Case Report

Toripalimab plus lenalidomide for central nervous system recurrence in refractory CD5$^+$ diffuse large B-cell lymphoma with *MYD88* and *CD79B* comutation: a case report

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Background: CD5-positive (CD5$^+$) non-germinal center B-cell-like diffuse large B-cell lymphoma (non-GCB DLBCL) is heterogeneous with a poor prognosis. For refractory DLBCL, the median overall survival was only 6.3 months. Therefore, there is a need for approaches to elongate the survival in this subgroup of relapsed DLBCL patients.

Case Description: Here, we present a rare case of a 72-year-old patient with stage IV CD5$^+$ non-GCB DLBCL with myeloid differentiation primary response 88 (*MYD88*) and cluster of differentiation 79B (*CD79B*) comutations. Zanubrutinib and rituximab therapy was initially administered until disease progression. Subsequently, zanubrutinib plus rituximab together with attenuated standard chemotherapy (miniCHOP) was applied and a notable response was observed. The patient tolerated the treatment well and exhibited a complete response in lung for about 5 months. Afterwards, the patients experienced relapse in the brain and started programmed death protein 1 (PD-1) regimens of toripalimab plus lenalidomide, which also exhibited a good response with decreased lesions in brain after half-year treatment. However, the patient experienced relapse again in the brain 3 months later and started chemotherapy with methotrexate plus rituximab. The patient had survived for over 2 years since the initial diagnosis of stage IV DLBCL and has continued to survive after experiencing a relapse in the brain for approximately 11 months till now.

Conclusions: These findings suggest that toripalimab may be a new therapeutic option for central nervous system recurrence in refractory CD5$^+$ DLBCL with *MYD88* and *CD79B* comutation. Further clinical trials are warranted to confirm these results.

Keywords: Diffuse large B-cell lymphoma (DLBCL); central nervous system recurrence; toripalimab; *MYD88* and *CD79B* mutations; case report

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Introduction

Diffuse large B-cell lymphoma (DLBCL) is a highly heterogeneous malignancy and accounts for approximately 30% of all lymphomas worldwide (1). DLBCL can be classified into germinal center B-cell-like (GCB) and non-GCB [which includes activated B-cell-like (ABC) and unclassified] subtypes according to the Hans algorithm (2). Non-GCB DLBCL comprises approximately 60% of all cases and is associated with an inferior prognosis compared to the GCB subtype (3). CD5 is a pan-T-cell surface marker in approximately 5% to 22% of all DLBCL cases (4). CD5 positivity ($CD5^+$) is also of poor prognosis and is mainly observed in cases of the ABC subtype (4). For refractory DLBCL patients, the median overall survival is reported to be only 6.3 months (5). However, for refractory $CD5^+$ non-GCB DLBCL patients, it is crucial to prioritize efforts towards prolonging their survival.

Molecular genetics subtyping of lymphoma cases via next-generation sequencing (NGS) has been widely applied in clinical practice (6). Co-occurrence of mutations changing leucine at position 265 to proline (L265P) in myeloid differentiation primary response 88 (*MYD88*) and cluster of differentiation 79B (*CD79B*) double mutations type (MCD type) is a genetic subtype (7), which is associated with inferior outcomes under current standard immunochemotherapy (8). Heterogeneity is a prominent feature of MCD among different types and primary sites of lymphoma. The co-occurrence of *MYD88* and *CD79B* mutations is more commonly observed in primary central nervous system (CNS) DLBCL (9). In addition, patients with $CD5^+$ DLBCL have a higher incidence of carrying both $MYD88^{L265P}$ and *CD79B* mutations (10).

R-CHOP therapy (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone) is widely used as a standard regimen for DLBCL, especially in newly diagnosed DLBCL (11). R-miniCHOP, an attenuated regimen, is recommended for patients over 80 years without cardiac dysfunction (12). However, standard R-CHOP chemotherapy or stem cell transplantation has not been shown to benefit patients with the $CD5^+$ DLBCL subtype (4,10,13). Recently, novel targeted agents such as ibrutinib, bortezomib, and lenalidomide have been added to R-CHOP to improve DLBCL outcomes (14).

