková A, Belada D, et al. Survival of Patients with Primary Mediastinal B-Cell Lymphoma Treated By Immunochemotherapy with or without Radiotherapy. *Blood* .2022; 140: 3831–3832.

[32] Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood*. 2016; 127(20): 2375-2390. PMID: 26980727.

[33] Yu Y, Dong X, Tu M, et al. Primary mediastinal large B cell lymphoma. *Thorac Cancer.* 2021; 12: 2837.

[34] Chen H, Pan T, He Y, et al. Primary Mediastinal B-Cell Lymphoma: Novel Precision Therapies and Future Directions. *Front Oncol.* 2021; 11: 654854. PMID: 33869061.

[35] Gaulard P, Harris NL, Pileri SA. Primary mediastinal (thymic) large B cell lymphoma. In: Swerdow SH, Campo E, Harris NL, et al. (eds) *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. Lyon: IARC Press; 2017: 314–316.

[36] El Hussein S, O'Malley DP. Classic Hodgkin lymphoma: An illustrative review of select diagnostic limitations and immunomorphological challenges. *Hum Pathol* .2025; 156: 105678. PMID: 39491628.

[37] Munir F, Hardit V, Sheikh IN, et al. Classical Hodgkin Lymphoma: From Past to Future—A Comprehensive Review of Pathophysiology and Therapeutic Advances. *Int J Mol Sci.* 2023; 24(12): 10095. PMID: 37373245

[38] Angelopoulou MK, Mosa E, Pangalis GA, et al. The significance of PET/CT in the initial staging of hodgkin lymphoma: Experience outside clinical trials. *Anticancer Res.* 2017; 37(10): 5727-5736. PMID: 28982893.

[39] Triumbari EKA, Morland D, Cuccaro A, Maiolo E, Hohaus S, Annunziata S. Classical Hodgkin Lymphoma: A Joint Clinical and PET Model to Predict Poor Responders at Interim Assessment. *Diagnostics (Basel).* 2022; 12(10): 2325. PMID: 36292014.

[40] Sarkozy C, Molina T, Ghesquières H, et al. Mediastinal gray zone lymphoma: clinico-pathological characteristics and outcomes of 99 patients from the Lymphoma Study Association. *Haematologica* 2017; 102(1): 150-159. PMID: 27758822.

[41] Wang SS. Epidemiology and etiology of diffuse large B-cell lymphoma. *Semin Hematol.* 2023; 60(5): 255–266. PMID: 38242772.

[42] Chen J, Lin F, Dai Z, et al. Survival prediction in diffuse large B-cell lymphoma patients: multimodal PET/CT deep features radiomic model utilizing automated machine learning. *J Cancer Res Clin Oncol.* 2024; 150(10): 452. PMID: 39382750.

[43] Lambert L, Wagnerova M, Vodicka P, et al. Whole-body magnetic resonance imaging provides accurate staging of diffuse large B-cell lymphoma, but is less preferred by patients. *World J Radiol.* 2025; 17(1): 99207. PMID: 39876887.

[44] Si J, Wang H, Xie M, et al. Distinguishing diffuse large B-cell lymphoma from Hodgkin's lymphoma in children using an enhanced computed tomography radiomics approach. *Transl Pediatr.* 2024; 13(5): 716-726. PMID: 38840678.

[45] Ferrer-Lores B, Lozano J, Fuster-Matanzo A, et al. Prognostic value of genetic alterations and 18F-FDG PET/CT imaging features in diffuse large B cell lymphoma. *Am J Cancer Res.* 2023; 13(2): 509-525. PMID: 36895981.

[46] Cottereau AS, Nioche C, Dirand AS, et al. 18F-FDG PET Dissemination Features in Diffuse Large B-Cell Lymphoma Are Predictive of Outcome. *J Nucl Med.* 2020; 61(1): 40-45. PMID: 31201248.

