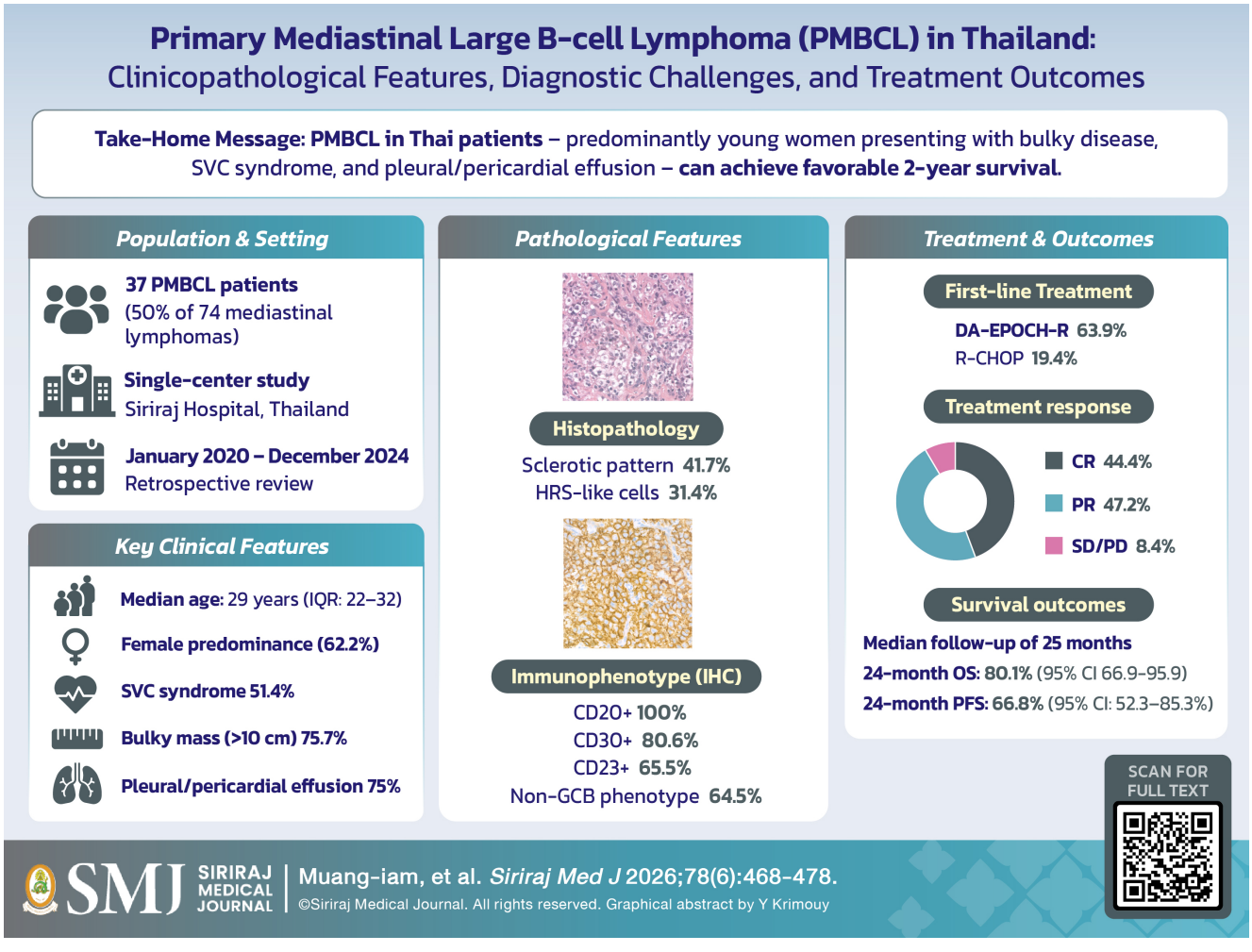
Clinicopathological Features of Primary Mediastinal Large B-cell Lymphoma: A 5-Year Retrospective Study

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ABSTRACT

Objective: To describe the clinicopathological features and treatment outcomes of primary mediastinal large B-cell lymphoma (PMBCL) at Siriraj Hospital, Thailand.

Materials and Methods: This retrospective study included all patients diagnosed with PMBCL during 2020–2024. Clinical, pathological, treatment, and survival data were retrieved from medical records and pathology reports. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan–Meier method.

Results: PMBCL accounted for 37 of 74 mediastinal lymphoma cases (50%). Median age was 29 years (IQR: 22–32), with female predominance (62.2%). Presentations included cough (79.4%), dyspnea (74.3%), and SVC syndrome (51.4%). Pleural or pericardial effusion was found in 75.0%. Bulky disease (>10 cm) and elevated LDH were 75.7% and 91.4%, respectively. Histologically, sclerotic pattern and HRS-like cells were observed in 41.7% and 31.4%, respectively. All cases were CD20-positive; CD23 and CD30 were expressed in 65.5% and 80.6%, respectively. A non-GCB phenotype was identified in 64.5% by the Hans algorithm. DA-EPOCH-R was the most common first-line regimen (63.9%). At a median follow-up of 25 months, the 24-month OS and PFS rates were 80.1% and 66.8%, respectively.