A first-generation Bruton's tyrosine kinase (BTK) inhibitor ibrutinib monotherapy shows an 80% objective response rate in MCD tumors carrying both *CD79B* and $MYD88^{L265P}$ mutations (15). Moreover, the *in vitro* mechanism study also confirms that cell lines of *CD79A/B* and $MYD88^{L265P}$ confer ibrutinib sensitivity, indicating that they are likely to be derived through a B cell receptor (BCR)-dependent pathway (15). Additionally, ibrutinib plus R-CHOP shows a 100% 3-year event-free survival rate in younger DLBCL patients (age ≤60 years old) than R-CHOP alone (42.9%) in MCD tumors (7). Zanubrutinib, a second-generation BTK inhibitor, reaches 50% overall response rate (ORR) in relapsed or refractory DLBCL with oncogenic mutations in both *CD79B* and $MYD88^{L265P}$ (16). Moreover, higher ORR is observed in older subgroup (age ≥65 years old, 38.5% versus 25.0% age <65 years old) (16). Zanubrutinib plus R-CHOP therapy has also been applied for the treatment of naïve lymphomas in recent clinical trials (17).

Toripalimab is a monoclonal antibody to selectively target programmed death protein 1 (PD-1), which has shown promising anti-tumor effects in a range of cancer types, including melanoma, lung cancer, digestive tract tumors, hepatobiliary and pancreatic tumors, neuroendocrine neoplasms, nasopharyngeal carcinoma and urothelial carcinoma (18). Furthermore, toripalimab exerts its function by binding to PD-1 and block the interaction with its ligands, thereby blocking downstream pathways and restoring the anti-tumor response of T cells (18). According to the results of the Phase II TREND trial, the combination of toripalimab and rituximab as a first-line treatment, followed by R-CHOP, demonstrated a high complete response (CR) rate and manageable toxicities in elderly patients (aged 60–85 years) who were newly diagnosed with DLBCL (NCT04058470) (19). The elevated expression

Highlight box

Key findings

- Toripalimab may be a new therapeutic option for central nervous system (CNS) recurrence in refractory CD5-positive ($CD5^+$) diffuse large B-cell lymphoma (DLBCL) with myeloid differentiation primary response 88 (*MYD88*) and cluster of differentiation 79B (*CD79B*) comutation.

What is known and what is new?

- The median overall survival time was short for refractory DLBCL.
- Third-line treatment with toripalimab combined with rituximab helped to prolong the patient's survival after CNS relapse.

What is the implication, and what should change now?

- This case provides crucial guidance for clinical practice and demonstrates a convincing response to a new treatment that may be useful for patients with relapsed DLBCL.

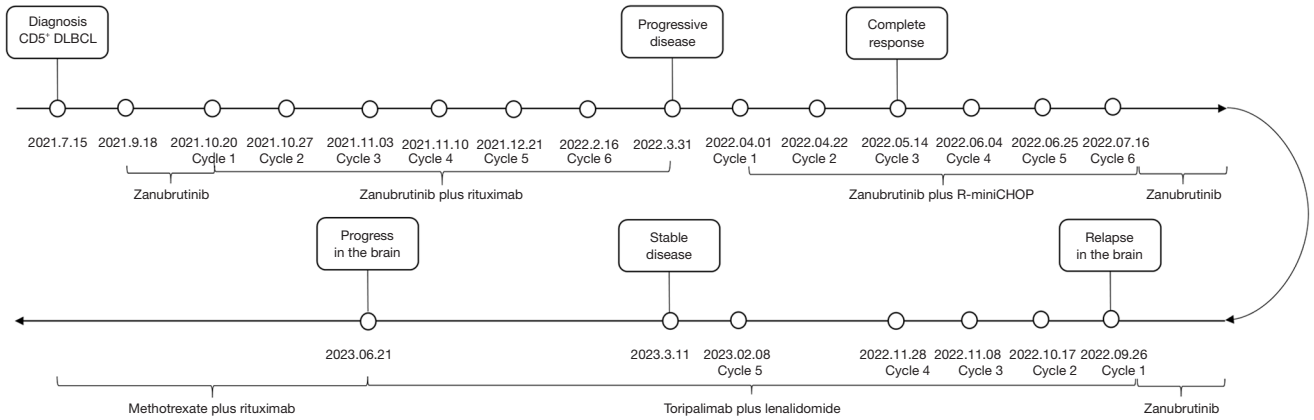

Figure 1 Timeline of the patient. DLBCL, diffuse large B-cell lymphoma; R-miniCHOP, rituximab plus attenuated standard chemotherapy.

of PD-1 in the peripheral blood of DLBCL patients is correlated with a worse prognosis (20). *In vitro* study has also demonstrated that blocking PD-1 can reverse the impaired proliferation and cytokine production of T cells in DLBCL cell lines which are positive for Epstein-Barr virus (21). Lenalidomide is an oral immunomodulator that has shown single-agent activity in relapsed/refractory aggressive non-GCB DLBCL (22). Recently, clinical trials of toripalimab combined with rituximab has been applied in treatment of relapsed CD20 positive DLBCL (NCT04425824) (23).