FIGURES

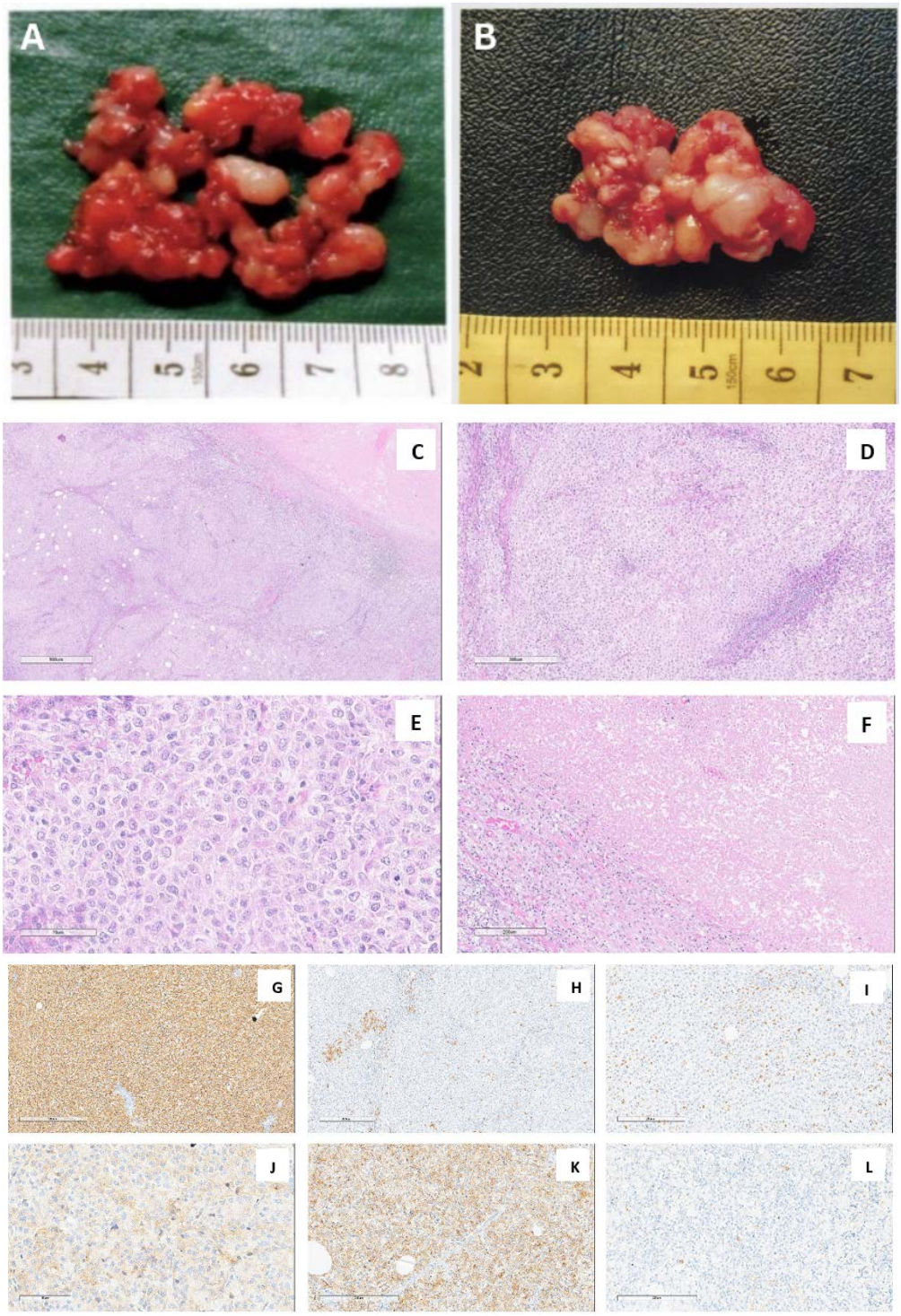

Figure 1: Macroscopic images: (A) Left subclavian lymph nodes of the first incisional biopsy, with a soft consistency and white color, measuring 4x3x0.6 cm. (B) The second excisional biopsy of newly diagnosed swollen lymph node measuring 30x15x5 mm. Histopathological features of primary mediastinal B-cell lymphoma (H&E stain): (C) The tumor exhibits a diffuse and vaguely nodular growth pattern with areas of fibrosis. (D) Tumor cells are arranged in sheets, appearing pale due to the presence of clear cytoplasm. (E) The cells are large with pleomorphic nuclei, coarse chromatin, and a combination of clear and eosinophilic cytoplasm. (F) Foci of tumor necrosis are also observed. Immunohistochemical profile of primary mediastinal large B-cell lymphoma: (G) Tumor cells show diffuse positivity for CD20. (H) CD3 staining is negative. (I) The Ki-67 proliferation index is high, indicating a high proliferative activity. (J, K) CD30 and CD23 expression demonstrate heterogeneous positivity. (L) CD10 staining is negative.