Conclusion: This study provides the first characterization of PMBCL in a Thai cohort, showing frequent SVC syndrome and pleural or pericardial effusion at diagnosis. Given the overlapping features and complexity of differential diagnosis, comprehensive immunohistochemical workup was essential for accuracy. DA-EPOCH-R was the dominant first-line therapy, with 2-year outcomes comparable to the rituximab era. Prompt recognition, diagnostic expertise, and multidisciplinary management are critical for optimizing PMBCL outcomes.

Keywords: Primary mediastinal large B-cell lymphoma; clinicopathological features; treatment outcomes; Thailand
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INTRODUCTION

Mediastinal lymphoma is the second most common primary mediastinal neoplasm after thymic epithelial tumors.[1] Several lymphoma subtypes can arise in this compartment, including classical Hodgkin lymphoma (CHL), primary mediastinal (thymic) large B-cell lymphoma (PMBCL), secondary involvement by diffuse large B-cell lymphoma (DLBCL), mediastinal gray zone lymphoma (MGZL), and T-lymphoblastic leukemia/lymphoma.[2,3] Among these, an incidence of PMBCL is approximately 2.38 per 1,000,000 population[4] and accounts for only 2–4% of all non-Hodgkin lymphomas (NHL).[5] Clinically, it typically affects young patients[4] and presents as a localized mediastinal mass, although direct invasion into adjacent structures or dissemination to extranodal sites may occur.[6] In addition, PMBCL harbors unique pathological and genetic features - including deregulation of the NF-κB and JAK/STAT signaling pathways alongside multiple mechanisms of immune escape, such as PDL1/PDL2 overexpression and MHC class II downregulation—that distinguish it from conventional DLBCL[6,7] and requires distinct treatment approaches.[8] However, its overlapping morphological and immunophenotypic features with CHL and MGZL may pose significant diagnostic challenges.[9]

Although the clinicopathological characteristics of PMBCL have been well described in studies from Western countries,[7] data on the Thai population remain limited. One previous study reported the frequency of PMBCL within a national NHL registry in Thailand,[10] and no study has specifically characterized its clinical or pathological features in this population. A better understanding of the clinical course and pathological characteristics of PMBCL in Thai patients may improve diagnostic accuracy, prognostic assessment, and therapeutic decision-making. Therefore, this study aimed to describe the clinical features, pathological findings, and treatment outcomes of PMBCL cases at Siriraj Hospital, the largest tertiary care center in Thailand.

MATERIALS AND METHODS

This retrospective descriptive study was approved by the Institutional Review Board of the Faculty of Medicine Siriraj Hospital, Mahidol University (COA no. Si 468/2025), and conducted at Siriraj Hospital, Bangkok, Thailand. All cases diagnosed between January 1, 2020 and December 31, 2024 were reviewed.

Case identification and selection

Cases were searched from the pathology laboratory information system (HCLAB) using the keywords "lymphoma", "mediastinum", and "mediastinal". Reports initially diagnosed as large B-cell lymphoma were reviewed,

and the final diagnosis of primary mediastinal large B-cell lymphoma (PMBCL) was confirmed by clinicopathological correlation documented in electronic medical records (SiIT). Owing to the rarity of PMBCL, all available cases were included. Cases with other lymphoma subtypes were excluded from further analysis and described only for determining disease frequency.

Clinical data and outcome assessment

Clinical data at diagnosis were collected from pathology request forms and electronic medical records (SiIT, Eclair, and SiPAC), including the following parameters: demographic characteristics (age and sex); presenting symptoms (cough, dyspnea, chest pain, superior vena cava [SVC] syndrome, B symptoms, and other reported symptoms) and duration of symptoms; laboratory parameters (hemoglobin, white blood cell [WBC] count, platelet count, and lactate dehydrogenase [LDH] level); imaging findings (mediastinal mass size, tumor invasion, and lymph node enlargement); Ann Arbor staging; Eastern Cooperative Oncology Group (ECOG) performance status; and International Prognostic Index (IPI) score. Treatment details and follow-up data were also retrieved. Treatment response at the end of first-line treatment was classified as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD). Overall survival (OS) and progression-free survival (PFS), including survival estimates at 2 years, were analyzed. OS was defined as the time from the date of diagnosis to death from any cause. PFS was defined as the time from the date of diagnosis to the first occurrence of disease progression, relapse following CR, or death from any cause, whichever occurred first. Cases with diagnostic uncertainty or complex clinical course were discussed with a hematologist (W.O.).