In the current case report, we present a woman with primary pulmonary $CD5^+$ DLBCL with *CD79B/MYD88*^{L265P} mutations who experienced disease progression of three times after combination treatment. Interestingly, ZR-miniCHOP therapy as second-line, and toripalimab combined with rituximab as third-line regimen helped to prolong the survival after central relapse. Patient specific information has been de-identified. We present this case in accordance with the CARE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1638/rc).

Case presentation

A 72-year-old Chinese woman was hospitalized in July 2021 due to cough and chest tightness. Her routine medical history included metformin, insulin, nifedipine, metoprolol, aspirin and isosorbide mononitrate for diabetes mellitus, hypertension and coronary heart disease. Timeline of the patient could be found in *Figure 1*. Computed tomography (CT) and the color and Doppler imaging results were presented in *Figure 2*. From *Figure 2A-2D*, the CT results indicated multiple metastatic lesions, including numerous solid nodular and mass-like soft tissue shadows with significantly increased metabolism in both lungs. Furthermore, in *Figure 2I*, the color and Doppler imaging presented no signals in the cervical lymph node. The hematoxylin-eosin (HE) staining of the biopsy showed the presence of "starry sky" phenomenon (Figure S1A,S1B), which was characterized by uniform, medium-sized lymphoma cells with multiple basophilic small, inconspicuous, centrally located nucleoli, and basophilic cytoplasm. From the immunophenotype results in Figure S1C-S1I, the tumor cells were positive for tumor protein 53 (P53, 50–60%+), B-cell lymphoma 2 protein (Bcl-2, 90%+), B-cell lymphoma 6 protein (Bcl-6, 30–35%+), CD5 (80–85%+), CD20 (diffusely positive), c-Myc (60–65%+), and Ki-67 (>95%+), respectively. Other positive results of multiple myeloma oncogene-1/interferon regulatory factor 4 (MUM1/IRF4, diffusely positive), and negative results for CD3, CD10, CD21, CD30, CyclinD1 and cytokeratin (CK) (pan) were not displayed. All procedures performed in this study were in accordance with the ethical standards of the institutional or national research committees and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Biopsies were taken simultaneously from the right upper lobe posterior lesion and bronchoalveolar lavage fluid (BALF) samples for 688-gene panel sequencing. The samples and NGS processing details have been described in previous publication (24). Comutations in *MYD88* (p. L265P) [variant allele frequency (VAF) =23.56%] and

