Journal of Cancer Research and Practice

journal homepage: https://journals.lww.com/jcrp

Case Report

Pembrolizumab as an Unconventional First-line Salvage Therapy in Primary Mediastinal Large B-cell Lymphoma: A Case Report

Szu-Chi Yao*, Yu-Hsuan Kuo

Division of Hematology and Oncology, Department of Internal Medicine, Chi Mei Medical Center, Tainan City, Taiwan

Abstract

Primary mediastinal large B-cell lymphoma (PMBCL) is a rare and aggressive subtype of non-Hodgkin lymphoma with unique clinical and molecular characteristics. We report the case of a young woman diagnosed with PMBCL who presented with a bulky mediastinal mass and responded favorably to pembrolizumab monotherapy after initial R-CEOP treatment was discontinued due to adverse effects. Over 24 months of follow-up, pembrolizumab monotherapy, later combined with rituximab, achieved a complete response and gradual clinical improvement. Despite experiencing severe complications throughout the clinical course, the patient demonstrated an excellent therapeutic response to immune checkpoint inhibitor monotherapy, underscoring the potential clinical value of this treatment approach.

Keywords: Cerebral edema, pembrolizumab, primary mediastinal large B-cell lymphoma, superior vena cava syndrome

Introduction

Primary mediastinal large B-cell lymphoma (PMBCL) is a rare subtype of B-cell lymphoma originating from thymic B-cells. It predominantly affects young women and typically presents as a rapidly enlarging mass in the anterior mediastinum. PMBCL is unique among B-cell non-Hodgkin lymphoma subtypes but shares certain features with classical Hodgkin lymphoma, including a peak incidence in adolescents and young adults, a mediastinal presentation, and molecular changes including dysregulation of the JAK-STAT and nuclear factor kappa B (NF-κB) signaling pathways, along with the overexpression of PD-1 ligands.[1] Clinical manifestations often include dyspnea, cough, chest pain, and dysphagia, which are typically related to the rapid growth of the mediastinal mass. In addition, serious complications may arise, including airway compression, superior vena cava (SVC) syndrome, and the development of pericardial and pleural effusions. Here, we report the case of a woman in her 20s who presented with a bulky mediastinal mass and SVC syndrome. Following evaluation, she was diagnosed

Submitted: 10-Mar-2025 **Revised:** 14-Jun-2025
Accepted: 03-Jul-2025 **Published:** 14-Aug-2025

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jcrp

DOI: 10.4103/ejcrp.eJCRP-D-25-00011

Address for correspondence: Dr. Szu-Chi Yao, Division of Hematology and Oncology, Department of Internal Medicine, Chi Mei Medical Center, No. 901, Zhonghua Road, Yongkang Dist., Tainan City 710402, Taiwan.
E-mail: s46457978@gmail.com

How to cite this article: Yao SC, Kuo YH. Pembrolizumab as an unconventional first-line salvage therapy in primary mediastinal large B-cell lymphoma: A case report. J Cancer Res Pract 2025;12:94-7.

with PMBCL. Despite the presence of a significant tumor burden and multiple complications, she responded favorably to pembrolizumab monotherapy, suggesting its potential role as an alternative salvage treatment option for patients with PMBCL.

