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The Impact of Early Corticosteroid Pretreatment Before Initiation of Chemotherapy in Patients With Primary Central Nervous System Lymphoma

BACKGROUND: The optimal timing of corticosteroid (CS) treatment in patients with primary central nervous system (CNS) lymphoma (PCNSL) remains controversial. While poor clinical presentation may justify early treatment with CS, this may ultimately result in reduced concentrations of chemotherapeutic agents via perturbations in the permeability of the blood-brain barrier.

OBJECTIVE: To investigate whether early CS exposure is associated with beneficial outcomes and/or reduced occurrence of adverse events as opposed to delayed/concomitant administration.

METHODS: Herein we performed a retrospective observational analysis using patients that were prospectively entered into a database. All patients whom were admitted to the University Hospital between 2009 and 2015 with newly diagnosed PCNSL were included within our study.

RESULTS: Our cohort included 50 consecutive patients diagnosed with PCNSL; of these, in 30 patients CS administration was initiated prior to chemotherapy (early), whilst in the remaining 20 patients CS administration was initiated concomitantly with their chemotherapeutic regimen (concomitant). Within the early vs concomitant CS administration groups, no significant differences were observed with regard to progression-free survival (PFS) ($P = .81$), overall survival (OS) ($P = .75$), or remission ($P = .68$; odds ratio 0.76 and confidence interval [95%] 0.22-2.71). Critically, the timing of CS initiation was not associated with either PFS ($P = .81$) or PFS ($P = .75$).

CONCLUSION: Early CS administration was not associated with a deterioration in response to chemotherapy, PFS, or OS. As such, administration of CS prior to initiation of chemotherapy is both reasonable and safe for patients with newly diagnosed PCNSL.

KEY WORDS: Primary CNS lymphoma, Corticosteroids, Systemic therapy, Treatment response, Survival, Complete response

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Primary central nervous system (CNS) lymphoma (PCNSL) is a rare variant of extranodal non-Hodgkin lymphoma (NHL) that involves the brain, leptomeninges, eyes, and/or spinal cord, without additional evidence suggestive of systemic disease.[1] PCNSL accounts for approximately 3% of all newly diagnosed primary brain tumors and 3% of all cases of NHL.[2]

Historically, patients with PCNSL have been associated with a poorer prognosis compared to patients with aggressive systemic lymphomas.[3] However, recent data have come to suggest improvement in outcomes for patients with lymphoma.[4-7] While current clinical trials have focused primarily on the development and/or combination of chemotherapeutic agents,[8] little attention has been paid to the administration of corticosteroids (CS) in PCNSL.

ABBREVIATIONS: BBB, blood-brain barrier; **CI,** confidence interval; **CNS,** central nervous system; **CS,** corticosteroid; **CSF,** cerebrospinal fluid; **ECOG,** Eastern Cooperative Oncology Group; **HIV,** human immunodeficiency virus; **HR,** hazard ratio; **KPS,** Karnofsky performance scale; **NHL,** non-Hodgkin lymphoma; **OR,** odds ratio; **OS,** overall survival; **PCNSL,** primary central nervous system lymphoma; **PFS,** progression-free survival

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In contrast to the treatment paradigms employed for other intracranial lesions, wherein CSs are principally employed to reduce perilesional edema, CS employed in the treatment of PCNSL exhibit cytolytic effects on lymphoma cells.[9,10] Such findings are also reflected in a number of multicenter prospective trials that have incorporated CS administration into chemotherapeutic cycles.[11]

Of note, CSs have been shown to impact several critical properties of the blood-brain barrier (BBB), including tight junction integrity.[12] Consequently, CS administration not only influences brain hemostasis, but also the delivery/bioavailability of CNS-targeted therapeutics.[12] Despite such findings, the literature lacks focus on the impact of treatment with CS prior to the initiation of chemotherapy in PCNSL. As such, we herein assess the association of patient outcomes with the timing of the initiation of CS administration (ie, prior to chemotherapy vs concomitant with chemotherapy).