Pathological evaluation

All available histologic slides were reviewed for morphologic features and immunohistochemical findings by hematopathology fellow in training (M.M.) and a board-certified hematopathologist (S.S.). In diagnostically challenging cases, additional review was performed with a thoracic pathology specialist (R.R.). When histologic and/or immunohistochemical slides were incomplete, results were obtained from the original reports.

Statistical analysis

Descriptive statistics were used to summarize the data. Survival analysis was performed using the Kaplan-Meier method with RStudio (version 2026.01.1).

RESULTS

Over a 5-year period, 74 patients presenting with a mediastinal mass were diagnosed with malignant lymphoma, including primary mediastinal B-cell lymphoma (37, 50%), classic Hodgkin lymphoma (9, 12.2%), diffuse large B-cell lymphoma (9, 12.2%), T-lymphoblastic leukemia/lymphoma (5, 6.8%), mediastinal gray zone lymphoma (2, 2.7%), follicular lymphoma (2, 2.7%), ALK-negative anaplastic large cell lymphoma (2, 2.7%), Burkitt lymphoma (1, 1.4%), and blastoid variant of mantle cell lymphoma (1, 1.4%).

Demographic and clinical characteristics

A total of 37 patients with primary mediastinal large B-cell lymphoma were included over a 5-year period (Table 1). The median age at diagnosis was 29 years (IQR: 22-32), with a female predominance (23/37, 62.2%). The median duration of symptoms prior to diagnosis was 2 months (IQR: 0.7–3). The most common presenting symptoms were cough (27/34, 79.4%) and dyspnea (26/35, 74.3%), followed by superior vena cava (SVC) syndrome (18/35, 51.4%). Pleural or pericardial effusion and lymphadenopathy were each present in approximately three-quarters of patients, while B symptoms in approximately one-quarter. Less common symptoms included hoarseness and progressive back pain. Notably, two patients were pregnant at gestational ages of 19 and 21 weeks. In two additional patients, mediastinal masses were incidentally detected on pre-employment screening chest imaging.

Elevated LDH was present in 91.4% of patients. The mean mediastinal mass size was 11.7 ± 3.1 cm, with bulky disease (>10 cm) in 75.7%. Tumor invasion was documented in the pleura (2/36, 5.6%), pericardium (10/36, 27.8%), and other structures (15/36, 41.7%) including the brachiocephalic vein, chest wall, SVC, lung parenchyma, aortopulmonary window, left pulmonary artery, left internal jugular vein, and right phrenic nerve. Mediastinal and supraclavicular lymph node enlargement were identified in 48.6% (mean size: 2.7 ± 1.3 cm) and 58.3% (mean size: 2.0 ± 1.1 cm) of patients, respectively.

Regarding disease staging and risk stratification, the majority of patients presented with early-stage disease, with Ann Arbor stage I and II accounting for 83.3% of cases (38.9% and 44.4%, respectively). Most patients had a good performance status, with an ECOG performance score of 0-1 in 94.4% of cases. By IPI score, the majority were low-risk, with 74.3% scoring 0-1.

Pathological features

Histopathological features are summarized in Table 2.

TABLE 1. Baseline demographic, clinical, and laboratory characteristics.

Characteristic	Number (%)
Demographics	
Age at diagnosis (years) [median (IQR)] (n=37)	29 (22–32)
Sex	
Female	23/37 (62.2)
Male	14/37 (37.8)
Clinical Presentation	
Duration of symptoms (months) [median (IQR)] (n=34)	2 (0.7–3)
Cough	27/34 (79.4)
Chest pain	10/31 (32.3)
Dyspnea	26/35 (74.3)
B symptoms	9/35 (25.7)
SVC syndrome	18/35 (51.4)
Pleural/pericardial effusion	27/36 (75.0)
Lymphadenopathy	28/36 (77.8)
Laboratory & Imaging Findings	
Hemoglobin (g/dL) (mean ± SD) (n = 34)	12.13 ± 1.6
WBC ($\times 10^9$/L) (mean ± SD) (n = 34)	8.32 ± 4.3
Platelets ($\times 10^9$/L) (mean ± SD) (n = 34)	351.94 ± 111.8
Elevated LDH	32/35 (91.4)
Mediastinal mass size (cm) (mean ± SD)	11.7 ± 3.1
Bulky disease (mass size > 10 cm)	28/37 (75.7)
Tumor invasion	
Pleura	2/36 (5.6)
Pericardium	10/36 (27.8)
Other	15/36 (41.7)
Mediastinal lymph node enlargement	18/35 (48.6)
Supraclavicular lymph node enlargement	21/36 (58.3)
Ann Arbor Staging	
Stage I	14/36 (38.9)
Stage II	16/36 (44.4)
Stage III	2/36 (5.56)
Stage IV	4/36 (11.1)
ECOG PS 0–1	34/36 (94.4)
IPI score	
0-1	26/35 (74.3)
2	4/35 (11.4)
3	2/35 (5.7)
4-5	3/35 (8.6)

TABLE 2. Pathological features.