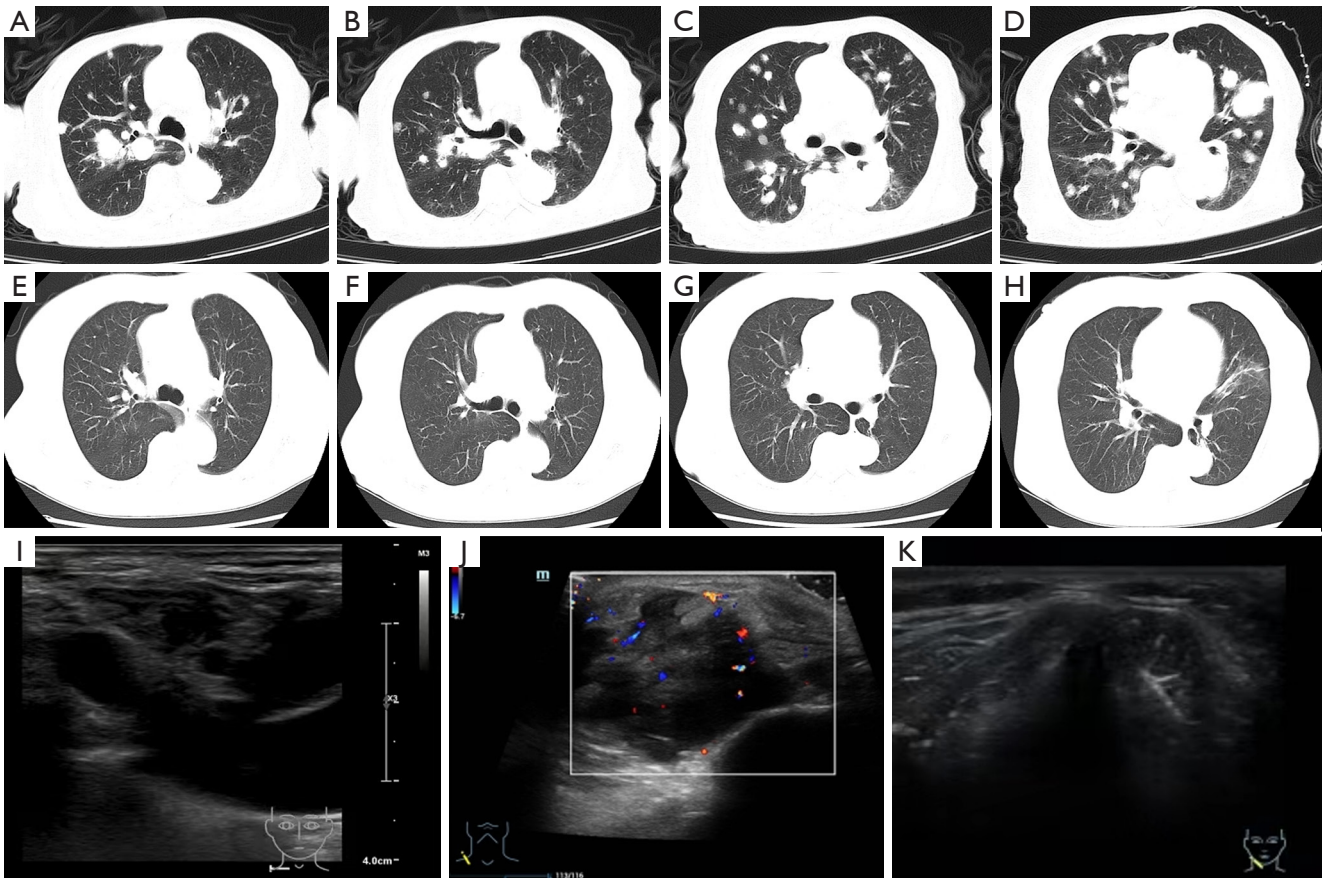

Figure 2 CT of the lung and the color and Doppler imaging of the left clavicle for the patient. (A-D) CT images at the diagnosis stage in July 2021. (E-H) CT images after the combination of zanubrutinib and R-miniCHOP therapy in May 2022. (I-K) Color Doppler imaging at the diagnosis stage in July 2021 (I), disease progression in March 2022 (J) and complete response in May 2022 (K). CT, computed tomography; R-miniCHOP, rituximab plus attenuated standard chemotherapy.

CD79B (p. Y197H) (VAF =22.04%) were identified in the tissues. Other mutated genes, such as PR domain zinc finger protein 1 (*PRDM1*, VAF =27.91%), beta-2-microglobulin (*B2M*, VAF: 24.85%), ETS variant transcription factor 6 (*ETV6*, VAF =24.65%), proviral integration of Moloney virus 1 (*PIM1*, VAF =22.35%), FAT atypical cadherin 1 (*FAT1*, 20.74%), TATA-box binding protein associated factor 1 like (*TAF1L*, VAF =18.27%), X-linked alpha thalassemia mental retardation (*ATRX*, VAF =18.02%), B-cell lymphoma 2 (*BCL2*, VAF =17.54%), ryanodine receptor 2 (*RYR2*, VAF =21.82%), zinc finger MYM-type containing 3 (*ZMYM3*, VAF =16.04%), and the gene fusion cyclin dependent kinase inhibitor 2A-cyclin dependent kinase inhibitor 2B antisense RNA 1 (*CDKN2A-CDKN2B-AS1*, VAF =63.48%) were detected in the tissues. In BALF, the gene mutations vascular endothelial growth factor A (*VEGFA*, VAF =0.91%), serine protease 1 (*PRSS1*, VAF =2.83%) and AT-rich interactive domain-containing protein 1A (*ARID1A*, VAF =0.63%) were identified. The details for the NGS results could be found in Table S1.

After the patient was diagnosed with stage IV group lymphoma with an International Prognostic Index (IPI) score of 5, she was treated with zanubrutinib (160 mg, *bid*) orally in September 2021 as shown in *Figure 1*, followed by rituximab administered for six courses (0.5 mg per week for 4 weeks and titrated to 0.5 mg per month for 2 weeks). However, 1 month after completion of the 6-month therapy regimen, the patient reported feeling a lump in the left clavicle. Subsequent color Doppler imaging and biopsy results revealed progressive disease (PD) of $CD5^+$ DLBCL that had spread to the right clavicle and distal epigastric nodule, as shown in *Figure 2J* in March 2022. The patient