METHODS

Patients

All patients with newly-diagnosed, histologically-confirmed PCNSL who presented at the corresponding author's institution between January 2009 and December 2015 were prospectively entered into a curated institutional database as per approval of the institutional ethics committee (reference # 04/09 SNO 01/08). Patient follow-up was sustained via outpatient hematology/oncology and neurosurgery departments. For the purposes of this study, additional follow-up was performed via a standardized phone call. Beyond baseline demographics, the patients' Karnofsky performance scale (KPS) and Eastern Cooperative Oncology Group (ECOG) statuses were obtained at admission by an attending neurosurgeon. Moreover, histopathologic features, extra-CNS-manifestations, and the clinical course of each patient were recorded.

Within the indicated inclusion period, 62 patients were diagnosed with CNS lymphoma manifesting as an intracerebral lesion. We excluded patients with lymphoma manifestations outside of the CNS from our analysis (n = 8) and patients without documented CS treatment during their clinical course (n = 4). Fifty patients with newly diagnosed PCNSL remained, and were subsequently used to populate our retrospective cohort. All patients received dexamethasone as per the institutional standard. For the diagnostic procedure, stereotactic biopsy, written informed consent was obtained from the patient or the patient's legal representative. Clinical indications for or against perioperative CS treatment were determined by at least two experienced specialists in neurosurgery, based on clinical parameters and the expected clinical course of the patient.

Procedures

Attending neuropathologists participated in every stereotactic biopsy to confirm that tissue was obtained from the pathological lesion of interest. Stereotactic trajectories were planned and performed by the attending neurosurgeon. The surgeon accounted for tumor location, contrast enhancement, peritumoral edema, central necrosis, and patient history. Stereotactic planning was performed as has been published.[13] For all stereotactic biopsies, a stereotactic frame was utilized (Leksell Coordinate Frame G; Elekta Instruments, Stockholm, Sweden). The procedure was performed and/or supervised by 1 of 3 experienced neurosurgeons with clinical expertise in stereotactic procedures as previously described.[14] All tumor specimens were evaluated using classic hematoxylin/eosin staining, and selected specimens were investigated using immunohistochemistry. All specimens were examined by at least 2 board-certified neuropathologists and at least 2 board-certified pathologists at the local referral center at the Senckenberg Institute for Surgical Pathology.

The number of biopsies, trajectories, and all results from histopathological and molecular analyses were prospectively entered into the above-mentioned institutional database.

Outcomes

Data were collected in both primary neurosurgery and follow-up hematology/oncology centers (ie, where patients were transferred for management after their initial diagnosis of PCNSL). Obtained data were entered into the database by either the treating physician or study nurse. Outcome parameters were response, progression-free survival (PFS), and overall survival (OS). Progress was defined clinically or radiologically as per standard criteria.[15]

Statistical Analyses

We defined 2 cohorts for statistical analysis: patients with the first administration of CS prior to the initiation of chemotherapy patients were assigned to the early treatment group, whereas patients with the first administration of CS concomitant with their chemotherapeutic regimen were assigned to the concomitant treatment group.

The Mann–Whitney *U*-test was employed for nonparametric data. Binary parameters were analyzed using a χ^2-test and binary logistic regression was employed for multivariable analysis. Sex, age, KPS at admission, ECOG at admission, marker expression, immunocompetency status, cerebrospinal fluid (CSF) manifestations, other CNS manifestations, systemic therapy, biopsy-related parameters, time/onset of CS treatment, and histology were considered independent variables. Dependent variables were defined as treatment response, PFS, and OS for the analysis of outcomes. OS was defined as the time between stereotactic biopsy for the definitive diagnosis of lymphoma and the date of death; PFS was defined as the time between stereotactic biopsy for the definitive diagnosis of lymphoma and the date of clinical or radiological progression. For both OS and PFS, subjects were censored at the time of their last clinical follow-up appointment.

Groups were compared using a log rank test and pointwise 95% confidence intervals (CIs). A multivariable Cox's proportional hazards regression backward stepwise model (likelihood ratio) was performed to find independent predictors for outcome parameters.

Results with $P < .05$ were considered to be statistically significant. To rule out potential confounding factors in the univariate analysis, we performed multivariable analysis to determine independent risk factors and included parameters identified in univariate with a P value of $P < .1$.

All calculations/analyses were performed with SPSS (Version 22, IBM, Armonk, New York).