Pathological Features	Number (%)
Microscopic Architecture	
Diffuse	21/36 (58.3)
Sclerotic	15/36 (41.7)
Immunohistochemistry – B-cell Markers	
CD20 positive	37/37 (100)
PAX5 positive	16/16 (100)
PAX5 strong intensity	14/15 (93.3)
Immunohistochemistry – Other Markers	
CD23 positive	19/29 (65.5)
CD30 positive	29/36 (80.6)
CD23 and CD30 positive	16/29 (55.2)
CD15 positive	0/17 (0)
CD45 positive	20/20 (100)
CD10 positive	5/32 (15.6)
BCL6 positive	29/34 (85.3)
MUM1 positive	24/35 (68.6)
BCL2 positive	19/34 (55.9)
EBER positive	0/15 (0)

Tissue diagnosis was established predominantly via core needle biopsy of the mediastinal mass (32/37, 86.5%). Two cases were biopsied from supraclavicular lymph nodes in patients presenting with an anterior mediastinal mass and were subsequently diagnosed as PMBCL based on clinicopathological correlation. One patient required mediastinal mass resection following an inconclusive initial biopsy; however, the biopsy specimen was unavailable for review in our laboratory system. Another patient was initially diagnosed with thymic carcinoma at an outside institution, but upon review with expanded immunostaining, the diagnosis was revised to PMBCL. Histologically, a sclerotic architectural pattern was observed in 15/36 cases (41.7%). (Fig 1) The lymphoma cells ranged in size from medium to large, with a median proportion of large-sized cells of 60% (IQR 30–80). Hodgkin/Reed-Sternberg (HRS)-like cells were identified in 11/35 cases (31.4%), comprising a median of 1% of the tumor cellularity (IQR 1–5%). Tumor necrosis was present in 5/36 cases. Bone marrow involvement was uncommon, detected in only 2/31 (6.5%) of evaluable cases.

Immunohistochemically, CD45, CD20, and PAX5 were positive in all tested cases. CD30 was expressed in 80.6% of cases, CD23 in 65.5%, and co-expression of both CD30 and CD23 in 55.2%. (Fig 1) No case demonstrated EBV positivity by EBER in situ hybridization. Cell-of-origin classification using the Hans algorithm identified a non-germinal center B-cell (non-GCB) phenotype in the majority of cases (20/31, 64.5%). The tumor microenvironment showed a modest inflammatory infiltrate, with a median T-cell component of 5% (IQR 5–10) and a median histiocyte component of 5% (IQR 1–5). Notably, one case exhibited cytoplasmic kappa light chain restriction with negative lambda staining. An additional case showed CD117 expression (reported sporadically in DLBCL); PAX8 positivity was interpreted as nonspecific, reflecting polyclonal antibody used in this study cross-reactivity with lymphoid cells (Fig 2).