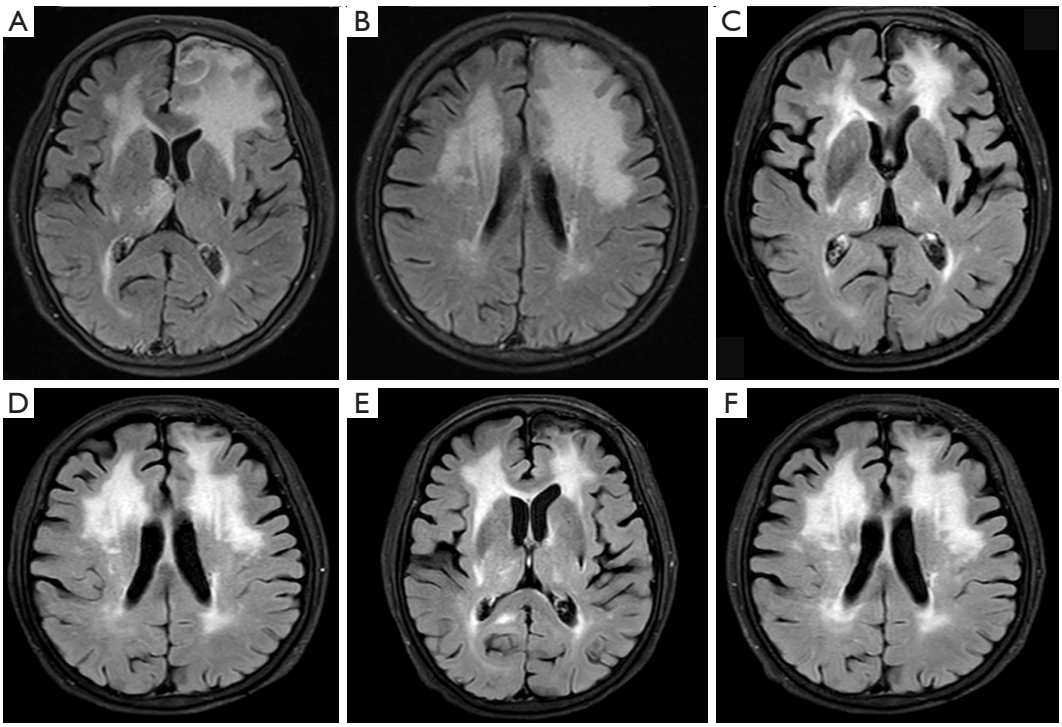

Figure 3 MRI of the brain for the patient. (A,B) MRI with relapse in September 2022. (C,D) MRI after toripalimab and rituximab treatment in January 2023. (E,F) MRI of progressive disease in June 2023. MRI, magnetic resonance imaging.

was then immediately switched to second-line therapy with ZR-miniCHOP, which was well tolerated with no adverse events reported. After three courses of the ZR-miniCHOP regimen, the patient underwent CT (*Figure 2E-2H*) and color Doppler imaging (*Figure 2K*), which showed a CR in May 2022. Then, ZR-miniCHOP therapy was adopted for another three courses till July 2022.

In September 2022, the patient became "less talkative" and the magnetic resonance imaging (MRI) results suggested a central recurrence with diffuse and nodular gray matter swelling with perilesional edema (measuring 28 mm × 20 mm) in left frontal lobe (*Figure 3A,3B*). Afterwards, she was administrated four courses of toripalimab (240 mg q3w) in combination with lenalidomide (15 mg/day for the first course and, 115 mg/14/21 days for the next three courses). During the treatment period, the last course was delayed due to coronavirus disease 2019 (COVID-19) infection. In January 2023, the MRI results suggested stable disease (SD) with a decrease of lesion in brain (*Figure 3C,3D*). Next the toripalimab was continued (240 mg q3w) together with lenalidomide (15 mg 14/21 days). In March 2023, the CT results of lung (Figure S2A-S2D) also showed that the patchy density shadows with slightly increased metabolic activity had regressed. Treatment of toripalimab and lenalidomide were continued afterwards. In June 2023, according to the new MRI results (*Figure 3E,3F*), there was new in relapse in the brain, with a new lesion appeared in the left basal ganglia area and the right hippocampus near the splenium. The CT results of lung (Figure S2E-S2H) showed that the patchy density shadows had increased with enlarged lesions. Afterwards, the regimen changed to chemotherapy including methotrexate (3g q2w) plus rituximab (500 mg q2w). To date, this patient remains survival for 11 months after central relapse till now. In addition, this regimen of toripalimab and lenalidomide decreased the lesions in brain during treatment, although it relapsed finally. The toripalimab plus lenalidomide therapy showed promising effect for central relapsed DLBCL patient carrying *MYD88* (p. L265P) and *CD79B* (p. Y197H) comutations.

Discussion

NGS has been widely applied in clinical assessment of DLBCL (25), while the feasibility of using BALF samples has not yet been evaluated in MCD tumors. *CD79B* and

MYD88 comutations contribute to the heterogeneity of the disease (26). In our case, paired BALF samples and tissue biopsies were both evaluated for variation detection of primary pulmonary DLBCL. The mutated genes revealed were totally inconsistent for these samples, which also validates the heterogeneity of this lymphoma subtype. In addition, the VAF for *CDKN2A-CDKN2B-AS1* gene fusions identified in this patient reached 63.48%. This fusion is more common in glaucoma than in tumors (27).

