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Impact of radiation response on survival in pediatric medulloblastoma with residual or disseminated disease

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Abstract

Background This study aimed to determine the clinical impact of radiation response on survival in patients with medulloblastoma (MB) and to explore the predictive factor of radiation response.

Methods Data from 170 pediatric patients with MB and residual disease or metastasis before radiotherapy (RT) were analyzed.

Results The median follow-up period was 5.2 years. A total of 74 (43.5%) patients achieved CR, 85 (50.0%) patients achieved PR, 8 (4.7%) patients had SD, and 3 (1.8%) patients developed PD after RT. The five-year post-RT progression-free (prtPFS) and overall survival (prtOS) were superior in patients who achieved CR compared to those who did not (prtPFS: 67% ± 6% vs. 42% ± 6%, $P < 0.001$; prtOS: 82% ± 5% vs. 44% ± 6%, $P < 0.001$). Multivariable logistic regression analysis showed that residual disease site was the predictive factor for radiation response, patients who had residual disease in both the brain and spinal cord before RT had higher non-CR rate (OR: 7.312, 95%CI 3.375–15.845, $P < 0.001$). Multivariate Cox analysis revealed that radiation response and large cell/anaplastic subtype were independent prognostic factors for survival ($P < 0.05$).

Conclusions Radiation response was an independent prognostic factor for survival in patients with MB. Patients who did not achieve CR after RT should receive intensified adjuvant chemotherapy to improve survival.

Keywords Medulloblastoma, Radiation response, Prognosis, Predictive factor

Background

Medulloblastoma (MB) is the most prevalent intracranial embryonal tumor in pediatric patients, exhibiting notable heterogeneity [1, 2]. The current standard of care for children over the age of three is a maximum safe excision of the tumor, followed by craniospinal irradiation (CSI) and adjuvant chemotherapy [3]. A multidisciplinary approach to treatment has led to a considerable increase in the long-term survival of patients with MB. Patients in the standard-risk (SR) group have achieved a 5-year overall survival (OS) rate of over 75%, while the prognosis for patients in the high-risk (HR) group, particularly those with residual disease and metastases, remains unsatisfactory [4–6]. The clinical outcome of MB is highly dependent on the efficacy of radiotherapy (RT). Omission of RT is associated with an unacceptable neuraxial failure even in patients with the best prognosis [7, 8]. However, few studies have reported the clinical impact of radiation response on survival in patients with MB especially those

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with residual disease prior to RT [9]. In this study, we retrospectively evaluated a cohort of 170 patients with MB who had measurable residual disease and/or metastases before RT to assess the impact of radiation response on prognosis. On the other hand, we explored the risk factors predicting radiation response.

Methods

Patient cohort

This retrospective study included all consecutive MB patients with residual disease (>1.5 cm^2 of enhancing lesion present at the primary site) or disseminated lesions (M2/3) or both who received RT at Xinhua Hospital between 2009 and 2022. Baseline assessments were conducted via cranial and spinal MRI scans prior to the initiation of RT. The irradiation volume encompassed CSI with a boost to the tumor bed or whole posterior fossa (WPF). The gross tumor volume (GTV) was defined as the initial extent of disease before surgery or any other treatment. The GTV was extended by 1–1.5 cm in all directions to define the clinical target volume (CTV) that included all risk areas for microscopic disease as indicated by surgical reports and pathological examinations, taking into account anatomical constraints. The planning target volume (PTV) consisted of a geometric extension (0.3–0.5 cm) of the CTV to account for setup error or patient movement and was intended to be covered by the 95% isodose line. The CSI doses ranged from 23.4 Gy to 40 Gy (median 36 Gy), delivered in 1.8–2.0 Gy per fraction. Patients who were treated prior to April 2016 underwent RT using intensity modulated radiation (IMRT), while those treated subsequently received treatment using the helical Tomo-therapy. Cranial and spinal MRI scans were reperformed within 3 days after the end of RT and every three months thereafter for the initial two years, every six months during years three to five, and annually thereafter. The therapeutic effect was classified as complete response (CR) or non-CR (including partial response (PR), stable disease (SD), and progressive disease (PD)) according to the RAPNO (Response Assessment in Pediatric Neuro-Oncology) criteria [10]. Alkylator and platinum-based adjuvant chemotherapy was administered at our hospital or at an external facility after RT. Vincristine was used for concomitant chemotherapy. Patients younger than 3 years at diagnosis received chemotherapy first to delay RT and reduce long-term toxicity. Patients who had severe postoperative complications and could not tolerate CSI also received chemotherapy first. The patients' survival status was followed up by telephone, with the endpoint of follow-ups occurring in October 2024.