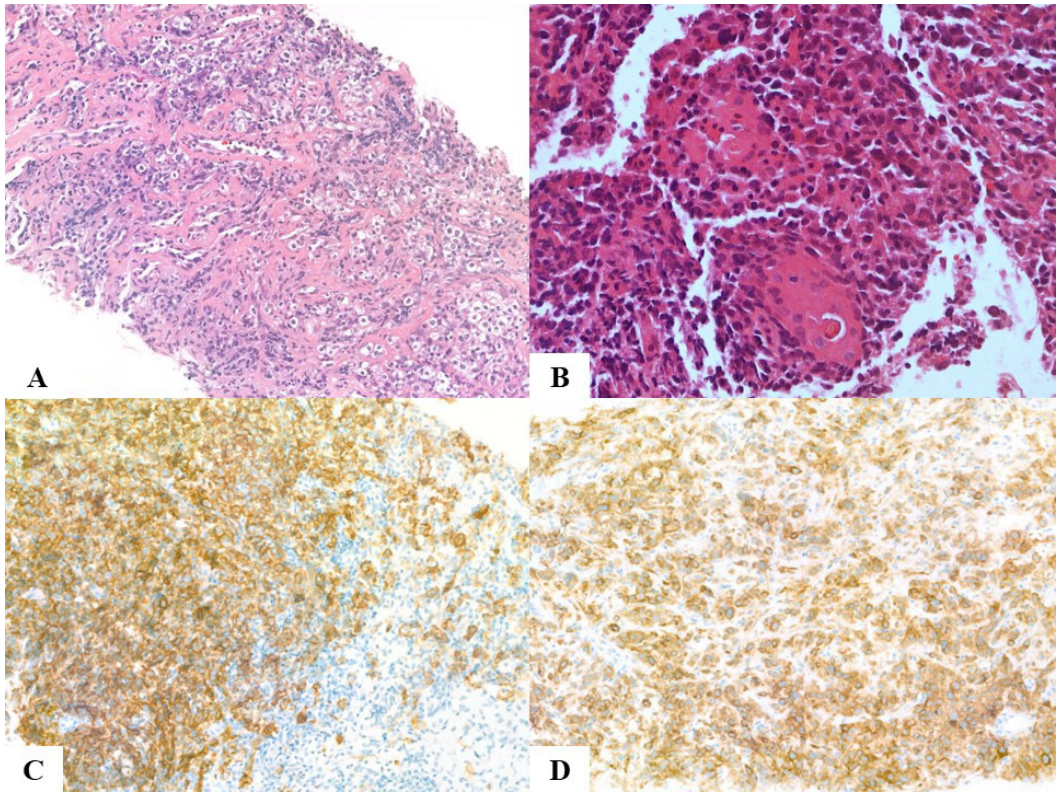


Fig 1. Infiltration of medium to large clear cells in sclerotic background, H&E, 20x (A). Remnants of thymic epithelium among diffuse infiltration by lymphoma cells, H&E, 40x (B). Example of case with CD23 expression, 20x (C). Example case with CD30 expression, 20x (D).

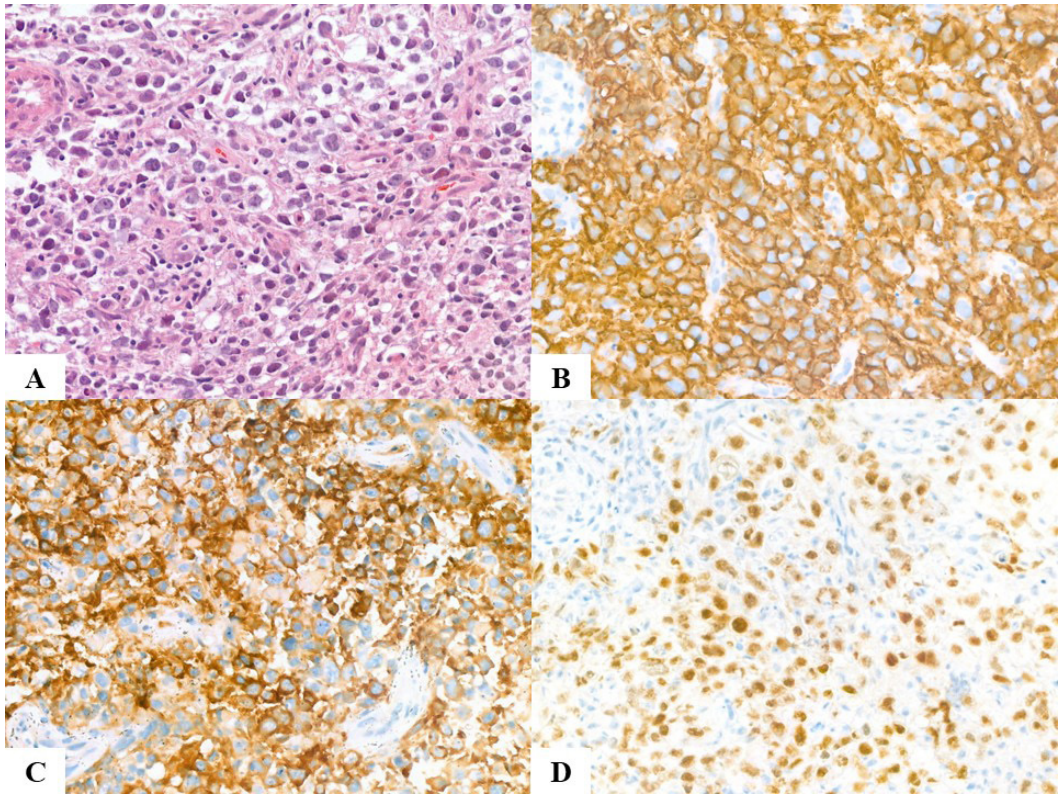


Fig 2. Primary mediastinal large B-cell lymphoma with aberrant expression of CD117 and PAX8. Delicate reticular fibrosis with compartmentalization of groups of neoplastic tumor cells with clear cytoplasm, H&E, 40x (A). CD20 expression confirmed B-cell lineage, 40x (B). CD117 expression, 40x (C). PAX8 expression, 40x (D)