MYD88^{L265P} is present in approximately 29% of DLBCL cases (28), and *MYD88* mutations selectively involve *L265P* and often occur together with *CD79B* mutations (29). Studies have indicated that the BTK inhibitor ibrutinib is more sensitive to *MYD88/CD79B* double-mutant DLBCLs, probably due to *CD79B*-dependent BCR activation (8,15). Most primary CNS DLBCL cases are reported to contain the double *MYD88*^{L265P} and *CD79B*$^{Y196C/D/H}$ mutations, which could trigger the NF-κB signaling pathway (9). In addition, the *MYD88*^{L265P} mutation prompts the progression of DLBCL to the CNS (30). It has also been confirmed that the incidence of CNS recurrence is high in CD5$^+$ DLBCL, and that it is mainly included in the non-GCB type of DLBCL (31). In our case, the patient was relapsed in the right upper lobe after ZR-miniCHOP therapy, which might be the result of her physiological background of CD5$^+$ and *MYD88*^{L265P}/*CD79B* mutations (32).

The NF-κB signaling pathway is crucial in distinct lymphoma entities, including DLBCL (33). BTK inhibitors can prevent the proliferation, migration, and activation of NF-κB in B-cell malignancies (34). Study on mechanisms for ibrutinib-responsive biopsies shows that oncogenic BCR signaling could mediate and cooperatively activate NF-κB via the MYD88-TLR9-BCR (My-T-BCR) multiprotein signaling complex (35). Zanubrutinib, a highly selective and potent BTK inhibitor, when combined with R-miniCHOP therapy, demonstrates a remarkable response in treating refractory DLBCL. It might possibly function by inhibiting NF-κB signaling. However, further investigation is required to fully understand the intrinsic molecular mechanisms.

DLBCL with *MYD88*^{L265P} and *CD79B* comutations has inferior outcomes with current standard immunochemotherapy (8). In addition, *MYD88* (L265P) (36,37) and CD5$^+$ DLBCL subtype (4,10,13) are both inferior prognostic factor in DLBCLs under current R-CHOP regimens. Zanubrutinib monotherapy has shown promising results in treating relapsed and refractory DLBCL (16). In our study, we observed disease progression after zanubrutinib plus rituximab therapy. However, the combination of zanubrutinib with R-miniCHOP therapy as second-line therapy produced a remarkable response in this patient. Afterwards, the disease migrated to CNS and the regimen of toripalimab and lenalidomide also showed response during treatment, although it relapsed finally. Tumor mutation burden (TMB) values quantified by targeted gene panels have been widely applied in clinical use as for its lower cost than whole exome sequencing (38). The TMB value were 6.45 mutations/Mb, and the micro-satellite instability (MSI) status was low in this patient, which might explain the efficacy of PD-1 in this case. In this study, we also observed that the TMB value in BALF was lower compared to the tissue sample (24). Currently, the PD-1 toripalimab plus rituximab has been used as a first-line treatment, followed by R-CHOP for elderly patients in primary DLBCL (NCT04058470) (19).

Administration of ibrutinib plus R-CHOP in patients over 60 years old has been associated with increased toxicity and worse outcomes (14). In those younger than 60 years old, ibrutinib plus R-CHOP therapy could improve outcomes (14). For older subgroup (age ≥65 years old) with relapsed or refractory MCD tumors, zanubrutinib monotherapy shows higher ORR (16). In our case, the use of zanubrutinib plus R-miniCHOP therapy yielded positive results in a 72-year-old female, which might be of great clinical significance. Additionally, administration of toripalimab plus lenalidomide prolonged the survival status of this stage IV DLBCL patient with an IPI score of 5, the patient remains survival for 11 months after central relapse till now. In addition, she had survived for over 2 years since the initial diagnosis. Our findings might be useful in developing an improved biomarker strategy for targeting this population. Further investigation is warranted.