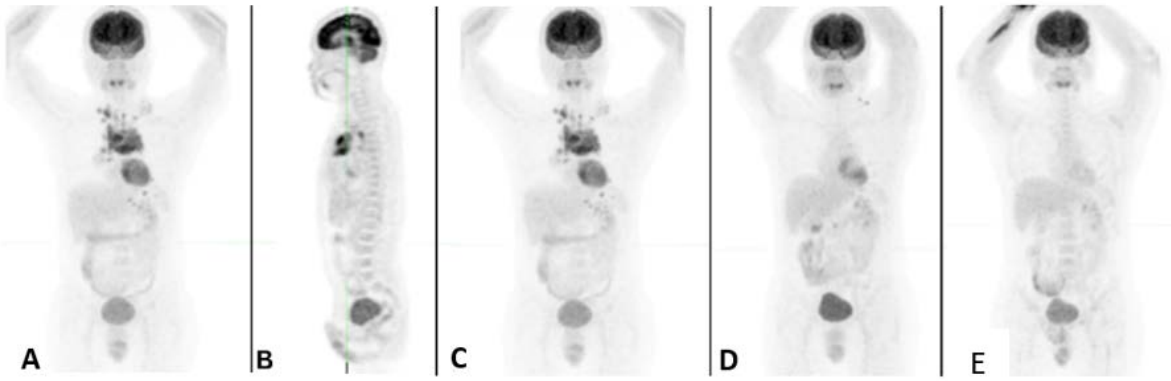

Figure 2: Heterogeneous uptake with increased ^{18}F-Fluorodeoxyglucose (^{18}F-FDG) accumulation in a large anterior mediastinal mass, as shown by the maximum intensity projection (MIP) PET image (A) and sagittal plane PET image (B). MIP PET images: (C) 10 July 2020 Pre-chemotherapy PET scan revealed a mass with high FDG uptake filling the anterior mediastinum and multifocal FDG-avid lesions in the supra-diaphragmatic and infra-diaphragmatic regions. (D) 18 January 2021, an end-of-treatment PET scan following first-line R-CHOP chemotherapy indicated that the anterior mediastinal mass had resolved, but some new hypermetabolic lymph nodes were seen. (E) 27 April 2021 Interim PET scan evaluation after two cycles of second-line R-ICE chemotherapy showed a complete metabolic response (DS-1).