RESULTS

Of the 50 patients included within our study, CS were administered prior to chemotherapy in 30 patients (early), whilst the remaining 20 patients received CS concomitantly with their chemotherapeutic regimen (concomitant).

TABLE 1. Patient Characteristics

	Early corticosteroids (n = 30)	Concomitant corticosteroids (n = 20)	
Age (yr[IQR])	67.5 (53-78)	69 (60-74)	$P = .84$
Female sex (n[%])	12 (40%)	10 (50%)	$P = .49$
KPS (n[%])			$P = .56$
100-70	22 (73.4%)	17 (85%)	
60-50	4 (13.3%)	1 (5%)	
<50	4 (13.3%)	2 (10%)	
ECOG (n[%])			$P = .49$
0	9 (30.3%)	7 (35%)	
1	13 (45.5%)	8 (40%)	
2	1 (3.3%)	3 (15%)	
3	3 (10%)	1 (5%)	
4	4 (13.3%)	1 (5%)	
Preoperative CS (n[%])	3 (10%)	0 (0%)	$P = .15$
Immunosuppression (n[%])	5 (16.7%)	2 (10%)	$P = .69$
CNS manifestation (n[%])			$P = .9$
CSF	2 (46.7%)	1 (40%)	
Other	6 (13.3%)	3 (40.0%)	
Histology (n[%])			$P = .15$
Diffuse large B cell lymphoma	30 (100%)	18 (90%)	
T cell rich B cell lymphoma	0 (0%)	2 (10%)	
Ki67 (n[%])			$P = .7$
90%	6 (20%)	3 (15%)	
80%	7 (23.3%)	7 (35%)	
70%	1 (3.3%)	2 (10%)	
≤60%	16 (53.3%)	8 (40%)	
Systemic therapy (n[%])			$P = .32$
MTX/radiotherapy	4 (13.3%)	0 (0%)	
Rituximab/MTX/procarbazine	13 (43.3%)	12 (60%)	
Other	13 (43.3%)	8 (40%)	
Response (n[%])			$P = .77$
Complete response	14 (46.7%)	11 (55%)	
Partial response	4 (13.3%)	3 (15%)	
Failed response	12 (40%)	6 (30%)	

CNS, central nervous system; CS, corticosteroid medication; CSF, cerebrospinal fluid; ECOG, Eastern Cooperative Oncology Group score; IQR, indicates interquartile range; KPS, Karnofsky performance scale

Data are given as means except for age which is presented as the median. Data comparisons were made with Mann–Whitney *U*-test or χ^2-test, where applicable.

Baseline Characteristics

All patients included within our analyses underwent stereotactic biopsy for the diagnosis of lymphoma; none of the patients underwent microsurgical resection of their lesions. Further analysis of the administration of CS revealed that 3 patients within the early CS group (10%) received steroids prior to biopsy (Table 1). Five patients (16.7%) within the early CS group and 2 patients (10%) within the concomitant CS group were in an immunocompromised state at the time of diagnosis (eg, human immunodeficiency virus (HIV) infection). The majority of the patients were diagnosed with a diffuse large B-cell lymphoma in both the early CS (n = 30/100%) and concomitant CS (n = 18/90%) cohorts. Only 2 patients (10%) within the concomitant CS treatment group were diagnosed with a T-cell rich B-cell lymphoma. Further, the majority of patients within both early CS (n = 17/56.7%) and concomitant CS (n = 12/60%) were treated with high-dose methotrexate (HD-MTX)-containing regimens and included in clinical trials whenever possible. Median time from administration of CS to initiation of systemic chemotherapy was 9.1 d (SD 4.4 d, range 1-18 d) in the early CS group (**Figure**, **Supplemental Digital Content 1**).