Conclusions

Our case report highlights the treatment of a stage IV CD5$^+$ non-GCB DLBCL patient with an IPI score of 5. We found that only tissue biopsy samples were appropriate for identifying relevant mutations due to the heterogeneity of this disease, as revealed by our comparison of genomic profiles of tissue biopsy and BALF samples. With genomic background of *MYD88*^{L265P} and *CD79B* comutations, the patient experienced relapse in CNS (the left frontal lobe). Third-line treatment with toripalimab combined with rituximab helped to prolong the patient's survival after CNS relapse. This case provides crucial guidance for

clinical practice and demonstrates a convincing response to a new treatment that may be useful for patients with relapsed DLBCL.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1638/rc

Peer Review File: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1638/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1638/coif). Y.X. and B.C. are current employees of BGI Genomics. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional or national research committees and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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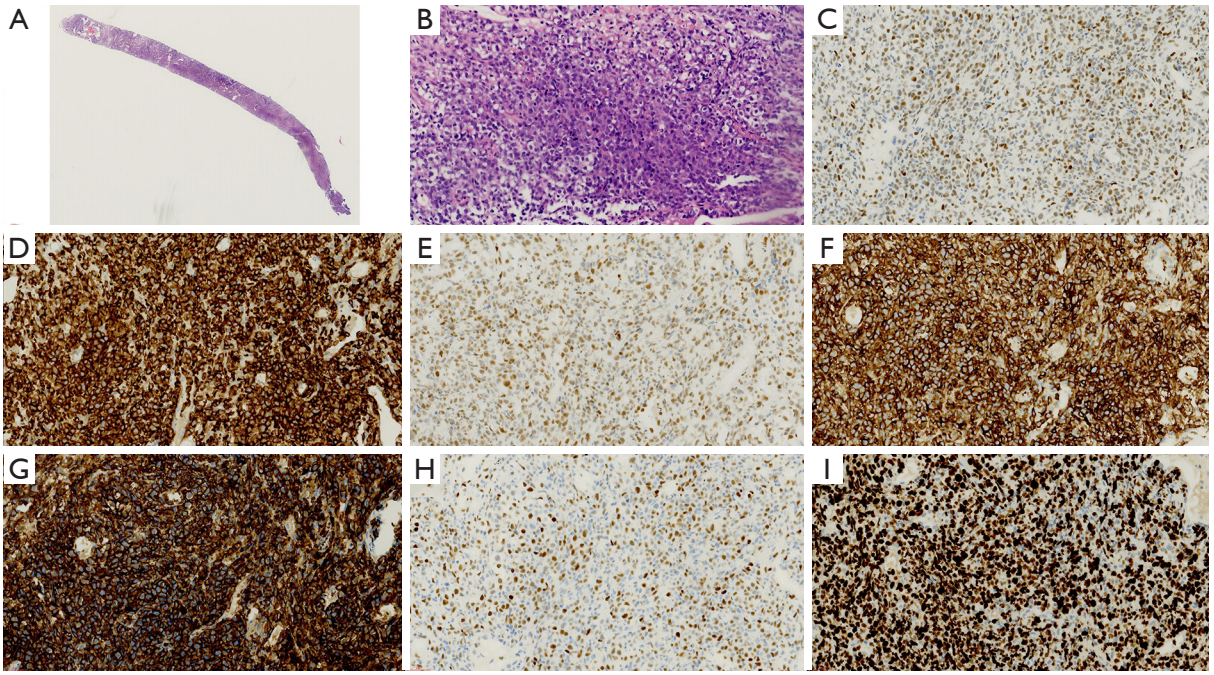

Figure S1 Hematoxylin-eosin and immunohistochemical staining results for the patients. (A,B) Hematoxylin-eosin staining of the biopsy showed the presence of "starry sky" phenomenon (scale bar: 1,000 μm for A and 40 μm for B). (C-I) Immunohistochemical staining results (scale bar: 40 μm) for P53 (C), Bcl-2 (D), Bcl-6 (E), CD5 (F), CD20 (G), c-Myc (H), and Ki-67 (I). Bcl-2, B-cell lymphoma 2 protein; Bcl-6, B-cell lymphoma 6 protein; P53, tumor protein 53.

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Table S1 Detailed description of the mutations