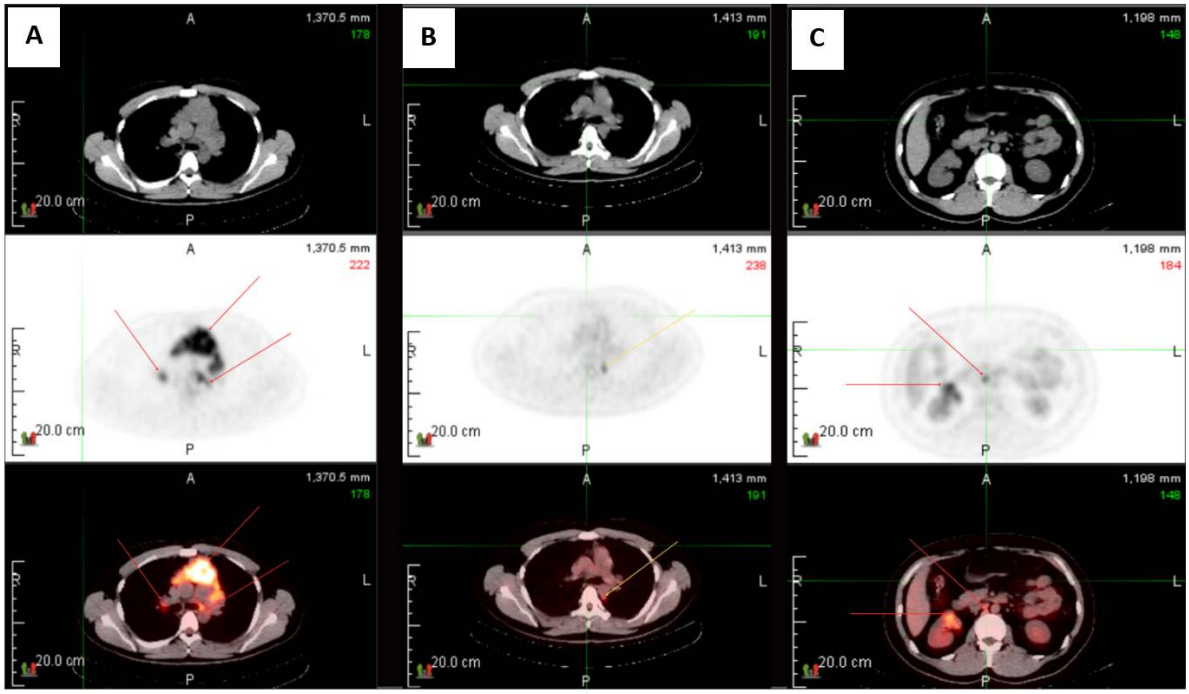

Figure 3: Axial CT (top), PET (middle), and fused PET/CT images (bottom): (A) 10 July 2020 PET image showed increased FDG uptake in the paratracheal, paraesophageal, and paracardial region (red arrow). (B) 18 January 2021 After completing chemotherapy, it showed a significant but incomplete response with some residual disease and a new nodal focus localized in the paravertebral region at the T-V level (SUV: 6.51) (yellow arrow). (C) 18 January 2021, a new intense focus of FDG avidity (SUV: 7.32) in the aortocaval region at the L-II level (red arrow) and a new irregular nodule (± 1x2 cm) in the inferior pole of the right kidney (red arrow), suggestive of the metastatic process.

Table 1: Summary table for PMBL

Etiology	PMBL is a distinct subtype of diffuse large B-cell lymphoma (DLBCL)
Incidence	2–4% of all non-Hodgkin lymphomas (NHLs) and about 10% of all large B-cell lymphomas
Gender ratio	female-to-male ratio of approximately 2:1
Age predilection	- predominantly adolescents and young adults - median age at diagnosis around 30-35 years
Risk factors	- Immunodeficiency states - autoimmune disorders - celiac disease - scleroderma - viral infections (HIV, EBV) - family history, - mutation in the MLL gene - exposure to radiation for the treatment of solid tumors - occupational chemical exposure - tobacco use
Treatment	- The first-line therapy is the R-CHOP regimen, with the option of consolidative radiotherapy or dose-adjusted R-EPOCH regimen. - The second-line therapy is the R-ICE regimen followed by **autologous stem cell transplantation (ASCT)** or chimeric antigen receptor T-cell (CAR-T).
Prognosis	- The prognosis is very favorable - 5-year survival rate exceeding 80% in most reports
Imaging findings	- CT typically demonstrates a masses in nodal or extranodal sites, rapid growth, displaying low attenuation due to necrosis, cystic degeneration, or hemorrhage. Infiltration of adjacent structures, including the lungs, chest wall, pleura, and pericardium, occurs in 70–80% of cases. - Relapse often presents as new hypermetabolic lymph nodes or extranodal lesions.