No significant differences in baseline or clinical parameters were observed between either of the treatment groups (Table 1). Specifically, no significant differences in prebiopsy CS medication, the number of immunocompromised patients, CSF, other CNS manifestations, or systemic therapy were observed. No significant differences regarding histology (Ki67 as a molecular marker) were observed (Table 1). No significant differences were observed with regard to intraoperative parameters

TABLE 2. Univariate and Multivariate Analysis of Parameters Associated With Complete Response (Nagelkerke $R^2 = 0.242$)

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age > 68 yr	0.96 (0.27-3.36)	.95		
KPS < 90	0.38 (0.1-1.4)	.1		.72
ECOG < 1	0.08 (0.01-0.69)	.007	0.08 (0.01-0.69)	.022
Early CS	0.76 (0.22-2.71)	.68		
Immunosuppression	0.75 (0.09-5.9)	.79		
CSF manifestation	1.7 (0.14-20.4)	.67		
Other CNS manifestation	3.79 (0.38-37.3)	.23		
Intracerebral blood on CT	1.78 (0.29-11)	.53		
New postop deficit	0.81 (0.05-13.9)	.88		
T cell rich B cell lymphoma	0.52 (0.39-0.71	.19		
Ki 67 ≥ 80%	0.78 (0.16-3.67)	.75		
Rituximab/MTX/procarbazine	0.8 (0.1-6.3)	.82		

CNS, central nervous system; CI, confidence interval; CS, corticosteroid medication; CSF, cerebrospinal fluid; ECOG, Eastern Cooperative Oncology Group score; OR, odds ratio
OR is displayed in significant outcome parameters/where applicable.
Data comparisons were made with χ^2-test for univariate analysis and binary logistic regression with stepwise exclusion was used for multivariable analysis.

or perioperative complications (**Table**, **Supplemental Digital Content 2**).

Biopsy-related Characteristics

Altogether, 6 patients (12%) displayed an intraoperative effusion of blood via the sampling cannula despite thorough planning of the stereotactic procedure (**Table**, **Supplemental Digital Content 2**). In all of these patients, postoperative signs of blood were demonstrated on postoperative CT (k = 1, $P < .001$, and data not shown). Two patients, both of whom were among the early CS treated patients (4%), displayed postoperative neurological deficits. No significant differences were observed regarding the above-named biopsy-related parameters when comparing both groups.

Effect of CS Administration Timing on Response

In the early CS group, 14 patients (46.7%) achieved complete response, compared to 11 patients within the concomitant CS treatment group (55%). No significant differences in response were observed when analyzing the influence of CS medication before the initiation of chemotherapy for PCNSL ($P = .77$; Table 1).

Those patients who attained a complete response had a significantly better clinical status upon presentation, reflected by the significant association of a poor ECOG status with a lack of complete response (odds ratio [OR] 0.08, 95% CI, 0.01-0.69, $P = .007$, and univariate, Table 2). Moreover, a trend was observed suggesting that a poor KPS upon presentation is associated with lack of complete response (OR 0.38, 95% CI, 0.1-1.4, and $P = .1$).

Critically, no association with the timing of initiation of CS treatment with regard to a complete response was observed (OR 0.76, 95% CI, 0.22-2.71; $P = .68$, and univariate).

Furthermore, only ECOG status (OR 0.08, 95% CI, 0.01-0.69, and $P = .022$) was confirmed as an independent parameter associated with complete response via multivariable analysis (Nagelkerke $R^2 = 0.242$). KPS status ($P = .72$) was not associated with the achievement of complete response.

Effect of CS Timing on PFS

No significant difference was observed in the PFS between the early and concomitant CS groups (Figure 1A). Progression did not occur earlier in the early CS group, with a median time of 348 d (95% CI, 75-620 d) in the early group and a median time of 553 d (95% CI, 256-850 d) in the concomitant group ($P = .81$; test for proportional hazard assumption $P = .46$). Multivariable analysis identified the postoperative detection of blood as an independent parameter associated with early progression (hazard ratio (HR) 3.5; 95% CI, 1.22-10; $P = .04$; Table 3, including univariable analysis).

Effect of CS Timing on OS

No significant differences in OS between the early and concomitant CS groups were observed (Figure 1B). OS was not significantly decreased in the early CS group, with a median of 573 d in the early group and a median of 1885 d in the concomitant CS group (95% CI, 1524-2246 d, $P = .75$; test for proportional hazard assumption $P = .3$). Multivariable analysis demonstrated that the occurrence of a newly developed postoperative deficit (HR 10.84; 95% CI, 2.24-52.5; $P = .02$) was