Case Report

A 25-year-old female student of traditional Chinese medicine with no comorbidities presented with a 1-month history of cough, wheezing, orthopnea, and progressive swelling of the right side of the face, bilateral neck, and right lower limb. She had taken symptomatic medications based on traditional Chinese medicine; however, worsening symptoms forced her to seek medical care. A chest radiograph showed a widening mediastinum and mass-like opacity over the left upper lung. Further chest computed tomography (CT) revealed a large anterior mediastinal mass approximately 10 cm in size, tumor invasion of the SVC with stenosis, and regional metastatic lymphadenopathy of the left supraclavicle with pleural and left upper lung invasion. The tumor had also invaded the pericardium and visceral pleura, with pericardial effusion and bilateral pleural effusion [Figure 1]. Subsequently, the patient underwent video-assisted thoracoscopic surgery (VATS) to biopsy the mediastinal tumor. However, postoperative airway collapse led to sudden respiratory failure, necessitating emergency endotracheal intubation to relieve tumor-induced airway compression. The pathological diagnosis confirmed PMBCL with invasion to the lung. Additional biomarker analysis demonstrated strong programmed death-ligand 1 (PD-L1) expression in more than 90% of tumor cells by immunohistochemical staining [Figure 2]. Comprehensive staging evaluations, including abdominal CT and bone marrow biopsy, revealed no further disease involvement. According to the Lugano classification, the disease was staged as IIE. Following diagnosis, the patient began first-line systemic treatment with the R-CEOP regimen in January 2023 (rituximab 375 mg/m² on day 1; cyclophosphamide 750 mg/m², epirubicin 75 mg/m², and vincristine 2 mg on day 2; prednisone 100 mg daily on days 1–5). Despite the prophylactic administration of filgrastim, the patient developed severe neutropenic fever, complicated by a urinary tract infection (urine culture: *Candida tropicalis*) and subsequent bacteremia (blood culture: *Candida tropicalis*). Her condition rapidly deteriorated to septic shock, requiring the use of three vasopressors to maintain hemodynamic stability by day 7 postchemotherapy. This critical state persisted for several days. Given the life-threatening severity of the infectious complication, her family ultimately declined further chemotherapy due to concerns about the risk of repeated severe infections. Two weeks after initiating therapy, the patient developed pupil dilation and a diminished light reflex. Emergency brain CT revealed diffuse cerebral edema, reduced gray-white matter differentiation in the bilateral basal ganglia, and mass effect leading to tonsillar herniation with impending uncal herniation [Figure 3]. Cerebral hypoperfusion secondary to SVC syndrome was considered the most likely

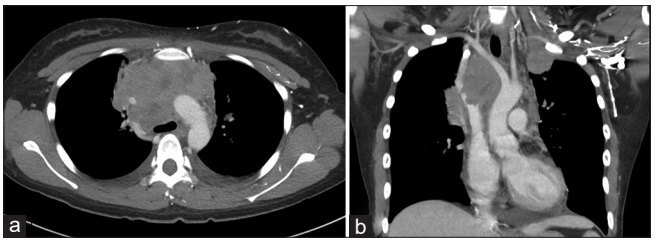

Figure 1: (a) A large anterior mediastinal mass of about 10 cm in size, (b) The tumor had invaded the superior vena cava with stenosis, and there was left supraclavicular metastatic lymphadenopathy

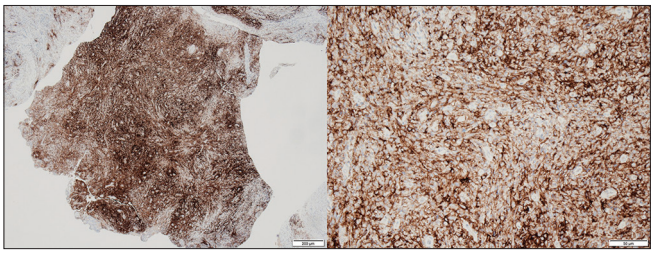

Figure 2: Immunohistochemical staining showed strong PD-L1 expression in over 90% of tumor cells

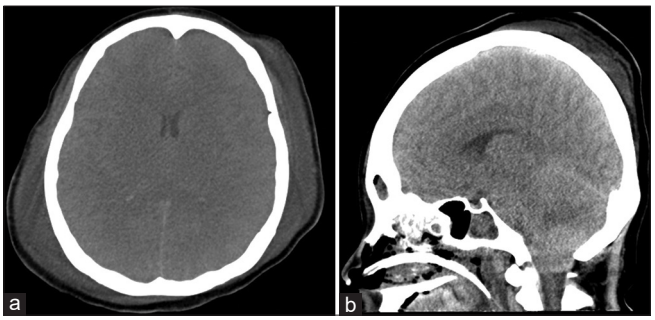

Figure 3: Brain computed tomography showed (a) diffuse brain swelling with reduced gray-white matter differentiation in the bilateral basal ganglia, (b) along with a mass effect causing tonsillar herniation and impending uncal herniation

