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Case Report

Central nervous system metastasis in a young female patient with primary mediastinal large B-cell lymphoma: A case report and literature review

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ABSTRACT

Background: Primary mediastinal B-cell lymphoma (PMBCL) is a subtype of diffuse large B-cell lymphoma that originates from a B cell in the thymus. It usually affects young female.

Case description: A 30-year-old woman presented with mediastinal mass with history of shortness of breath and chest pain. blood analysis showed low levels of hemoglobin, hematocrit, and mean corpuscular volume and high red cell distribution width. A computed tomography (CT)-guided mediastinal core biopsy disclosed primary mediastinal large B-cell lymphoma (PMLBL) with a nongerminal center phenotype and lung tissue infiltrate. Moreover, after undergoing six cycles of rituximab, cyclophosphamide, hydroxydaunomycin, Oncovin, and prednisone (R-CHOP) chemotherapy and mediastinal radiotherapy, the patient presented with headache and visual disturbance due to multiple supratentorial lesions.

Conclusion: Till date, only a few cases of central nervous system (CNS) metastasis have been reported in the literature. Moreover, CNS metastasis of refractory PMBCL is an uncommon event with a poor prognosis. Brain metastases are often the ultimate fatal consequence of many aggressive cancers, so early detection and treatment are important.

Keywords: Central nervous system metastasis, Primary mediastinal B-cell lymphoma, Radiotherapy, R-CHOP regimen

INTRODUCTION

Primary mediastinal B-cell lymphoma (PMBCL) is characterized by a diffuse proliferation of medium- to large-sized B cells and is accompanied by sclerosis and some degree of compartmentalization.[3] It has a worldwide distribution and is classified separately in the most recent World Health Organization classification of lymphoid cancers.[12] Patients suffering from the disease are often young, mostly female, and have a bulky mediastinal mass that causes cough, dyspnea, and superior vena cava syndrome.[1] Moreover, at the time of diagnosis, extranodal

diseases are frequently present and commonly involve lung lesions, with the potential for contagious spread to different intrathoracic locations.[7]

Brain metastases are often the ultimate fatal consequence of many aggressive cancers.[6] This category of central nervous system (CNS) disease typically manifests early, with a median interval of 5–12 months from diagnosis to the onset of CNS involvement. Approximately one-third of patients experience CNS involvement during the course of their primary treatment. The two primary types of CNS disease are parenchymal and leptomeningeal.[4] In this paper, we report an isolated CNS metastasis of refractory PMBCL in a young female patient who presented at our institution after completing six cycles of R-CHOP chemotherapy and mediastinal radiotherapy.

CASE DESCRIPTION

A 30-year-old woman presented at our institution with a mediastinal mass. She had a history of shortness of breath and chest pain. The physical examination was normal. Further investigations started with blood analysis, which showed low levels of hemoglobin, hematocrit, and mean corpuscular volume and high red cell distribution width. A peripheral blood smear report indicated moderate microcytic hypochromic anemia. A computed tomography (CT)-guided mediastinal core biopsy disclosed primary mediastinal large B-cell lymphoma (PMLBL) with a nongerminal center phenotype and lung tissue infiltrate. Immunohistochemistry showed the following target cells: CD20, CD23 (with focal weak positivity), CD30 (present in a subset of cells), BcI2 (with focal positive staining), Bcl6++, and MUM1++. Further analysis included a bone marrow aspiration, which revealed no signs of infiltration or abnormal cells. The final diagnosis was PMLBL located in the anterior mediastinum. The patient received six cycles of R-CHOP chemotherapy and 18 sessions of radiotherapy. The only remarkable event was stomatitis, which was promptly treated with an oral doxycycline gargle and fluconazole.

Five months later, she presented at the emergency department with a headache and episodes of vision changes lasting seconds for the past 4 days. A cranial CT scan was performed, which indicated multiple supratentorial lesions [Figure 1]. The patient was then advised to undergo multisequence intravenous contract brain magnetic resonance imaging (MRI), which revealed lesions located in the right frontal and occipital lobes [Figure 2]. There was no evidence of herniation, midline shift, or acute intracranial abnormalities. Moreover, the orbits, paranasal sinuses, and mastoid air cells appeared normal. A positron emission tomography/CT (PET/CT) scan reported a decrease in the metabolic activity of the anterior mediastinal mass on the right side. Compared to the previous image, it also showed new, intensely metabolically active intracranial lesions that corresponded to the lesions noted in the recent brain CT and MRI. These findings were found to be consistent with disease progression. The Deauville score determined the stage as 5B and cerebrospinal fluid (CSF) showed only mature T-cells and monocytes.