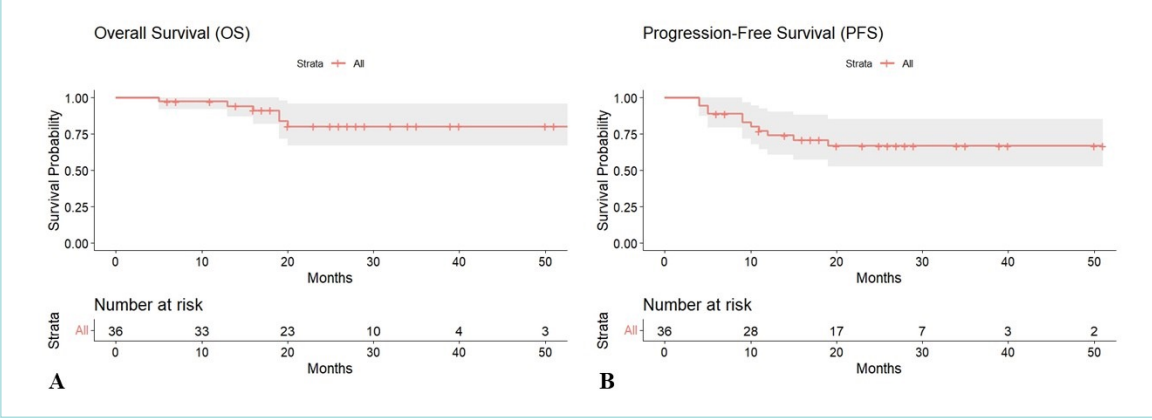


Fig 3. Kaplan-Meier survival curves. Overall survival (A). Progression-free survival (B).

Treatment and outcome

The regimen with 6 cycles of DA-EPOCH-R (dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab) was the most common (23/36, 63.9%). The regimen with 6 cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) (7/36, 19.4%) was the second most common. The remaining 6 patients (16.7%) received alternative regimens— 2 patients with R-CHOP x1 cycle followed by DA-EPOCH-R x5 cycles, 2 patients with R-HyperCVAD (rituximab, hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone), 1 patient with R-EPOCH, and 1 patient with R-CHOP x3 cycles, followed by ICE (ifosfamide, carboplatin, and etoposide) x3 cycles.

At the end of first-line treatment, CR was achieved in 16/36 (44.4%) patients, PR in 17/36 (47.2%), SD in 2/36 (5.6%), and PD in 1/36 (2.8%). Among patients who did not achieve CR following first-line therapy, a variety of salvage regimens were used. ICE-based regimens were the most frequently used, often combined with other salvage chemotherapy including DHAP (dexamethasone, high-dose cytarabine, and cisplatin), ESHAP (etoposide, methylprednisolone, high-dose cytarabine, and cisplatin), and GDP (gemcitabine, dexamethasone, and cisplatin).

Radiotherapy was used in some patients, either as a sole salvage modality or in combination with chemotherapy. Notably, immunotherapy-based approaches including nivolumab and brentuximab vedotin were incorporated in 4 patients, autologous stem cell transplantation (ASCT) was performed in 5 patients, and 2 patients proceeded to CAR-T cell therapy.

Among the 4 patients who experienced relapse, salvage regimens included radiotherapy, DHAP followed by BV-ICE (brentuximab vedotin, ifosfamide, carboplatin, and etoposide), R-nivolumab-ICE leading to ASCT, and R-DHAP followed by ASCT. One patient who underwent mediastinal mass resection subsequently relapsed with nodular sclerosis classic Hodgkin lymphoma, proven by left groin lymph node excision. Review of the diagnostic materials at the time of PMBCL diagnosis revealed a separate nodule adjacent to the main mediastinal mass, showing morphology suspicious for classic Hodgkin lymphoma. However, immunostaining could not be performed, as only slides were received from the referring hospital without the corresponding tissue block.

A total of 36 patients were included in the survival analysis (one patient was excluded due to missing data). The median follow-up time (reverse Kaplan-Meier method) for OS and PFS was 25 months [95% confidence interval (CI): 20–34 months] and 23 months (95% CI: 20–34 months), respectively. Because less than 50% of patients had experienced the events, median OS and PFS were not reached, suggesting favorable outcomes and limited follow-up. There were six deaths with an overall survival (OS) rate at 24 months of 80.1% (95% CI: 66.9–95.9%). Eleven events were reported for progression-free survival (PFS), with a 24-month PFS rate was 66.8% (95% CI: 52.3–85.3%). Kaplan-Meier curves demonstrated OS was around 80% after month 20 and stable, while PFS declined rapidly initially within the first 10 months before reaching a steady state at approximately 68%.

DISCUSSION

This study summarizes the clinicopathological characteristics and treatment outcomes of patients with PMBCL at Siriraj Hospital, a main referral center of Thailand, including one of the largest cohort from a single institution in Southeast Asia over 5 years. Compared with previous epidemiological data from our institution reporting 332 mediastinal masses, PMBCL remained the most common mediastinal lymphoma subtype.[3]