Acute hematologic toxicity

Blood cell data were collected retrospectively from complete blood counts performed before and weekly during RT. Average blood cell counts were used when more than one complete blood count was performed in each week. The Common Toxicity Criteria for Adverse Events version 5.0 (CTCAE5) was used to grade hematologic toxicities.

Statistical analysis

Overall survival was defined as the time interval between the end of RT and death from any cause, or the date of the last follow-up (prtOS). Progression free survival was defined as the time interval starting from the end of RT to the date of disease progression or last follow-up (prtPFS). Survival analyses were performed using the Kaplan-Meier method. Univariate and multivariate analyses were performed with Cox proportional hazards models. Multivariable logistic regression analyses were used to explore the factors predicting radiation response. Statistical evaluations were performed using SPSS version 23.0 software, and a *P*-value of less than 0.05 was considered statistically significant.

Results

Clinicopathologic characteristics

The clinicopathological characteristics of the cohort are summarized in Table 1. Of the 170 patients, 106 (62.4%) patients were male; 141 (82.9%) patients were older than 3 years of age at diagnosis; 122 (71.8%) patients had metastatic disease at diagnosis; Most of the tumors (45.3%) were classic histological subtypes and non-WNT/non-SHH molecular subtypes occupied the major types in patients with molecular evidence. All patients had residual diseases before RT and the residual lesions were distributed in the brain (32.9%), spinal cord (19.4%) or both (47.6%).

Treatment characteristics

A total of 35 (20.6%) patients received chemotherapy prior to RT, 11 (6.5%) patients had concurrent chemotherapy. IMRT was employed in 33 (19.4%) cases, while Tomo-therapy was utilized in 137 (80.6%) cases. The median dose of CSI was 36 Gy (range 23.4–40 Gy, only one patient received 23.4 Gy CSI), and the median dose of boost was 54 Gy (range 52.2–57.6 Gy). 74 (43.5%) patients achieved CR, 85 (50.0%) patients achieved PR, 8 (4.7%) patients exhibited SD, and 3 (1.8%) patients developed PD after RT.

Survival and prognostic factors

The median follow-up period after the end of RT for survivors ($n = 107$) was 5.2 years (range: 0.5–14.8 years). During the observational period of the study, 71 (41.8%)

Table 1 The clinicopathological characteristics of the entire cohort

Characteristics	Entire cohort (*N* = 170)
Sex	
Female	64 (37.6%)
Male	106 (62.4%)
Age at diagnosis	
< 3 y	29 (17.1%)
≥ 3 y	141 (82.9%)
Histology	
Classic	77 (45.3%)
Nodular/ desmoplastic	21 (12.4%)
MBEN	2 (1.2%)
Large cell/anaplastic	7 (4.1%)
Not specified	63 (37.1%)
Molecular grouping	
WNT	7(4.1%)
SHH	25 (14.7%)
Non WNT/SHH	59 (34.7%)
Not specified	79 (46.5%)
M stage at diagnosis	
M0	48 (28.2%)
M+	122 (71.8%)
Residual disease site before RT	
Brain	56 (32.9%)
Spinal cord	33 (19.4%)
Borth	81 (47.6%)
Chemotherapy before RT	
No	135 (79.4%)
Yes	35 (20.6%)
Concurrent chemotherapy	
No	159 (93.5%)
Yes	11 (6.5%)
Radiotherapy mode	
IMRT	33 (19.4%)
TOMO	137 (80.6%)
CSI dose	
< 36 Gy	8 (4.7%)
≥ 36 Gy	162 (95.3%)
Radiotherapy dose	
≤ 54 Gy	163(95.9%)
> 54 Gy	7 (4.1%)
Radiotherapy efficacy	
CR	74 (43.5%)
PR	85 (50.0%)
SD	8 (4.7%)
PD	3 (1.8%)