An excisional biopsy was performed through a right frontoparietal mini-craniotomy. During the surgery, a bulging layer of the cortex covered the tumor. The tumor was firm and yellow, with a clear plane identified, and histopathology confirmed the presence of lymphoma cells. The biopsy showed diffuse sheets of large neoplastic cells with round nuclei. These cells exhibited vesicular chromatin and prominent central nucleoli, as well as membrane-bound multiple nucleoli. Mitotic figures were observed [Figure 3].

Immunohistochemistry indicated the presence of large cells with positive staining for CD20, CD30, BCL6, MUM1, and C-MYC (40%) and negative staining for BCL2 and CD23. The Ki67 Proliferative Index was found to be positive in 80% of tumor cells. Based on these findings, the final diagnosis was progressive secondary CNS large B-cell lymphoma. After the diagnosis, the patient underwent salvage chemotherapy MATRIX/RISE for two cycles, followed by an auto-stem cell transplant.

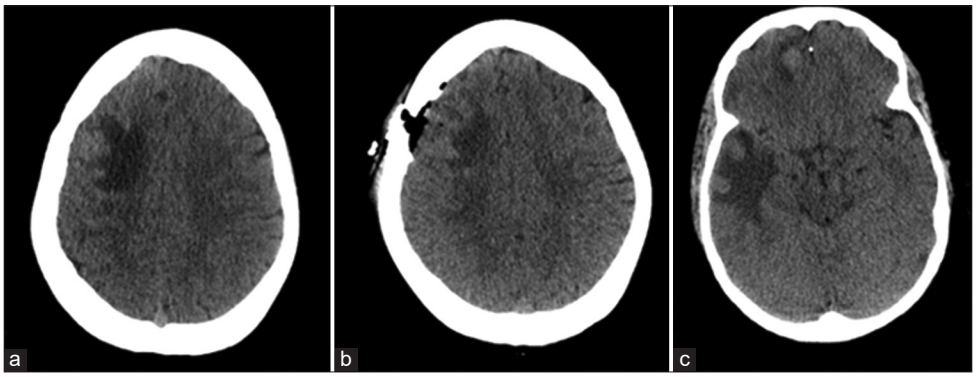

Figure 1: Brain axial computed tomography shows (a and b) multiple supratentorial enhacing lesions associated with edema causing effacement of adjacent sulci. (c) The largest lesion in the right parietal lobe 2.1 × 1.8 × 1.5 cm.