cause. Consequently, the patient underwent decompressive craniectomy, SVC stent placement, and ventriculoperitoneal shunt procedures. Recurrent seizures were managed with anti-seizure medications. Despite these interventions, her neurological condition remained impaired, characterized by fluctuating consciousness, intermittent seizures, and hydrocephalus requiring multiple shunt revision surgeries. Serial imaging consistently demonstrated persistent brain edema, infarctions, and hemorrhages [Figure 4], which were managed with nimodipine and mannitol. Meanwhile, she developed a left-sided hemothorax with organized blood clot formation, along with prolonged dependence on mechanical ventilation. Surgical interventions, including VATS for pleural decortication and tracheostomy, were subsequently performed. Owing to the previous severe complications and her family's strong refusal of chemotherapy due to its associated risks, she was started on pembrolizumab 200 mg every 3 weeks as an alternative treatment in March 2023. Despite extensive medical

and surgical interventions, her prognosis remained guarded due to recurrent infections, persistent neurological deficits, and ventilator dependency. When her condition had stabilized, she was transferred to the respiratory care ward, where she continued to receive pembrolizumab therapy to control lymphoma. Serial CT scans from May 2023 to April 2024 demonstrated stable disease regression. The tracheostomy was successfully removed in June 2024. Over time, her consciousness and cognitive function gradually improved. A positron emission tomography (PET) scan later confirmed a partial response with residual mediastinal tumor [Figure 5a].

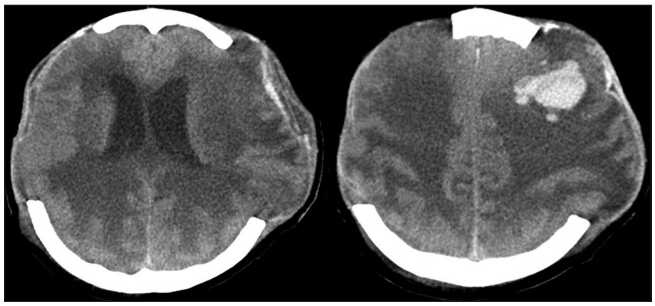

Figure 4: With clinically worsening consciousness and intermittent seizures, brain computed tomography consistently revealed brain infarcts, edema, and hemorrhage

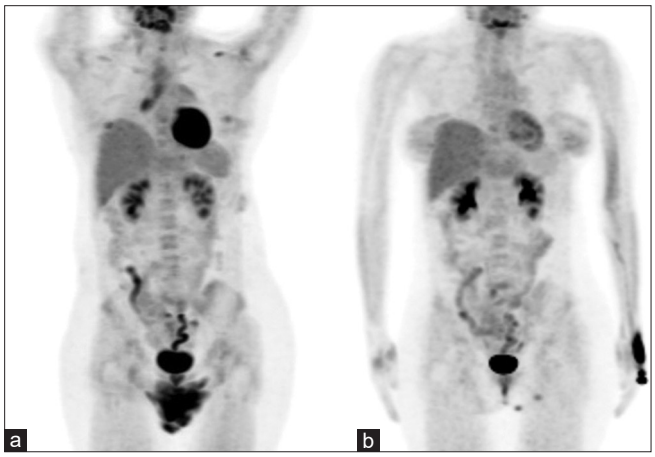

Figure 5: Imaging after 15 months of pembrolizumab monotherapy indicated a partial response, characterized by residual tumor in the mediastinum (a). Compared with the previous positron emission tomography (PET) scan, the PET scan obtained after the 2-year course of pembrolizumab demonstrated a complete response, with no evidence of residual tumor in the mediastinum (b)

To further consolidate treatment, rituximab (375 mg/m²) was added to pembrolizumab starting in July 2024 for a total of six cycles. A follow-up CT scan in October 2024 demonstrated an almost complete response [Figure 6]. After a thorough discussion, her family remained hesitant to pursue R-CEOP chemotherapy. Consequently, the treatment plan was adjusted to complete a full 2-year course of pembrolizumab monotherapy, and a subsequent PET scan showed no evidence of residual disease [Figure 5b]. Remarkably, despite previously being in a nearly vegetative and bedridden state, she is now able to walk independently and is preparing to return to school.