patients suffered disease progression at a median time of 12.0 months after RT. Among these patients, 50 individuals still demonstrated residual disease after RT, with 17 cases occurring in the brain, 10 cases in the spinal cord, and 23 cases involving both the brain and spinal cord. A total of 63 (37.1%) patients died. Of these, 60 patients died due to tumor-related causes, 2 patients died due to severe pneumonia and 1 patient died due to intracranial hypertension without disease progression. For the entire cohort, the 5-year prtPFS and prtOS were 57% ± 4.0% and 60% ± 4%, respectively. In the univariate Cox analyses, patients with residual disease in both brain and spinal cord before RT ($P = 0.006$) and non-CR after RT ($P = 0.001$) were associated with poorer prtPFS. Large cell/anaplastic subtype ($P = 0.042$), metastases ($P = 0.045$), residual disease in both brain and spinal cord before RT ($P = 0.001$) and non-CR after RT ($P < 0.001$) were associated with poorer prtOS (Table 2; Fig. 1). Gender, age at diagnosis, pre-RT chemotherapy, concurrent chemotherapy, radiotherapy mode and radiotherapy dose had no significant difference on prognosis. Forward stepwise multivariate Cox analysis revealed that non-CR after RT (HR, 2.204; 95% CI, 1.222–3.974; $P = 0.009$) was an independent adverse prognostic factor for prtPFS. Furthermore, non-CR after RT (HR, 3.596; 95% CI, 1.722–7.662; $P < 0.001$) and large cell/anaplastic subtype (HR, 3.180; 95% CI, 1.104–9.163; $P = 0.032$) were adverse prognostic factors for prtOS (Table 3).

The 5-year prtPFS for patients who achieved CR after RT was significantly higher than those who did not achieve CR (67% ± 6% vs. 42% ± 6%, $P < 0.001$). Similarly, the five-year prtOS was also superior in the CR group (82% ± 5% vs. 44% ± 6%, $P < 0.001$). Subsequently, the demographic and clinical characteristics of the two subcohorts with disparate radiation responses were compared (Table 4). A greater proportion of patients in the non-CR group had metastasis at diagnosis compared to the CR group (81.2% vs. 59.5%). Similarly, a greater proportion of patients in the non-CR group had residual diseases in both the brain and spinal cord before RT (67.7% vs. 21.6%). In univariable logistic regression analyses, patients with stage M+ (OR, 2.955; 95%CI, 1.480–5.899, $P = 0.002$) and residual diseases in both sites (OR, 7.312; 95%CI, 3.375–15.845, $P < 0.001$) were associated with non-CR. No significant differences were observed in the distribution of patients regarding gender, age, histology, concurrent chemotherapy, or RT mode. In multivariable analyses, the residual diseases site prior to RT was the independent predictor of radiation response in both the all-inclusive model and forward-stepwise models (Table 5). Patients with residual disease in both brain and spinal cord exhibited a higher likelihood of having non-CR after RT.

With the development of genomics, molecular typing of medulloblastoma has received increasing attention. Molecular typing became popular in our center after 2017, and 91 out of 170 patients had molecular subgroup based on targeted mutation and CNV analysis ($n = 61$) or NanoString gene expression assay ($n = 30$) in our study. We then collected molecular information, including *MYC* or *MYCN* amplification status, CNV profiles (event