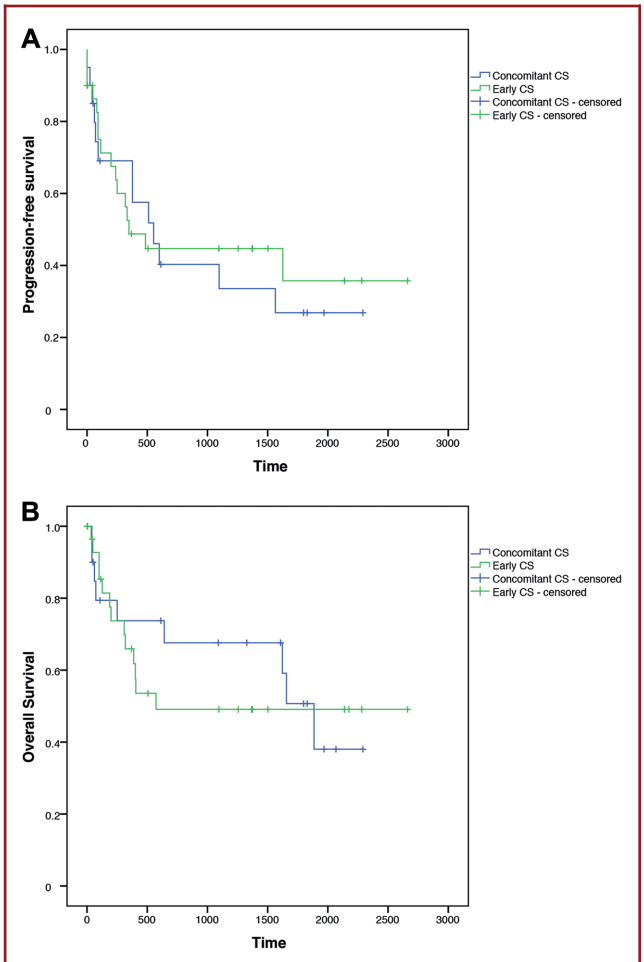

FIGURE 1. *Kaplan–Meier estimates.* **A**, *Progression-free survival (logrank test* $\chi^2 = 0.058$, $P = .81$*).* **B**, *Overall survival (logrank test* $\chi^2 = 0.102$, $P = .75$*).*

an independent factor associated with reduced OS (Table 4, including univariable analysis).

DISCUSSION

PCNSL accounts for 3% of all systemic lymphomas and for 3% of all primary brain tumors.[16] Of note, PCNSL mainly affects elderly patients,[16] and the optimal therapeutic regimen for PCNSL continues to be a matter of clinical debate.

Unfortunately, while standalone whole-brain irradiation results in complete remission in 50% of patients with PCNSL, more than 90% of these patients go on to develop a recurrent tumor.[17] Therefore, standalone radiation therapy is not an ideal first treatment in those patients diagnosed with PCNSL.[18] Meanwhile, several studies have demonstrated the value of combinational chemotherapeutic approaches with regard to PCNSL. For example, studies that combined HD-MTX with other chemotherapeutic agents demonstrated a higher response rate and a prolonged PFS compared to those studies that employed HD-MTX monotherapy.[11,19-22] Due to the poor prognosis of PCNSL patients as compared to patients with aggressive systematic lymphomas, an expanded chemotherapeutic regimen has been evaluated.[6,7] While the results are encouraging, the experience with high-dose chemotherapy supported by autologous stem cell transplantation is still limited to phase II trials.[23]

While these highly sophisticated therapeutic regimens have been a matter of intense study, there has been little attention towards evaluating the administration of CS. Interestingly, CS have demonstrated a highly cytolytic action on lymphoma cells in vitro.[24] The mechanism involves DNA fragmentation and the induction of apoptosis in a p53-independent fashion,[25-28] as has been extensively reviewed.[29] Beyond the induction of apoptosis, other studies have come to suggest an induction of autophagy after treatment with CS.[30,31] In line with the aforementioned, PCNSL patients display a highly-responsive clinical course upon administration of CS. Initial treatment with CS may produce rapid symptomatic improvement, coupled with a dramatic radiographic response in approximately 40% of patients[22,32]; such cytolytic activity may result in changes to tissue pathology, altering that which may be detected by a pathologist.[33] As such, it is critical to refrain from CS administration in suspected PCNSL cases until a diagnostic biopsy has been performed.[34-36]