Discussion

PMBCL is a rare and aggressive subtype of non-Hodgkin large B-cell lymphoma, accounting for approximately 2%–4% of all cases globally, and around 2.6% in Taiwan.[2,3] It typically affects young adults and is characterized by a bulky mediastinal mass. Genetically, PMBCL frequently harbors copy number gains and translocations at the 9p24.1 locus, resulting in the overexpression of PD-L1, PD-L2, and JAK2,[4] which has spurred interest in immune checkpoint inhibitors (ICIs) as a potential therapeutic approach.

Despite its distinct clinical and molecular profile, the optimal frontline treatment for PMBCL remains uncertain due to the lack of randomized controlled trials. Current guidelines recommend either six cycles of dose-adjusted EPOCH-R (consisting of dose-adjusted etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone, and rituximab) or 4–6 cycles of R-CHOP (rituximab combined with cyclophosphamide, doxorubicin, vincristine, and prednisone) as standard frontline regimens.[5-7] The use of ICIs such as pembrolizumab and nivolumab has been primarily explored in the relapsed or refractory setting.[8,9] In the KEYNOTE-170 trial, pembrolizumab achieved an overall response rate (ORR) of 42% and a complete response rate (CRR) of 21%, with a median progression-free survival (PFS) of 4.3 months and median overall survival of 22.3 months during long-term follow-up.[10] The CheckMate-436 study also demonstrated promising results, with the combination of nivolumab and brentuximab vedotin (BV) yielding an ORR of 73% and CRR of 40% in patients with relapsed or refractory PMBCL.[11]

In our case, the patient developed a series of life-threatening complications, including SVC syndrome and cerebral edema with impending herniation, attributable to the underlying

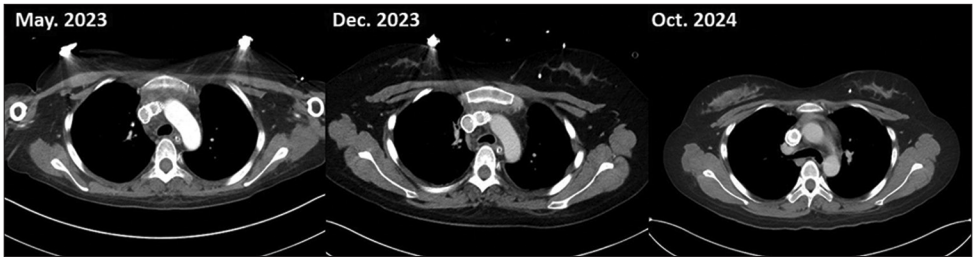

Figure 6: Subsequent computed tomography scans demonstrated regression of the mediastinal tumor, indicating a near-complete response

PMBCL and disseminated infections, culminating in septic shock shortly after the initial cycle of R-CEOP. Although DA-EPOCH-R is associated with favorable outcomes in patients with PMBCL, it requires close inpatient monitoring and carries a substantial risk of hematologic toxicity. Administering this regimen in a critically ill, immunocompromised patient, such as in our case, would have risked further complications, including opportunistic infections and treatment-related mortality. Accordingly, due to her critical clinical status, standard frontline regimens such as DA-EPOCH-R or R-CHOP were deemed unsuitable. In addition, her family opted against further cytotoxic chemotherapy. In light of these factors, pembrolizumab monotherapy was selected as a less toxic alternative. Although ICIs are currently approved for relapsed or refractory PMBCL, their favorable toxicity profile and mechanistic relevance offer a rational therapeutic option in this high-risk setting. At the time of initiating treatment, there were no established guidelines or clinical data to inform the optimal duration of pembrolizumab treatment in the first-line salvage context. Therefore, following the KEYNOTE-170 study protocol, a 2-year treatment plan was chosen following shared decision-making with the patient's family.