Table 2 Univariate Cox analyses of prognostic factors of survival

Characteristic	Univariate analyses			
	prtPFS		prtOS	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Sex				
Female	Ref		Ref	
Male	0.958(0.591–1.553)	0.861	0.904(0.543–1.504)	0.697
Age at diagnosis				
< 3 y	Ref		Ref	
≥ 3 y	1.081(0.568–2.056)	0.813	0.817(0.435–1.534)	0.529
Histology				
Non-large cell/anaplastic	Ref		Ref	
Large cell/anaplastic	2.097(0.762–5.776)	0.152	2.895(1.039–8.072)	0.042
Molecular grouping				
WNT	Ref		Ref	
SHH	1.961(0.434–8.851)	0.381	1.344(0.285–6.334)	0.709
Non WNT/SHH	1.497(0.351–6.387)	0.586	1.145(0.263–4.983)	0.857
M stage at diagnosis				
M0	Ref		Ref	
M+	1.322(0.774–2.258)	0.308	1.905(1.014–3.576)	0.045
Chemotherapy before RT				
No	Ref		Ref	
Yes	1.179(0.675–2.057)	0.563	1.169(0.645–2.118)	0.606
Residual disease site before RT				
Brain	Ref		Ref	
Spinal cord	1.036(0.474–2.263)	0.929	1.321(0.556–3.136)	0.528
Borth	2.180(1.245–3.819)	0.006	2.904(1.528–5.520)	0.001
Concurrent chemotherapy				
No	Ref		Ref	
Yes	0.787(0.287–2.159)	0.641	0.697(0.218–2.222)	0.541
Radiotherapy mode				
IMRT	Ref		Ref	
TOMO	0.765(0.390–1.169)	0.161	0.688(0.389–1.218)	0.200
CSI dose				
< 36 Gy	Ref		Ref	
≥ 36 Gy	1.271(0.400-4.045)	0.684	1.271(0.396–4.077)	0.686
Radiotherapy dose				
≤ 54 Gy	Ref		Ref	
> 54 Gy	1.103(0.346–3.516)	0.868	1.162(0.362–3.734)	0.801
Radiation response				
CR	Ref		Ref	
Non-CR	2.465(1.478–4.110)	0.001	3.773(2.075–6.861)	< 0.001

number ≥ 5), and integrated these molecular data into our statistical analysis to evaluate their impact on radiation response and prognosis. The results showed that patients with 17p loss ($P < 0.001$) and *MYC* amplification ($P = 0.051$) had poor prtPFS compared to wild-type patients, whereas patients with 7p gain ($P = 0.024$), 7q gain ($P = 0.094$) and 17p gain ($P = 0.067$) had good prtPFS compared to wild-type patients (Table S1). While none of the molecular characteristics can predict the radiation response (Table S2).

Hematologic toxicity

Hematologic toxicity is a well-documented adverse effect of CSI. Our analysis of hematologic data during RT in 158 patients revealed that most patients exhibited grade 3 leukopenia, grade 3 neutropenia, grade 1 anemia, grade 0 thrombocytopenia and grade 4 lymphopenia (Table 6). No patients died because of hematologic toxicity during RT.

Several studies have indicated that RT-associated lymphopenia is associated with poorer clinical outcomes in patients with solid tumors [11–14]. Subsequently, we explored the dynamic change of lymphocyte during RT. As shown in Fig. 2, the median baseline absolute lymphocyte count (ALC) prior to RT was 1.5×10^9/L (range 0.56–3.52), and no patient had grade 3/4 lymphopenia. In comparison to the baseline, the ALC exhibited a notable decline during the initial three weeks of RT, with a median ALC of 0.61×10^9/L (range 0.18–4.06), 0.32×10^9/L (range 0.13–2.32), and 0.25×10^9/L (range 0.08-3.00), respectively. The ALC ceased its decline from the fourth week of RT and recovered to 0.48×10^9/L (range 0.09–2.61) at the seventh week of RT. Accordingly, the proportion of grade 3/4 lymphopenia in our cohort exhibited a notable increase during the initial four-week period, followed by a gradual decline during the subsequent treatment phase. The ALC exhibited no significant difference between the CR and non-CR groups during RT, while the ALC nadir was observed to be higher in patients who achieved CR (0.19 ± 0.13) $\times 10^9$/L compared to those who did not (0.15 ± 0.07) $\times 10^9$/L ($t = 2.445$, $P = 0.016$) (Supplementary Fig. S1). Patients were divided into two groups according to the median ALC nadir. There was no significant difference in survival between the two groups (Supplementary Fig. S2).