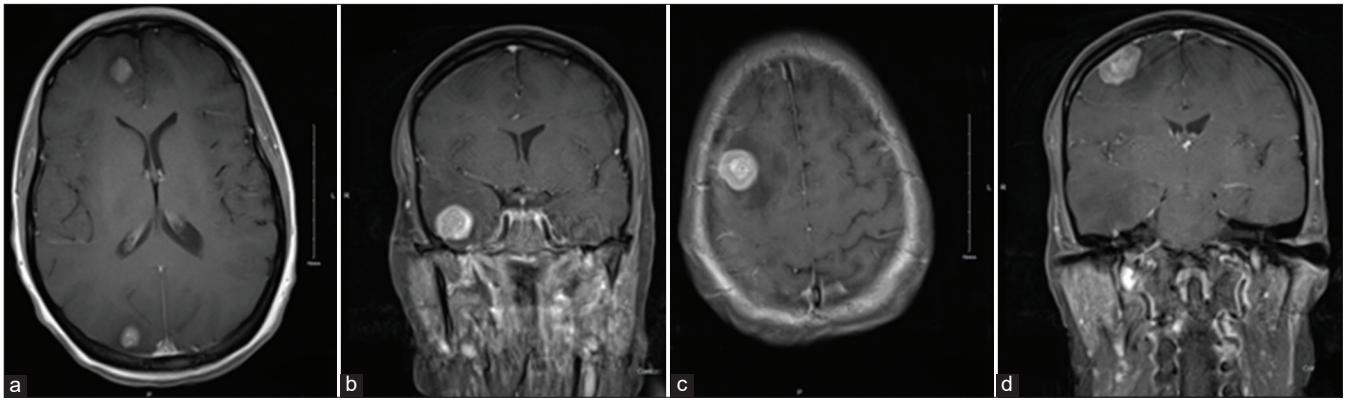

Figure 2: Brain magnetic resonance imaging (a) axial (b) coronal section intermediate T2 signals shows multiple enhaced scattered mass lesions involving the right frontal and occipital lobes. (c) Axial (d) coronal section shows largest lesion in the right temporal lobe measures 2.3 × 1.9 × 2.0 cm.

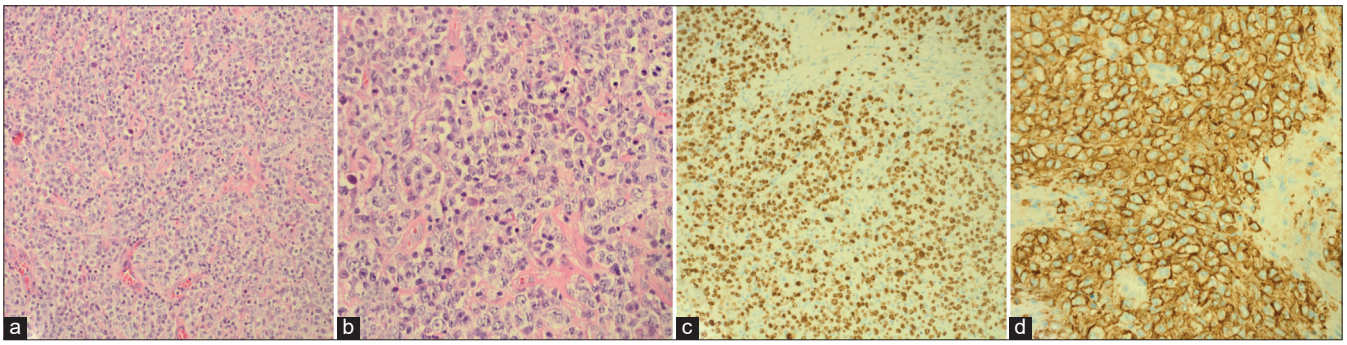

Figure 3: (a and b) H&E stained sections show diffuse sheets of large neoplastic cells with round nuclei that exhibit vesicular chromatin and prominent central nucleoli to membrane bound multiple nucleoli. Mitotic figures are seen. (c) Immunohistochemistry shows large cells with positive for CD20, CD30, BCL6, MUM1, and C-MYC (40%), while negative for BCL2 and CD23. (d) Immunohistochemistry shows Ki67 proliferative index that is positive in 80% of tumor cells.

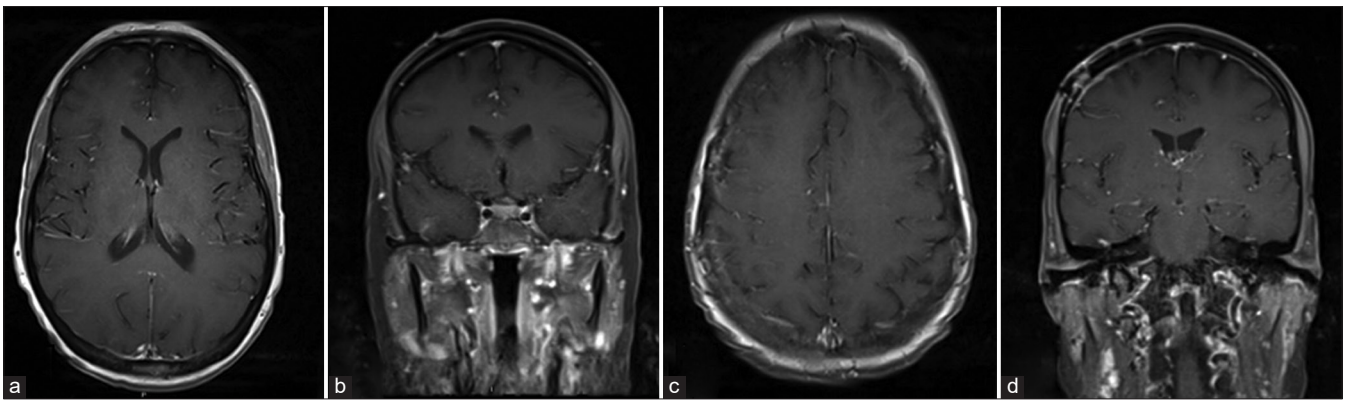

Figure 4: Follow-up postsurgical magnetic resonance imaging (a) axial (b) coronal section shows occipital lesions very small to measure. (c) Axial section shows resolution of the right temporal lesion. (d) Coronal section shows craniotomy site right frontal meningeal enhancement.