While ICIs are not currently approved for first-line use in PMBCL, emerging studies are exploring its incorporation into frontline regimens. The ALLG-PACIFIC trial, a phase II study, is evaluating the safety and efficacy of pembrolizumab combined with R-CHOP in treatment-naïve PMBCL patients.[12] This ongoing trial is evaluating the safety and efficacy of pembrolizumab combined with R-CHOP, with the aim of improving event-free survival. A phase III randomized trial (NCT04759586) is also underway to assess the addition of nivolumab to standard first-line therapy. The study enrolment, safety, and efficacy analyses are ongoing. Results from these studies may help define the role of ICIs in the upfront management of PMBCL.

In conclusion, this case suggests a potential role for pembrolizumab as an alternative treatment option in selected patients with PMBCL who are ineligible for standard regimens such as DA-EPOCH-R or R-CHOP. In our patient, pembrolizumab monotherapy was initiated following the early discontinuation of R-CEOP due to significant comorbidities and complications, and after shared decision-making with her family. Although the patient received pembrolizumab over a 2-year period based on a schedule adapted from the KEYNOTE-170 protocol, the optimal timing, duration, and positioning of ICIs in the frontline setting remain undefined. Further prospective studies are warranted to evaluate their efficacy, safety, and long-term outcomes in this subset of patients.

Declaration of patient consent

This study was performed in accordance with and conforming to the Declaration of Helsinki. The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Data availability statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Giulino-Roth L. How I treat primary mediastinal B-cell lymphoma. Blood 2018;132:782-90.
2. Savage KJ. Primary mediastinal large B-cell lymphoma. Blood 2022;140:955-70.
3. Chuang SS, Chen SW, Chang ST, Kuo YT. Lymphoma in Taiwan: Review of 1347 neoplasms from a single institution according to the 2016 revision of the World Health Organization classification. J Formos Med Assoc 2017;116:620-5.
4. Joos S, Otaño-Joos MI, Ziegler S, Brüderlein S, du Manoir S, Bentz M, *et al*. Primary mediastinal (thymic) B-cell lymphoma is characterized by gains of chromosomal material including 9p and amplification of the REL gene. Blood 1996;87:1571-8.
5. Dunleavy K, Pittaluga S, Maeda LS, Advani R, Chen CC, Hessler J, *et al*. Dose-adjusted EPOCH-rituximab therapy in primary mediastinal B-cell lymphoma. N Engl J Med 2013;368:1408-16.
6. Camus V, Rossi C, Sesques P, Lequesne J, Tonnelet D, Haioun C, *et al*. Outcomes after first-line immunochemotherapy for primary mediastinal B-cell lymphoma: A LYSA study. Blood Adv 2021;5:3862-72.
7. Network NCC. B-Cell Lymphomas (Version 1.2025): National Comprehensive Cancer Network. Available from: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. [Last accessed on 2024 Dec 30].
8. Armand P, Rodig S, Melnichenko V, Thieblemont C, Bouabdallah K, Tumyan G, *et al*. Pembrolizumab in relapsed or refractory primary mediastinal large B-cell lymphoma. J Clin Oncol 2019;37:3291-9.
9. Zinzani PL, Santoro A, Gritti G, Brice P, Barr PM, Kuruvilla J, *et al*. Nivolumab combined with brentuximab vedotin for relapsed/refractory primary mediastinal large B-cell lymphoma: Efficacy and safety from the phase II CheckMate 436 study. J Clin Oncol 2019;37:3081-9.
10. Zinzani PL, Thieblemont C, Melnichenko V, Bouabdallah K, Walewski J, Majlis A, *et al*. Pembrolizumab in relapsed or refractory primary mediastinal large B-cell lymphoma: Final analysis of KEYNOTE-170. Blood 2023;142:141-5.
11. Zinzani PL, Santoro A, Gritti G, Brice P, Barr PM, Kuruvilla J, *et al*. Nivolumab combined with brentuximab vedotin for R/R primary mediastinal large B-cell lymphoma: A 3-year follow-up. Blood Adv 2023;7:5272-80.
12. Lewis KL, Giri P, Marconi T, Blombery P, Keane C, Sungala NP, *et al*. Interim safety analysis of ALLG-Pacific (NHL35): An open label phase II study of pembrolizumab and chemo-immunotherapy as first-line therapy for primary mediastinal B-cell lymphoma. Blood 2024;144 Suppl 1:1721.