Discussion

The current standard of care for MB includes initial surgery followed by a combination of radiation and chemotherapy. Despite advances in systemic therapy and neurosurgical techniques, radiation therapy remains essential. Omission of upfront CSI or radiation is associated with unacceptable neuraxial failure, even in low-risk WNT MB with the best prognosis [7, 8]. Here, we

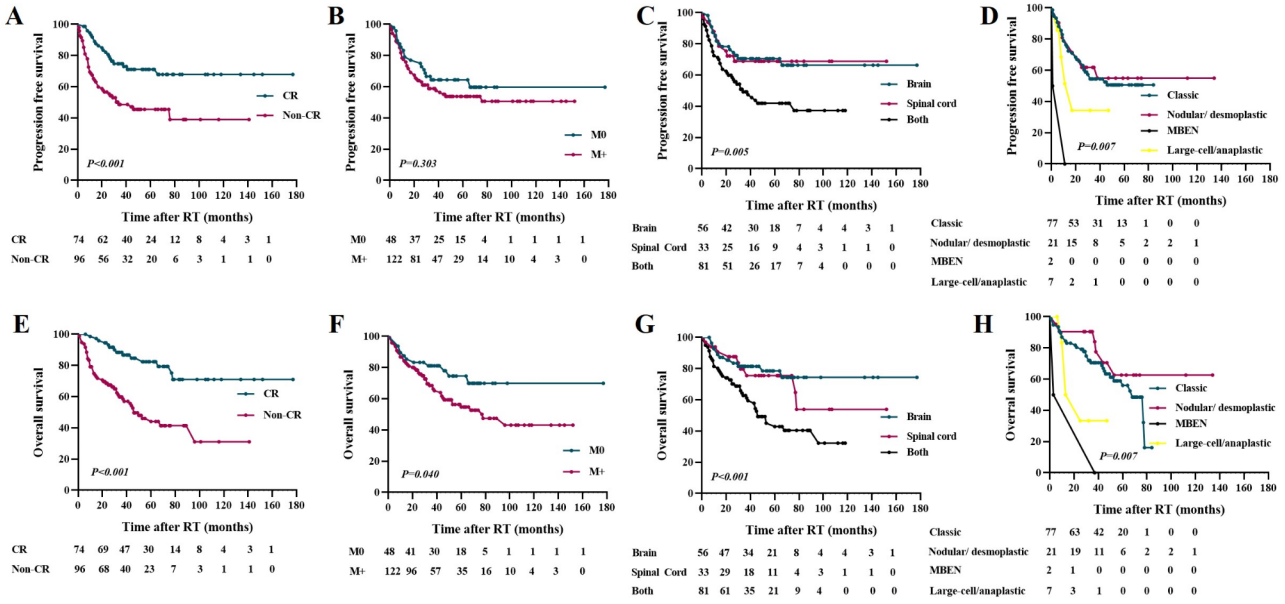

Fig. 1 Patient outcomes after RT for medulloblastoma with residual or dissimilated diseases. The prtPFS for patients achieved CR and non-CR after RT (**A**), metastatic status at diagnosis (**B**), residual disease site before RT (**C**) and histological subtype (**D**). The prtOS for patients achieved CR and non-CR after RT (**E**), metastatic status at diagnosis (**F**), residual disease site before RT (**G**) and histological subtype (**H**)

Table 3 Multivariate Cox analyses of prognostic factors of survival

Characteristic	Multivariate analyses			
	prtPFS		prtOS	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Histology				
LC/A *VS* non-LC/A			3.180(1.104–9.163)	0.032
Radiotherapy response				
Non-CR *VS* CR	2.204(1.222–3.974)	0.009	3.596(1.722–7.662)	< 0.001

LC/A: Large cell/anaplastic

provided the real-word data of MB, analyzed the clinical characteristics of patients with residual or disseminated disease before RT and evaluated the effect of radiation response on prognosis. A total of 170 patients were enrolled in the study, and the 5-year prtPFS and prtOS were 57% and 60%, respectively, for the entire cohort. These results are comparable to those of previous studies [15–19].