Seven weeks after surgical resection, the patient was observed to be recovering well. The MRI scan indicated that the right frontal lymphomatous lesions had resolved and that there had been a reduction in the size of the other lesions [Figure 4].

DISCUSSION

PMBCL is characterized by a diffuse proliferation of medium- to large-sized B cells and is accompanied by sclerosis and some degree of compartmentalization.[6] At the time of PMBCL diagnosis, extranodal diseases are often

Table 1: Reviewing the cases of large B-cell lymphoma with CNS metastasis in the litterateurs.

Year	Author	No. of patients	Age	Gender	Initial presentation	Stage	CNS involvement	Period between initial diagnosis and CNS involvement
1999	Philippe C. Bishop[2]	23	Median age 29	61% F	48% B symptoms	43% III/IV	Only in 6 patients	Median 9.6 months Range 5.7 to 16.8 months
2003	Thierry A.G.M Huisman[5]	1	12	M	-	-	yes	-
2009	Vittori Stefoni[11]	1	50	F	Progressively increasing asthma Dyspnoea Hacking cough	-	yes	10 Months
2010	Makoto Sasaki[10]	1	19	M	Persistent cough	IIA	Yes	9 Months
2012	Sotrios G. Papageogiou[9]	1	30	F	-	IA	Yes	-
		1	41	M	-	IIA	Yes	-
		1	33	F	Dry cough and Superior vena cava syndrome	IIEA	Yes	-
		1	25	M	-	IIIA	Yes	5 Months
2019	Mariam Marangon[8]	1	25	F	Hacking Cough facial edema conjunctival swelling	IV	Yes	6 Months
2023	Our case	1	30	F	Shortness of breath and Chest pain		Yes	5 Months

CNS: Central nervous system, M: Male, F: Female

present and involve lung lesions, with the potential for contagious spread to different intrathoracic locations.[7] CNS involvement usually occurs 5–12 months after the initial diagnosis.[9] In the reported case, the patient presented at the emergency department with neurological symptoms. At that time, we discovered multiple brain masses, which were later confirmed to be PMBCL metastases, 5 months after her primary diagnosis of PMBCL. In PMLBL, CNS metastasis is an extremely rare event associated with aggressive lymphoma and a poor outcome.[2,9] Literature review revealed that CNS metastasis of PMBCL primarily involves the leptomeningeal and dural surfaces in most cases (65%), while only 35% of the metastasis involves the parenchyma.[2] Although it is less common, in the reported case, the patient had involvement in multiple parenchymal areas [Table 1].[2,5,8-11]

The previous studies have identified some potential risk factors for CNS involvement, which include two or more extranodal involvements, especially if there is bone marrow involvement and elevated lactate dehydrogenase (LDH).[2,9] A study reported that many patients with PMLBL who did not have CNS involvement had elevated levels of LDH, and there were also a few cases of multiple extranodal involvement.[2] Although it is important for physicians to be aware of these risk factors, their sensitivity and specificity are still not high. Therefore, we recommend that physicians conduct a thorough evaluation using brain imaging and CSF cytology. They should also exercise medical judgment to determine appropriate prophylaxis for each patient individually. Further, it is important for physicians to avoid being misled by potential risk factors.

CONCLUSION

Brain metastases are often the ultimate fatal consequence of numerous aggressive cancers. Therefore, we encourage physicians to maintain a high level of suspicion for early detection and treatment of PMBCL so that the disease progression can be managed. We also recommend conducting further investigation and performing an MRI for any patient with PMBCL as part of the initial assessment and when they present with neurological symptoms. Furthermore, it is important to educate patients about the symptoms so that they can seek help and visit the hospital if they develop any of them.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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