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LETTER TO THE EDITOR

Secondary diffuse large B cell lymphoma of the central nervous system: retrospective review of case series

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Dear Editor,

The primary central nervous system (CNS) diffuse large B cell lymphoma (DLBCL) has a significantly more aggressive clinical course compared to systemic DLBCL. Secondary CNS DLBCL has been associated with immunosuppression, autoimmune disease, and transplantation [1, 2] and is excluded from primary DLBCL in the 2016 WHO classification of lymphomas [3]. Secondary isolated CNS relapse is rare, with poorly defined management strategies [4–7]. We set out to identify and further characterize secondary CNS DLBCL in our patient population. A search of our pathology archives from 2000 to 2016 identified 55 cases of DLBCL. After clinical and pathological review, patients were divided into primary and secondary CNS DLBCL. The secondary lymphomas were further subclassified as germinal center (GC) and activated B cells (ABC) using the Hans algorithm [8]. Clinical information is summarized in Table 1.

Forty-eight primary CNS DLBCLs were identified, with an average age of 67 and a slight male predominance of 1.2:1. Ninety-eight percent were Caucasian. Seven secondary DLBCLs were identified, and further divided into metachronous and synchronous lymphomas. Five metachronous CNS DLBCLs occurred at an average age of 58 and M:F ratio of 3:2. All showed ABC phenotypic expression and an average of 7 years between initial systemic presentation and CNS relapse. Two had a transplantation history (one of whom was treated with mycophenolate) and one had history of autoimmune disease. The time from the CNS diagnosis to last follow-up ranged from 5 to 48 months. Two of the seven metachronous cases had divergent lymphoma phenotypes, with initial diagnoses of mixed small and large cell lymphoma and cutaneous B cell lymphoma. The two synchronous DLBCLs both occurred in male patients at an average age of 52; one of these patients was HIV positive and showed EBER expression and GC phenotype. The second patient had no history of transplantation, autoimmunity, or immunosuppression. Variations in therapeutic chemotherapy, rituximab and radiation did not appear to affect the outcome in our limited data set.

The high prevalence of the ABC phenotype among these secondary CNS lymphomas partly explains the dismal outcome in these patients [9]. Although our case series is not large enough to perform statistical analysis, our findings indicate an increased incidence of secondary DLBCL in patients with autoimmunity, transplantation, and immunosuppression, which is concordant with previous reports [1, 2]. DLBCL of the CNS in these settings should be distinguished from primary DLBCL of the CNS [3]. The relatively long period before the CNS relapse is unique in the metachronous group and may result in under diagnosis of secondary CNS DLBCL. Further studies are required to understand the pathophysiology and prognosis of secondary DLBCL of the CNS.

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Table 1 Clinical information

	Subtype of 2 DLBCL	EBER	Time between systemic and 2 lymphoma	Type of systemic lymphoma	Stage of 1 lymphoma	History and type of transplant	Autoimmune disorders	History of immunosuppression	Time to last follow up
Metachronous DLBCL									
1	ABC	Neg	6 years	Mixed small and large cell lymphoma	Unknown	None	None	NA	48 months
2	ABC	NA	9 years	DLBCL	Unknown	Kidney	Lupus nephritis	Undocumented	1.7 months
3	ABC	Neg	8 years	DLBCL	IV	Unrelated donor peripheral stem cell transplant	None	Yes	37 months
4	ABC	Neg	5 years	Cutaneous B cell lymphoma	IV	None	None	NA	5.5 months
5	ABC	Neg	9 years	DLBCL	IA	None	None	NA	5 months
Synchronous DLBCL									
1	ABC	Neg	NA	DLBCL	IV	None	None	None	0 month
2	GC	Positive	NA	DLBCL	IV	None	None	None	3.6 months

ABC, activated B cell; *Neg*, negative; *NA*, not available; *GC*, germinal center

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. O'Neill BP, Vernino S, Dogan A, Giannini C (2007) EBV-associated lymphoproliferative disorder of CNS associated with the use of mycophenolate mofetil. Neuro-Oncology 9(3):364–369
2. Evens AM, Choquet S, Kroll-Desrosiers AR, Jagadeesh D, Smith SM, Morschhauser F et al (2013) Primary CNS posttransplant lymphoproliferative disease (PTLD): an international report of 84 cases in the modern era. Am J Transplant 13(6):1512–1522
3. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri S, Stein H, Thiele J (2017) WHO classification of tumours of haematopoietic and lymphoid tissues. International Agency for Research on Cancer, Lyon
4. Wudhikarn K, Bunworasate U, Julamanee J, Lekhakula A, Chuncharunee S, Niparuck P et al (2017) Secondary central nervous system relapse in diffuse large B cell lymphoma in a resource limited country: result from the Thailand nationwide multi-institutional registry. Ann Hematol 96(1):57–64
5. El-Galaly TC, Cheah CY, Bendtsen MD, Nowakowski GS, Kansara R, Savage KJ et al (2018) Treatment strategies, outcomes and prognostic factors in 291 patients with secondary CNS involvement by diffuse large B-cell lymphoma. Eur J Cancer 93:57–68
6. Kawano N, Ochiai H, Yoshida S, Yamashita K, Shide K, Shimoda H et al (2012) Clinical features and treatment outcomes of isolated secondary central nervous system lymphomas in Miyazaki Prefecture. Int J Clin Oncol 17(4):336–340
7. DeRosa P, Cappuzzo JM, Sherman JH (2014) Isolated recurrence of secondary CNS lymphoma: case report and literature review. J Neurol Surg Rep 75(1):e154–e159
8. Hans CP, Weisenburger DD, Greiner TC, Gascoyne RD, Delabie J, Ott G, Müller-Hermelink HK, Campo E, Braziel RM, Jaffe ES, Pan Z, Farinha P, Smith LM, Falini B, Banham AH, Rosenwald A, Staudt LM, Connors JM, Armitage JO, Chan WC (2004) Confirmation of the molecular classification of diffuse large B-cell lymphoma by immunohistochemistry using a tissue microarray. Blood 103(1): 275–282
9. Camilleri-Broët, Sophie, et al. A uniform activated B-cell–like immunophenotype might explain the poor prognosis of primary central nervous system lymphomas: analysis of 83 cases. Blood 107.1 (2006): 190–196