The demographic profile of this cohort is broadly consistent with the published literature, as PMBCL predominantly affects young female patients across all reported series.[4,11–15] A population-based SEER analysis reported a mean age of 36 years,[4] whereas our patients had a younger median age, comparable to that of a single-center study from Singapore (median age 27 years).[14] Cough and dyspnea were the most common presenting symptoms, reflecting the compressive effect of a bulky anterior mediastinal mass typical of PMBCL.[11] SVC syndrome was more prevalent in the present study than in most comparative series.[12,15] The multicenter Turkish study documented SVC syndrome in 27.4% of patients and identified it as an independent adverse prognostic factor for overall survival on multivariate analysis (HR 2.78, p = 0.028).[12] This finding warrants clinical attention, as SVC syndrome reflects significant vascular compression and may necessitate urgent intervention before definitive treatment can be initiated.[16] Pleural or pericardial effusion was markedly more prevalent in the present study than in previous series,[11-15] likely reflecting the high burden of bulky disease and extensive local tumor invasion at presentation. Effusion carries well-established adverse prognostic significance in PMBCL, independently predicting inferior PFS and higher rates of primary refractory or early relapse in three studies,[12,13,15] although this association was not observed in two others.[11,17] We further explored the nature of this phenomenon by comparing symptom duration between groups to determine whether a high rate of SVC syndrome and effusion was attributable to delayed presentation or aggressive biological behavior. There was no difference in median symptom duration between patients with effusion and without [2 months (IQR: 0.75–3) vs. 2 months (IQR: 0.75–3), p = 0.906]. The median duration of symptoms was lower in patients with SVC syndrome compared to those without [0.75 months (IQR: 0.5–2) vs. 2 months (IQR: 1–4); p = 0.034], possibly indicating rapid growth of the tumor as a contributory reason, but its interpretation must be done cautiously, given the smaller subgroup number. Most patients presented with early-stage disease, favorable performance status, and low IPI scores, consistent with the described characteristic clinical profile of PMBCL.[4,11-15,17] Although IPI has demonstrated prognostic significance in some series,[12,13,17] its discriminatory utility in PMBCL remains limited, likely because most affected patients are young and otherwise healthy, leaving little score variation to meaningfully stratify risk. Notably, two patients were pregnant at the time of diagnosis - a recognized but uncommon scenario given PMBCL's predilection for women of reproductive age. This underscores the importance of early recognition and multidisciplinary management in this setting, as delayed diagnosis during pregnancy can result in life-threatening cardiorespiratory complications.[18,19]

Diagnosis of PMBCL on core needle biopsy, the predominant specimen type, can be challenging due to sclerosis, crush artifact, and morphologic overlap with other mediastinal neoplasms.[2,20] Given the broad differential, accurate diagnosis relies on careful integration of histomorphology and immunohistochemistry; notably, AE1/AE3 cytokeratins may highlight entrapped native thymic epithelium within lymphomatous infiltrates, potentially leading to misdiagnosis. One case required resection after an inconclusive biopsy, and another, initially diagnosed as thymic carcinoma at an outside institution, was reclassified as PMBCL following expanded immunohistochemical evaluation. In a case with a sheet-like growth pattern and clear cell features, with CD117 expression and PAX8 positivity, the differential diagnosis included a germ cell tumor and thymic epithelial tumor. An extended panel demonstrated negativity for AFP, OCT4, SALL4, and Beta-HCG, excluding germ cell tumor. The diagnosis was supported by positive CD20, CD45, CD79a, and PAX5, confirming B-cell lineage. Thymic epithelial tumor was excluded by negative AE1/AE3 staining. Notably, the polyclonal PAX8 antibody used in this case may cross-react with the N-terminal region of PAX5;[21] therefore, PAX8 positivity was interpreted with caution as likely nonspecific in this context.[22] Two cases presenting with supraclavicular lymphadenopathy were diagnosed only after clinicopathologic correlation, underscoring the importance of clinical context, particularly mediastinal involvement, to avoid misclassification as DLBCL.[16,23]

The immunophenotypic profile was consistent with established PMBCL criteria.[5,24] Universal CD20 and PAX5 confirmed B-cell lineage. CD30 expression, while slightly higher than reported in some cohorts, characteristically showed weak, heterogeneous, and focal-to-patchy staining— contrasting with the diffuse strong positivity of CHL.[20,25,26] A comprehensive immunophenotypic comparison of CHL, PMBCL, and GZL, noting that CD30 is expressed in more than 80% of PMBCL cases with weak and heterogeneous staining, while CD15 is usually negative and CD45 is positive, in contrast to CHL where CD30 is strongly and diffusely positive and CD45 is absent.[20] CD23 expression supported thymic B-cell origin, with a reported sensitivity of 85% and positive predictive value of 92% for distinguishing PMBCL from CHL.[26] No case demonstrated EBV positivity, an important feature excluding EBV-associated lymphomas.

