Modern approaches to the management of brain metastases: embracing a multi-modal paradigm

Balamurugan Vellayappan[1], Jonathan P. S. Knisely[2], Simon S. Lo[3], Kevin Shiue[4]

[1]Department of Radiation Oncology, National University Cancer Institute Singapore, National University Hospital, Singapore, Singapore; [2]Stich Radiation Oncology, Weill Cornell Medical College, New-York-Presbyterian Hospital, New York, NY, USA; [3]Department of Radiation Oncology, University of Washington School of Medicine, Seattle, WA, USA; [4]Department of Radiation Oncology, Indiana University School of Medicine, Indianapolis, IN, USA

Correspondence to: Balamurugan Vellayappan. Department of Radiation Oncology, National University Cancer Institute Singapore, National University Hospital, Singapore, Singapore. Email: bala_vellayappan@nuhs.edu.sg.

Submitted Apr 18, 2022. Accepted for publication Apr 28, 2022.
doi: 10.21037/cco-2022-1
View this article at: https://dx.doi.org/10.21037/cco-2022-1

Brain metastases (BM) continue to be a dreaded complication of malignancy, affecting 20% of cancer patients (1). Symptomatic BM can have profound impact on the physical and functional state of patients and their caregivers. Primary cancers such as melanoma, breast, and lung cancer have the highest frequencies of BM (2). The management of BM has evolved from a largely fatalistic approach, where corticosteroids and whole-brain radiotherapy provided temporary palliation, to a more locally curative approach with surgical resection and stereotactic radiosurgery providing durable intra-cranial control. We can confidently say that we have arrived at the next paradigm—underscored by advancements in molecular diagnostics (such as next-generation sequencing) where driver mutations can be identified and selectively targeted using systemic therapeutics. Research and development into this field has led to highly specific drug molecules with good intra-cranial activity and, in some cases, offering the patient the convenience of continuous oral administration. Moreover, "maintenance therapy" may prolong the time to distant intracranial recurrences. This contrasts with focal therapy with SRS, where multiple salvage treatments may be required to achieve the same outcome.

Nevertheless, we believe there is a role for all the above modalities in the management of BM. The dilemma is to choose the appropriate tool, or tools, for the specific situation. The over-arching goal remains to achieve intracranial control (both locally and distantly), with minimal toxicities (including patient convenience and financial toxicity). All subspecialities may experience cognitive bias, as was elegantly put by Abraham Maslow in 1966—"if the only tool you have is a hammer, to treat everything as if it were a nail". As such, a major collaborative multidisciplinary effort between neurosurgeons, neuro-radiation oncologist and neuro-medical oncologists is needed to push the boundaries to achieve meaningful survival for our patients with BM.

In this special issue, we have assembled key topics in the management of BM, which will certainly help practicing oncologists decide on appropriate tools. Abdulhaleem *et al.* expound on the various models available to prognosticate the outcomes of patients with BM, based on nomograms and BM velocity. Diao *et al.* and Ye *et al.* discuss the complications associated with cranial radiation and proven mitigation strategies, respectively.

Unique situations of BM are discussed in the following articles. Giantini-Larsen *et al.* review the optimal management of 5–15 BM, Thomsen *et al.* discuss the management of large untreated BM (i.e., >2 cm diameter), and Lee *et al.* review the management of brain stem metastases.

A primary cancer specific approach to BM is warranted, given that driver mutations and targeted therapies are specific. Saleem *et al.* explore the management of BM from melanoma, Hau *et al.* discuss the BM from small cell lung cancer, and lastly Le *et al.* summarize the management of BM from germ cell tumors.

In summary, as technology advances and our understanding of the biology of BM evolves, radiation treatment (be it focal or comprehensive) will continue to

adapt and complement systemic therapies and immune checkpoint inhibitors.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Chinese Clinical Oncology*, for the series "The Modern Approaches to the Management of Brain Metastases". The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cco.amegroups.com/article/view/10.21037/cco-2022-1/coif). The series "The Modern Approaches to the Management of Brain Metastases" was commissioned by the editorial office without any funding or sponsorship. SSL served as the unpaid Guest Editor of the series and served as an unpaid editorial board member of *Chinese Clinical Oncology* from May 2021 to April 2023. BV, JPSK and KS served as the unpaid Guest Editors of the series. The authors have no other 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.

References

1. Achrol AS, Rennert RC, Anders C, et al. Brain metastases. Nat Rev Dis Primers 2019;5:5.
2. Cagney DN, Martin AM, Catalano PJ, et al. Incidence and prognosis of patients with brain metastases at diagnosis of systemic malignancy: a population-based study. Neuro Oncol 2017;19:1511-21.

Cite this article as: Vellayappan B, Knisely JPS, Lo SS, Shiue K. Modern approaches to the management of brain metastases: embracing a multi-modal paradigm. Chin Clin Oncol 2022;11(2):9. doi: 10.21037/cco-2022-1