Role of cyclophosphamide, doxorubicin, vincristine, and prednisolone regimen in patients of primary central nervous system lymphoma: Is it justifiable?

Sir,

I read with great interest the research article "survival and failure outcomes in primary central nervous system lymphoma (PCNSL) with whole brain radiation therapy (WBRT) followed by cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) chemotherapy: An alternative treatment approach in community settings in low resource countries" published in the July-August issue of your esteemed journal. The authors have concluded that though the standard of care in the management of PCNSL is high-dose methotrexate (HD-MTX) based chemotherapy; considering poor compliance and tolerability to treatment in low resource countries in routine clinical setting, WBRT, followed by systemic chemotherapy with standard CHOP regimen for treatment of PCNSL demonstrates reasonably good outcome. This study opens up the opportunities to conduct further larger randomized controlled studies in the poor resource settings to compare the standard treatment versus CHOP after WBRT.

However, there are some important issues which could have been addressed in this study. There was listing of various prognostic factors such as age, performance status (PS), location of the tumor and extent of the surgery, but there was no use of risk stratification strategy. international extranodal lymphoma study group has recommended the use of a combination of five independent predictors of response and survival, that is, age, PS, serum lactate dehydrogenase level, cerebro-spinal fluid protein concentration, and the involvement of deep structures, to distinguish three risk groups based on the presence of 0-1, 2-3, or 4-5 unfavorable features.[1] The table of patient characteristics shows that a patient of age as young as 30 years and five patients of Kernofsky performance score as good as 80 were included in the study. These patients, in the absence of other unfavorable features, could have been benefitted more with the use of standard of care HD-MTX based regimens. Even, Ferreri *et al*. have recommended the use of combination of HD-MTX and HD-cytarabine in patients of age <75 years with acceptable toxicity.[2] They obtained a complete remission rate of 18% (95% confidence interval [CI]: 6-30) in HD-MTX alone versus 46% (95% CI: 31-61) in the combination arm, (P = 0.006).

CHOP regimen exhibits negligible activity in PCNSL; this has been confirmed in a randomized trial with incomplete accrual.[3] In a retrospective series, the addition of CHOP to HD-MTX resulted in higher toxicity without improving outcome compared with HD-MTX alone.[4] Most patients treated with CHOP have an immediate radiographic response, followed by early progression, probably because of the normalization of the disrupted blood brain barrier (BBB). This suggests that the bulky tumor not protected by the BBB responds while the microscopic tumor is not adequately treated and progresses. In line with this evidence, CHOP chemotherapy has been abandoned in classic PCNSL. However, CHOP-rituximab combination may be prescribed with good CNS bioavailability agents to patients with neurolymphomatosis[5] or intravascular large B-cell lymphoma with CNS involvement as tumor cells of these lymphomas mostly grow in structures (nerves and blood vessels, respectively) variably, or not, protected by physiologic barriers.

To conclude, the possible use of standard CHOP regimen in the patients of PCNSL can be decided on the basis of prognostic scoring and the site of the disease. However, this needs to be confirmed by well-designed randomized prospective studies. The patients with good prognostic factors should be offered the standard of care HD-MTX based chemotherapy, unless otherwise indicated.

ACKNOWLEDGMENTS

The authors would like to thank consultants in department of Oncology Dr. Ajay Sharma, Dr. N. Sharma, Dr. S. L. Jakhar and Dr. S. Beniwal.

Akhil Kapoor, Prakash Singh Rajput[1], Satya Narayan, Harvindra Singh Kumar

Department of Radiation Oncology, Acharya Tulsi Regional Cancer Treatment and Research Institute, [1]Department of Pathology, Sardar Patel Medical College and Associated Group of Hospitals, Bikaner, Rajasthan, India

Correspondence to: Dr. Akhil Kapoor,
Room No. 73, PG Boys Hostel, PBM Hospital Campus,
Bikaner - 334 003, Rajasthan, India.
E-mail: kapoorakhil1987@gmail.com

REFERENCES

1. Ferreri AJ, Blay JY, Reni M, Pasini F, Spina M, Ambrosetti A, *et al.* Prognostic scoring system for primary CNS lymphomas: The international extranodal lymphoma study group experience. J Clin Oncol 2003;21:266-72.
2. Ferreri AJ, Reni M, Foppoli M, Martelli M, Pangalis GA, Frezzato M, *et al.* High-dose cytarabine plus high-dose methotrexate versus high-dose methotrexate alone in patients with primary CNS lymphoma: A randomised phase 2 trial. Lancet 2009;374:1512-20.
3. Mead GM, Bleehen NM, Gregor A, Bullimore J, Shirley D, Rampling RP, *et al.* A medical research council randomized trial in patients with primary cerebral non-Hodgkin lymphoma: Cerebral radiotherapy with and without cyclophosphamide, doxorubicin, vincristine, and prednisone chemotherapy. Cancer 2000;89:1359-70.
4. Glass J, Shustik C, Hochberg FH, Cher L, Gruber ML. Therapy of primary central nervous system lymphoma with pre-irradiation methotrexate, cyclophosphamide, doxorubicin, vincristine, and dexamethasone (MCHOD). J Neurooncol 1996;30:257-65.
5. Grisariu S, Avni B, Batchelor TT, van den Bent MJ, Bokstein F, Schiff D, *et al.* Neurolymphomatosis: An international primary CNS lymphoma collaborative group report. Blood 2010;115:5005-11.

Access this article online	
Quick Response Code:	Website: www.ccij-online.org
	DOI: 10.4103/2278-0513.142714