A series of studies have been conducted to assess the efficacy of postoperative neoadjuvant chemotherapy before RT in patients with high-risk MB, while the results are controversial. The SIOP/UKCCSG PNET-3 study involved the administration of two courses of chemotherapy, comprising vincristine, etoposide, carboplatin, and cyclophosphamide, followed by CSI of 35 Gy and a posterior fossa boost of 20 Gy. With a median follow-up period of 7.2 years, the 5-year EFS rate was 34.7%, and the 5-year overall survival OS rate was 43.9%. There was no apparent improvement in outcome for M2-3 patients undergoing pre-RT chemotherapy [17]. Kortmann et al. performed a prospective, multicenter, randomized trial by using postoperative neoadjuvant chemotherapy before RT to improve survival of patients with MB. However, the results demonstrated that the RT first group exhibited superior outcomes compared to the neoadjuvant chemotherapy group, particularly in patients between 3 and 5.9 years of age [20]. Postoperative neoadjuvant chemotherapy was usually accompanied by increased myelotoxicity of the subsequent RT and lead to a higher rate of interruptions and delayed RT which have a negative impact on outcome. The long-term outcome of the study also corroborated the excellent results in post-RT chemotherapy group compared with the neoadjuvant chemotherapy group [21]. In the prospective multicenter trial HIT 2000, intensified neoadjuvant induction chemotherapy, hyperfractionated CSI and additional four cycles of maintenance chemotherapy were used in patients with metastatic MB. In comparison to the HIT 91 trial, the HIT 2000 trial demonstrated superior OS and comparable EFS although the study did not further explore the impact of RT timing on survival [6]. In another randomized study, POG 9031, patients with high-risk MB were assigned to receive either chemotherapy before RT or chemotherapy after RT. The 5-year EFS and 5-year OS did not exhibit a statistically significant difference between the two groups, but RT first group achieved higher objective response rate than chemotherapy fist group (86% vs. 66%, $P = 0.01$) [22]. In our study, 79.4% of patients received post-operative RT directly. The

Table 4 Clinical and pathologic characteristics of the two subcohorts with different radiation response

Characteristics	Entire cohort (*n* = 170)	CR group (*n* = 74)	Non-CR group (*n* = 96)	*P* value
Sex				0.494
Female	64 (37.6%)	30 (40.5%)	34 (35.4%)	
Male	106 (62.4%)	44 (59.5%)	62 (64.6%)	
Age at diagnosis				0.504
< 3 y	29 (17.1%)	11 (14.9%)	18 (18.8%)	
≥ 3 y	141 (82.9%)	63 (85.1%)	78 (81.2%)	
Histology				0.883
Classic	77 (45.3%)	31 (41.9%)	46 (47.9%)	
Nodular/ desmoplastic	21 (12.4%)	11 (14.9%)	10 (10.4%)	
MBEN	2 (1.2%)	1 (1.4%)	1 (1.0%)	
Large cell/anaplastic	7 (4.1%)	3 (4.1%)	4 (4.2%)	
Not specified	63 (37.1%)	28 (37.8%)	35 (36.5%)	
Molecular grouping				0.058
WNT	7(4.1%)	2 (2.7%)	5 (5.2%)	
SHH	25 (14.7%)	15 (20.3%)	10 (10.4%)	
Non WNT/SHH	59 (34.7%)	30 (40.5%)	29 (30.2%)	
Not specified	79 (46.5%)	27 (36.5%)	52 (54.2%)	
M stage at diagnosis				0.002
M0	48 (28.2%)	30 (40.5%)	18 (18.8%)	
M+	122 (71.8%)	44 (59.5%)	78(81.2%)	
Residual disease site before RT				0.000
Brain	56 (32.9%)	36 (48.6%)	20 (20.8%)	
Spinal cord	33 (19.4%)	22 (29.7%)	11 (11.5%)	
Borth	81 (47.6%)	16 (21.6%)	65 (67.7%)	
Chemotherapy before RT				0.770
No	135 (79.4%)	58 (78.4%)	77 (80.2%)	
Yes	35 (20.6%)	16 (21.6%)	19 (19.8%)	
Concurrent chemotherapy				1.000
No	159 (93.5%)	69 (93.2%)	90 (93.8%)	
Yes	11 (6.5%)	5 (6.8%)	6(6.3%)	
Radiotherapy mode				0.594
IMRT	33 (19.4%)	13 (17.6%)	20 (20.8%)	
TOMO	137 (80.6%)	61 (82.4%)	76 (79.2%)	
CSI dose				0.080
< 36 Gy	8 (4.7%)	6 (8.1%)	2 (2.1%)	
≥ 36 Gy	162 (95.3%)	68 (91.9%)	94 (97.9%)	
Radiotherapy dose				1.000
≤ 54 Gy	163(95.9%)	71 (95.9%)	92 (95.8%)	
> 54 Gy	7 (4.1%)	3 (4.1%)	4 (4.2%)	