Table 2: Differential table of primary mediastinal large B-cell lymphoma

Differential diagnoses	Imaging findings	Clinical findings
Classic Hodgkin lymphoma (cHL)	- CT findings: Anterior mediastinal mass; lymphadenopathy - PET CT: High FDG uptake	- Bimodal: young adults (20–30s) & elderly (50–60s) - Often asymptomatic; B-symptoms (fever, weight loss, night sweats) in advanced stages - Mediastinal involvement: common, especially in nodular sclerosis subtype - Extranodal involvement: rare - Aggressiveness: indolent to moderate
Mediastinal grey zone lymphoma (MGZL)	- CT findings: Bulky anterior mediastinal mass, heterogeneous - PET-CT: High FDG uptake; heterogeneous appearance	- Primarily young adults (20–40s); male predominance - B-symptoms common; may present with fever, weight loss, night sweats - Mediastinal involvement: prominent, bulky anterior mediastinal mass - Extranodal involvement: sometimes seen; may involve adjacent structures - Aggressiveness: intermediate / aggressive
Diffuse large B-cell lymphoma (DLBCL)	- CT findings: Masses in nodal or extranodal sites; rapid growth - PET-CT: High FDG uptake; often more widespread	- Older adults (median age ~64); slight male preponderance - B-symptoms in ~30%; variable presentation - Mediastinal involvement: possible but less often dominant - Extranodal involvement: common (e.g., GI tract, CNS, bone) - Aggressiveness: aggressive

KEYWORDS

Non-Hodgkin Lymphoma, relapse, second-line chemotherapy, positron emission tomography/computed tomography, PET-CT

ABBREVIATIONS

ASCT = Autologous Stem Cell Transplant
BCL-6 = B-Cell Lymphoma 6
BEAM = Bis-Chloroethyl-Nitrosourea, Etoposide, Cytosine Arabinoside, And Melphalan
BV = Brentuximab Vedotin
CAR-T = Antigen Receptor T-Cell
CD = Cluster Of Differentiation
CHL = Classic Hodgkin Lymphoma
CMV = Cytomegalovirus
DLBCL = Diffuse Large B-Cell Lymphoma
DS-1= Deauville Score Of 1
EBV = Epstein-Barr Virus
FDG = Fluorodeoxyglucose
G-CSF = Granulocyte-Colony Stimulating Factor
HBsAg = Hepatitis B Surface Antigen
HCV = Hepatitis C Virus
HIV = Human Immunodeficiency Virus
MGZL = Mediastinal Grey Zone Lymphoma
MLL = Mixed Lineage Leukemia
MUM-1 = Multiple Myeloma Oncogene 1
NHL = Non-Hodgkin Lymphoma
PBSC = Peripheral Blood Stem Cells
PET-CT = Positron Emission Tomography/Computed Tomography
PMBL = Primary Mediastinal Large B-Cell Lymphoma
R-CHOP = Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Oncovin, And Prednisone
R-EPOCH = Rituximab, Etoposide, Doxorubicin, Cyclophosphamide, Vincristine, Prednisone
rG-CSF = Recombinant Human Granulocyte Colony-Stimulating Factor
R-ICE = Rituximab, Ifosfamide, Carboplatin, And Etoposide
R/R = Relapse/Refractory
SUVmax = Maximum Standardized Uptake Value

Online access

This publication is online available at:
www.radiologycases.com/index.php/radiologycases/article/view/5850

Peer discussion

Discuss this manuscript in our protected discussion forum at:
www.radiolopolis.com/forums/JRCR

Interactivity

This publication is available as an interactive article with scroll, window/level, magnify and more features.
Available online at www.RadiologyCases.com

Published by EduRad

www.EduRad.org