However, controversial recommendations regarding the administration of postdiagnostic CS in PCNSL continue to exist. Due to the cytotoxic and antiedematous effects described in detail above, CS are commonly used in the treatment of lymphomatous lesions within the CNS, and included in almost all chemotherapy protocols for lymphoid malignancies.[11,29] It is prudent to note that the administration of CS may also impact the delivery of other chemotherapeutic agents, as steroids have been shown to impact several critical properties related to the permeability of the BBB, such as tight junction integrity. Consequently, administration of CS not only influences brain hemostasis, but also the delivery/bioavailability of CNS-targeted therapeutics.[12]

In an experimental model of glioma, CS treatment resulted in diminished delivery of the chemotherapeutic agent MTX (ie, the most commonly-used agent in PCNSL regimens) to both the tumor and brain.[37] Hence, CS administration may in fact impact the administration of other agents via perturbations in BBB permeability when used as a systemic treatment in PCNSL. Therefore, we sought to analyze our cohort of patients with PCNSL for outcomes related to the timing of CS administration in their clinical course.

In our cohort, the majority of patients (n = 30) received CS prior to further chemotherapy for the treatment of their PCNSL. Clinical indications related to the administration of CS were apparently not based upon the clinical status at presentation, as no significant differences were observed with regard to KPS and ECOG between early and concomitant groups. Both treatment groups included patients with a state of

TABLE 3. Univariate and Multivariate Analysis of Parameters Associated With Progression-Free Survival

	Univariate analysis		Multivariate analysis	
	Median (95% CI)	*P* value	HR (95% CI)	*P* value
Age		.42		
Age > 68 yr	377 (133-621)			
Age < 68 yr	1564 (0-3685)			
KPS		.96		
KPS < 90	377 (0-1865)			
KPS ≥ 90	511 (227-795)			
ECOG		.71		
ECOG < 1	333 (0-684)			
ECOG ≥ 1	511 (209-813)			
CS administration		.81		
Early	348 (75-620)			
Concomitant	553 (256-850)			
Immunosuppression		.67		
Present	511 (226-796)			
Absent	1546 (0-3211)			
CSF manifestation		.11		
Present	–			
Absent	–			
Other CNS manifestation		.29		
Present	1097 (-)			
Absent	377 (149-605)			
Intracerebral blood on CT		.004	3.5 (1.22-10.0)	.04
Present	81 (58-104)			
Absent	553 (0-1390)			
New postop deficit		.005		.08
Present	0 (-)			
Absent	511 (260-762)			
Histology		.19		
T cell rich BCL	511 (213-808)			
Diffuse large cell BCL	70 (-)			
Ki 67		.19		
≥80%	377 (132-622)			
<80%	–			
Adjuvant therapy		.6		
Rituximab/MTX/procarbazine	511 (203-819)			
Other	348 (-)			

CI, confidence interval CNS, central nervous system; CS, corticosteroid medication; CSF, cerebrospinal fluid; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group score; HR, hazard ratio; KPS, Karnofsky performance scale

Data comparisons were made with Kaplan–Meier estimates for univariate analysis. Column median indicates median of parameter displayed. No median was calculated for "CSF manifestation" as all cases were censored. Cox-regression analysis with stepwise exclusion was used for multivariable analysis.

immunosuppression resulting from HIV or posttransplant lymphoproliferative disease. The relatively high number of patients with immunosuppression due to HIV infection may be attributed with the authors' institution, a primary center for HIV/infectious diseases in Germany.[38] Other clinical and pathological parameters such as distribution of sex, age, and histopathologic diagnosis are in line with those reported within the literature.[39]

When looking at complete response, no significant differences were observed between those patients who received early CS and those patients who received concomitant CS. Of the analyzed factors, only ECOG was associated with complete response in multivariable analysis. This finding is partly in line with the literature, where the performance status has been shown to be associated with survival.[19,20,40] However, age was not among the prognosticators associated with complete response in our population. This might be attributed to the combined analysis of immunocompromised and immunocompetent patients, who are significantly younger upon development of PCNSL.