Table 5 Multivariable logistic regression analysis of predictors of RT response

Characteristics	OR (95%CI)	*P* value
All-inclusive model		
Sex		
Female	Ref	
Male	1.170(0.544–2.517)	0.688
Age at diagnosis		
< 3 y	Ref	
≥ 3 y	0.855(0.296–2.468)	0.773
Histology		
Non-large cell/anaplastic	Ref	
Large cell/anaplastic	0.614(0.100-3.757)	0.598
Molecular grouping		
WNT	Ref	
SHH	0.137(0.017–1.079)	0.059
Non WNT/SHH	0.267(0.039–1.827)	0.179
NOS	0.322(0.044–2.363)	0.265
M stage at diagnosis		
M0	Ref	
M+	1.726(0.624–4.779)	0.293
Chemotherapy before RT		
No	Ref	
Yes	0.535(0.193–1.478)	0.227
Residual disease site before RT		
Brain	Ref	
Spinal cord	0.690(0.209–2.274)	0.542
Borth	6.481(2.261–18.581)	0.001
Concurrent chemotherapy		
No	Ref	
Yes	2.228(0.465–10.666)	0.316
Radiotherapy mode		
IMRT	Ref	
TOMO	0.885(0.268–2.926)	0.841
CSI dose		
< 36 Gy	Ref	
≥ 36 Gy	7.089(0.876–57.392)	0.066
Radiotherapy dose		
≤ 54 Gy	Ref	
> 54 Gy	2.656(0.345–20.444)	0.348
Forward-stepwise model		
Residual disease site before RT		
Brain	Ref	
Spinal cord	0.900(0.363–2.229)	0.820
Borth	7.312(3.375–15.845)	< 0.001

prognoses of the RT first group and the chemotherapy first group were found to be similar. Moreover, the objective response rate in our study exceeded 90%, which is higher than that observed in previous studies, may be attributed to the high dose of radiation therapy administered. Subgroup analysis revealed that the radiation response is an independent prognostic factor. Patients who achieved CR after RT exhibited a higher survival rate than those who did not achieve CR. Patients who still had residual disease after RT may require intensified adjuvant chemotherapy to improve survival. Admittedly, intensive treatment may lead to increased treatment-related toxicity [23], and the balance between treatment efficacy and treatment toxicity is an issue that needs to be further explored in the future.

Table 6 Grades of acute hematologic toxicity during radiotherapy

CTCAE grade of toxicity	Hematological toxicity (*N* = 158)				
	Leukopenia	Neutropenia	Anemia	Thrombocytopenia	Lymphopenia
Grade 0	4 (2.5%)	20(12.7%)	9(5.7%)	77(48.7%)	0(0%)
Grade 1	8 (5.1%)	7(4.4%)	70(44.3%)	39(24.7%)	1(0.6%)
Grade 2	27(17.1%)	31(19.6%)	63(39.9%)	30(19.0%)	2(1.3%)
Grade 3	104(65.8%)	77(48.7%)	14(8.9%)	11(7.0%)	45(28.5%)
Grade 4	15(9.5%)	23(14.6%)	2(1.3%)	1(0.6%)	110(69.6%)

In this study, we also explore the factors affecting radiation response. Multivariable logistic regression analyses indicated that the site of residual disease before RT was associated with radiation response. Patients with residual disease in both the brain and spinal cord had the lowest CR rate and the worst prognosis compared with the other two groups, which may be due to the high tumor burden. Concurrent chemotherapy is common practice in brain tumor, employed with the objective of sensitizing RT and improving survival [24]. In this study, a limited number of patients received concurrent chemotherapy, with the primary chemotherapy agent being vincristine. No significant difference in survival was observed between the patients who received concurrent chemotherapy and those who did not. In a previous study, Liu et al. found that the use of chemotherapy during CSI or the choice of alkylator had no significant impact on patient outcomes [18]. Jakacki and colleagues evaluated the feasibility of administering carboplatin as a radiosensitizer during CSI and proposed that the use of carboplatin represents a promising strategy for patients with metastasis [25]. A subsequent randomized clinical trial demonstrated that intensifying therapy with carboplatin only improved the survival of Group 3 patients [5]. For patients falling into other molecular subgroups, it would be beneficial to explore new radiosensitizers.

