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Reply to Letter to the Editor

Prognostic factors in leptomeningeal metastases

We appreciate the interest of our colleagues Dankner and Maritan in our efforts to delineate prognostic disease patterns in leptomeningeal metastasis. In their communication, they specifically address the role of prior surgery for brain metastasis in this patient population. The authors perceive a discrepancy between our findings and those of previous studies. These previous studies had reported that patients, who had surgery for brain metastases and developed leptomeningeal metastases thereafter, fared better if they had nodular disease rather than linear disease.

However, what we report is that only in the absence of tumor cells in the cerebrospinal fluid (CSF), nodular disease is an indicator of inferior outcome, which likely corresponds to tumor burden driving the disease course. The previous studies[1,2] report on imaging defined leptomeningeal metastases and did not distinguish patients with or without positive CSF cytology.

In our cohort, a history of brain metastases prior to the diagnosis of leptomeningeal metastases was noted in 32 type II patients (defined as patients without positive CSF cytology), of whom only 11 had surgery which was combined with radiotherapy in all cases: stereotactic radiosurgery (SRS) in 5, whole brain radiotherapy (WBRT) in 5, and SRS plus WBRT in 1 patient).

We understand the interest in the history of prior surgery, but to analyze these data would have been beyond the scope of our study, especially considering the small number of patients in this subgroup. Further, MRI was not centrally collected and re-reviewed, further, data on the location and distance of leptomeningeal nodules to the site of surgically approached brain metastases and the extent of resection, and surgical technique used, including potential opening of the ventricle during surgery, were not collected.

Accordingly, we fully agree with the authors that further efforts at better defining risk profiles for the development of leptomeningeal metastases are needed, but we also would like to caution against underestimating the complexity of such studies, notably in a multicenter retrospective design. Heterogeneity of patients and tumors included in such studies also need to be considered. Accordingly, ideally, well-planned prospective cohort studies could try to resolve some of the important issues raised by our colleagues.

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