Anyway, rare EBV-positive cases with PMBCL/MGL morphology and molecular genetic have been described. The EAHP workshop identified at least one EBV-positive case sharing a PMBCL-like gene expression signature with mutations supporting possible inclusion within the mediastinal thymic B-cell lymphoma spectrum.[27,28]

One case relapsed as nodular sclerosis CHL, potentially representing sequential lymphoma – a rare phenomenon reflecting shared JAK-STAT and NF-κB pathway dysregulation between PMBCL and CHL, with GZL representing the biological continuum between these entities.[28,29] The EAHP workshop highlighted that in both composite and sequential lymphomas, one component may exhibit gray zone morphology, and transitional areas can further complicate classification. All relapses should be confirmed by rebiopsy, as the second occurrence may represent a histologically distinct but clonally related entity requiring a fundamentally different treatment approach.[29]

DA-EPOCH-R was the predominant first-line regimen, reflecting institutional adoption of dose-intensive therapy to reduce toxicity on consolidative radiotherapy in this predominantly young female population. This practice is supported by a systematic review and meta-analysis of 4,068 patients demonstrating superior OS with dose-intensive chemoimmunotherapy compared with standard R-CHOP,[30] and a single-center DA-EPOCH-R cohort reporting excellent 3-year OS and PFS.[15] One study has reported comparable efficacy between DA-EPOCH-R and R-CHOP in real-world multicenter cohorts, with no statistically significant differences in PFS or OS demonstrated between regimens.[12] The studies found better CR rates than this cohort. Reduced CR rates seen here could be attributed to factors such as bulky disease, SVC syndrome or pleural /pericardial effusion. Nonetheless, variances in patient selection characteristics, disease documentation and scored prior to response comparison preclude direct comparison. Differences in treatment effectiveness or institutional practices are also possible types of bias that could require further evaluation with larger, matched cohorts.

Upon data collection, treatment response was assessed predominantly by PET/CT. It is important to note that a Deauville score of 4 on end-of-treatment PET/CT most likely represents post-treatment inflammatory uptake rather than active residual disease in PMBCL, and these patients may still achieve durable remission without further treatment escalation.[6,15] PET/CT was used by this cohort to assess treatment response, but the final treatment response classification was based on the clinical judgment of the treating hematologist, combining imaging results with clinical and laboratory parameters. As a result, patients with a Deauville score of 4 were defined as PR and actively treated rather than observed. Moreover, the treating team decided on active intervention because this was the institutional practice during the period from which the patients' data were obtained. None of the 17 documented as PR achieved and maintained long-term remission without therapy, reflecting this institution's practice of actively treating non-CR patients. The estimated 24-month OS rate of 80.1% was generally in line with published PMBCL outcomes in the rituximab era, where 2-year OS rates between 75-90% have been reported across retrospective cohorts.[4,31] The rapid early PFS decline stabilizing after approximately 10 months is consistent with the known relapse pattern of PMBCL, which predominantly occurs within the first 12 months following first-line therapy.[15]

Among patients who did not achieve CR, ICE-based salvage chemotherapy was most commonly used. ASCT and CAR-T cell therapy were utilized in eligible patients, reflecting their emerging roles as consolidative and salvage strategies.[16] Nivolumab combined with brentuximab vedotin was incorporated in a subset of patients. PMBCL expansion cohort of the CheckMate 436 trial demonstrated favorable response and survival outcomes in relapsed or refractory PMBCL.[32]

This study has several limitations, including its retrospective single-center design, relatively small sample size, and variable completeness of medical record documentation, all of which introduce selection bias and limit generalizability. The short median follow-up likely underestimates true long-term OS and PFS, as late relapses would not have been captured. Additionally, the absence of molecular profiling data precluded evaluation of biologically informed prognostic models and may have underestimated the proportion of patients with high-risk disease.

CONCLUSION

Despite the limitations, PMBCL in Thai patients shares key clinicopathological features with previously described cohorts, with DA-EPOCH-R delivering acceptable survival outcomes in this predominantly young population. Careful clinicopathological correlation remains essential given the diagnostic complexity inherent to anterior mediastinal lesions. Rebiopsy at relapse should be considered mandatory, as relapsed disease may represent a histologically distinct entity requiring a fundamentally different treatment approach. Future multicenter collaboration across Thailand is essential to increase sample size, extend follow-up, and incorporate

molecular profiling with standardized response assessment to optimize PMBCL management in this region.

Data Availability Statement

Data may be available from the corresponding author upon reasonable request and with the approval of the Siriraj Institutional Review Board.

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None.

DECLARATIONS

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Conflict of Interest

The authors declare no conflict of interest.

Registration Number of Clinical Trial

This is a retrospective study.

Author Contributions

Conceptualization and methodology, M.M., S.S; Data collection, M.M., S.S.; Formal analysis, M.M., S.S.; Visualization and writing – original draft, M.M ; Writing – review and editing, S.S., W.O., R.R.; Supervision, S.S. All authors have read and agreed to the final version of the manuscript.

Use of Artificial Intelligence

Artificial intelligence tools (Claude, Anthropic) were used solely to assist with grammar correction and language editing during manuscript preparation. All content was written, revised, and finalized by the authors.

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