Sample type	TMB (Muts/Mb)	Gene	Mutation type	cHGVS	pHGVS	Exon	Variant allele frequency	Transcriptome
Bronchoalveolar lavage	0.36	*VEGFA*	Deletion	c.19_22delGACA	p.D7Pfs*45	EX1	0.91%	NM_001025366.2
		PRSS1	SNV	c.637G>A	p.V213I	EX5E	2.83%	NM_002769.4
		ARID1A	Deletion	c.492_494delCGC	p.A167del	EX1	0.63%	NM_006015.4
Tissue	6.45	*MYD88*	SNV	c.794T>C	p.L265P	EX5E	23.56%	NM_002468.4
		PRDM1	Duplication	c.251_260dupCAAGGAATCT	p.L88Kfs*12	EX2	27.91%	NM_001198.3
		CDKN2A/CDKN2B-AS1	Gene fusion	N/A	N/A	IVS1-IVS1	63.48%	NM_000077.4-NR_003529.3
		B2M	SNV	c.345G>A	p.W115*	EX2	24.85%	NM_004048.2
		ETV6	SNV	c.33G>C	p.K11N	EX1	24.65%	NM_001987.4
		PIM1	SNV	c.4C>T	p.L2F	EX1	22.35%	NM_002648.3
		CD79B	SNV	c.589T>C	p.Y197H	EX5	22.04%	NM_001039933.1
		RYR2	SNV	c.3999C>A	p.D1333E	EX31	21.82%	NM_001035.2
		PIM1	SNV	c.72G>C	p.K24N	EX1	21.58%	NM_002648.3
		PIM1	SNV	c.68C>G	p.T23S	EX1	21.36%	NM_002648.3
		FAT1	SNV	c.12425G>A	p.C4142Y	EX25	20.74%	NM_005245.3
		TAF1L	SNV	c.3808C>A	p.P1270T	EX1E	18.27%	NM_153809.2
		ATRX	SNV	c.1397G>T	p.R466I	EX9	18.02%	NM_000489.3
		ETV6	SNV	c.16G>A	p.A6T	EX1	17.84%	NM_001987.4
		BCL2	SNV	c.10G>A	p.A4T	EX2	17.54%	NM_000633.2
		RYR2	SNV	c.11522G>A	p.R3841Q	EX85	16.12%	NM_001035.2
		ZMYM3	SNV	c.1025C>A	p.T342N	EX5	16.04%	NM_201599.2

TMB, tumor mutation burden; Muts, mutations; cHGVS, nucleic acid Human Genome Variation Society; pHGVS, protein Human Genome Variation Society; *VEGFA*, vascular endothelial growth factor A; *PRSS1*, serine protease 1; SNV, single nucleotide variant; *ARID1A*, AT-rich interactive domain-containing protein 1A; *MYD88*, myeloid differentiation primary response 88; *PRDM1*, PR domain zinc finger protein 1; *CDKN2A-CDKN2B-AS1*, the gene fusion cyclin dependent kinase inhibitor 2A-cyclin dependent kinase inhibitor 2B antisense RNA 1; N/A, not applicable; *B2M*, beta-2-microglobulin; *ETV6*, ETS variant transcription factor 6; *PIM1*, proviral integration of Moloney virus 1; *CD79B*, cluster of differentiation 79B; *RYR2*, ryanodine receptor 2; *FAT1*, FAT atypical cadherin 1; *TAF1L*, TATA-box binding protein associated factor 1 like; *ATRX*, X-linked alpha thalassemia mental retardation; *BCL2*, B-cell lymphoma 2; *ZMYM3*, zinc finger MYM-type containing 3.

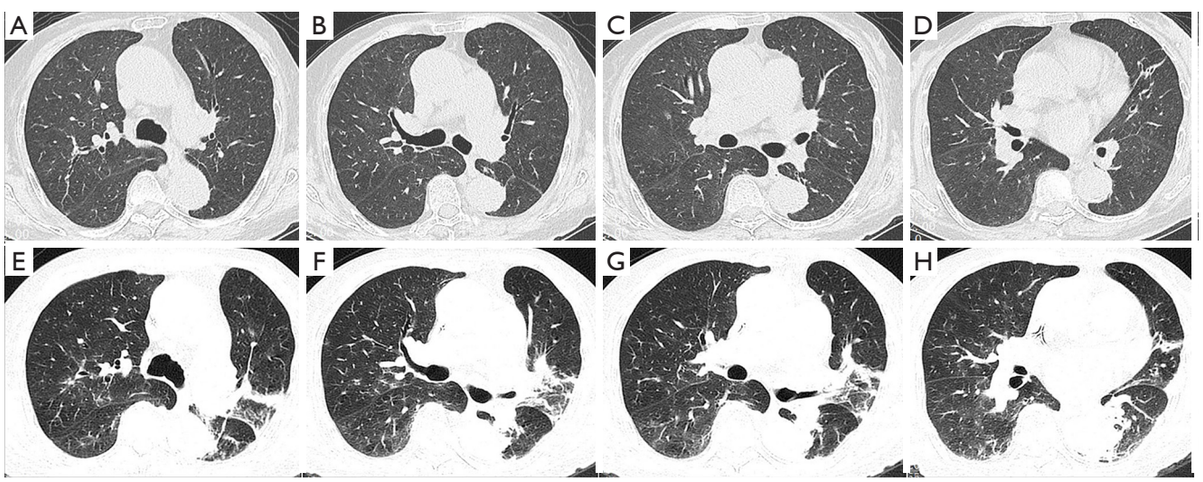

Figure S2 CT of the lung for the patient. (A-D) CT after toripalimab and rituximab treatment in March 2023. (E-H) CT of progressive disease in June 2023. CT, computed tomography.

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