TABLE 4. Univariate and Multivariate Analysis of Parameters Associated With Overall Survival

	Univariate analysis		Multivariate analysis	
	Median (95% CI)	*P* value	HR (95% CI)	*P* value
Age		.33		
Age > 68 yr	641 (0-1633)			
Age < 68 yr	1885 (-)			
KPS		.44		
KPS < 90	1856 (-)			
KPS ≥ 90	1801 (334-2909)			
ECOG		.82		
ECOG < 1	1881 (-)			
ECOG ≥ 1	1843 (234-3077)			
CS administration		.75		
Early	573 (-)			
Concomitant	1885 (1524-2246)			
Immunosuppression		.7		
Present	1885 (-)			
Absent	1656 (0-3345)			
CSF manifestation		.17		
Present	–			
Absent	–			
Other CNS manifestation		.19		
Present	–			
Absent	1622 (232-3012)			
Intracerebral blood on CT		.09		.13
Present	199 (0-405)			
Absent	1885 (1432-2338)			
New postop deficit		< .001	10.84 (2.24-52.5)	.02
Present	34 (-)			
Absent	1885 (325-3445)			
Histology		.22		
T cell rich BCL	–			
Diffuse large cell BCL	–			
Ki 67		.293		
≥80%	1622 (60-3184)			
<80%	–			
Systemic therapy		.98		
Rituximab/MTX/procarbazine	1885 (1428-2342)			
Other	401 (-)			

CI, confidence interval; CNS, central nervous system; CS, corticosteroid medication; CSF, cerebrospinal fluid; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group score; HR, hazard ratio; KPS, Karnofsky performance scale

Data comparisons were made with Kaplan–Meier estimates for univariate analysis. Column median indicates median of parameter displayed. No median was calculated for "Other CNS manifestation and CSF manifestation" as all cases were censored. Cox-regression analysis with stepwise exclusion was used for multivariable analysis.

The early administration of CS was not associated with a change in PFS or OS in our analysis. The detection of intracerebral blood on a postoperative CT scan, as an indicator for an intraoperative injury to intracerebral/intratumoral vessels, was the only parameter associated with PFS in our analysis. Moreover, the development of a new postoperative deficit was the only parameter in our analysis associated with OS. Both findings speak to the importance of thorough planning and careful execution of surgical biopsies, thereby avoiding the development of complications/deficits. As observed within the literature, other parameters such as meningeal dissemination were not associated with survival.[41]

While in general, treatment for PCNSL is carried out in oncology/neurooncology departments, the diagnosis of PCNSL is acquired with a neurosurgical biopsy. According to the data presented within this study, patients may be treated with CS postbiopsy as clinically warranted. However, future studies further assessing potential interactions of tumor cells with the immune system may be impeded by early CS administration prior to the initiation of chemotherapy for PCNSL.

Limitations

While this is the first series focused on the timing of CS administration in patients with PCNSL postbiopsy, it is nonetheless important to note that the study has several limitations. One limitation is the retrospective nature of the study and the lack of randomization with regard to early and concomitant CS groups. Furthermore, there are no standard clinical indications for initiation of CS in the early group, thereby introducing the possibility of selection bias. Finally, while the major strength of this study is the considerably large patient population relative to the limited incidence/prevalence of this neoplasm, the sample size of 50 patients may limit the power of our analyses.

CONCLUSION

To our knowledge, this is the first study focused on the timing of CS administration after biopsy derived sample acquisition in patients with PCNSL. Our data indicate that the early administration of CS in PCNSL is not associated with changes in achieving complete response, PFS, and/or OS. While our data substantiate the results and conclusions drawn from previous studies, discounting differentiation between early and concomitant administration of CS, future clinical trials investigating the induction of cell death and ultimately outcomes in PCNSL should take the onset of CS medication into account due to its broad clinical and biological implications.

Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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Supplemental Digital Content 1. Figure. Distribution of patients undergoing early CS administration. Early CS administration was defined as initiation prior to systemic therapy, concomitant CS administration was defined as initiation of CS concomitant with systemic therapy. In total, 30 patients underwent early CS treatment and 20 patients underwent concomitant CS treatment.

Supplemental Digital Content 2. Table. Surgical procedure-related characteristics. Data are given as means except for no. of samples that is presented as the median. Data comparisons were made with Mann–Whitney *U*-test or $\chi 2$-test, where applicable. OR is displayed in significant outcome parameters and where applicable. CT, computed tomography; CS, corticosteroid medication; IQR indicates Interquartile range.