Hematologic toxicity is the most common acute toxicity during RT. Patients with high-risk MB usually receive high dose of CSI and the hematologic toxicity is usually obvious. In this study, the grade 3–4 hematologic toxicities are leukopenia, neutropenia and lymphopenia, which are comparable to the previous study [14, 26]. Even through ALC nadir did not prove an effective predictor of prognosis in patients with MB, those with a high ALC nadir demonstrated a higher CR rate. Consequently, strategies to mitigate the risk of radiation-induced lymphopenia warrant consideration.

Conclusions

In conclusion, we summarized the clinical characteristics of MB with residual or disseminated disease before RT and evaluated the effect of radiation response on prognosis. Radiation response is an independent prognostic factor for patients with MB. Patients who achieved CR after RT had higher prtPFS and prtOS compared to those who did not. Patients with residual disease in both the brain and spinal cord exhibited a poorer CR rate and prognosis and may should receive intensified adjuvant chemotherapy. Admittedly, the relatively short follow-up period and the retrospective nature of the study are limitations of the analysis. A prospective randomized study with a long follow-up period is needed for further confirmation.

Abbreviations

MB	Medulloblastoma
CSI	Craniospinal irradiation
SR	Standard-risk
HR	High-risk
GTV	Gross tumor volume
CTV	Clinical target volume
PTV	Planning target volume
IMRT	Intensity modulated radiation

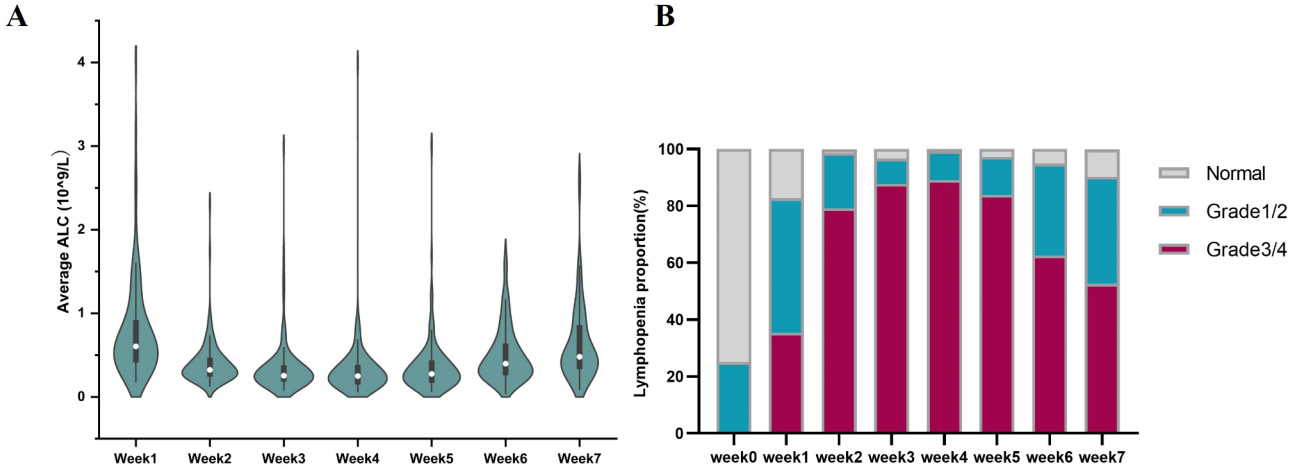

Fig. 2 Lymphocyte count and lymphopenia during RT. (**A**) The average absolute lymphocyte count (ALC) during RT, (**B**) the incidence of lymphopenia during RT

CR	Complete response
PR	Partial response
SD	Stable disease
PD	Progressive disease
prtPFS	Post-radiotherapy progression-free survival
prtOS	Post-radiotherapy overall survival
ALC	Absolute lymphocyte count

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13014-025-02632-9.

Supplementary Material 1

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Not applicable.

Author contributions
JMW concepted the study; Data collection was done by FWQ and DX; Data analysis was done by SXJ and SXY; SXJ drafted the manuscript; JMW revised the manuscript; All authors were involved in data visualization.

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Data availability
All data generated and analyzed during this study are available from the corresponding author on request.

Declarations

Ethical approval
This study was approved by the Ethics Committee of Xinhua Hospital (XHEC-D-2022-181).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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