Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines for the Treatment of Adults With Metastatic Brain Tumors: Executive Summary

BACKGROUND: The Congress of Neurological Surgeons systematic review and evidence-based clinical practice parameter guidelines for the treatment of adults with metastatic brain tumors was first published in 2010. Because of the time elapsed since that publication, an update of this set of guidelines based on literature published since is now indicated.

OBJECTIVE: To establish the best evidence-based management of metastatic brain tumors over all commonly used diagnostic and treatment modalities in regularly encountered clinical situations.

METHODS: Literature searches regarding management of metastatic brain tumors with whole brain radiation therapy, surgery, stereotactic radiosurgery, chemotherapy, prophylactic anticonvulsants, steroids, instances of multiple brain metastases, and emerging and investigational therapies were carried out to answer questions designed by consensus of a multidisciplinary writing group.

RESULTS: Recommendations were created and their strength linked to the quality of the literature data available thus creating an evidence-based guideline. Importantly, shortcomings and biases to the literature data are brought out so as to provide guidance for future investigation and improvements in the management of patients with metastatic brain tumors.

CONCLUSION: This series of guidelines was constructed to assess the most current and clinically relevant evidence for management of metastatic brain tumors. They set a benchmark regarding the current evidence base for this management while also highlighting important key areas for future basic and clinical research, particularly on those topics for which no recommendations could be formulated.

The full guideline can be found at: https://www.cns.org/guidelines-treatment-adults-metastatic-brain-tumors/chapter_1.

KEY WORDS: Chemotherapy, Guidelines, Metastatic brain tumor, Radiation therapy, Stereotactic radiosurgery, Surgery

In 2010 guidelines on the management of metastatic brain tumors were published and endorsed by the American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS). At that time plans for an update to these guidelines were made and this set of documents represents that revision. Guidelines for management of this entity are of value as it occurs commonly in the cancer patient community. Based on an official census of nearly 310 million people in the United States, the expected incidence of newly diagnosed patients with brain metastases is estimated to be between 21,651 and 43,301 per year.

These guidelines include sections similar to those previously published, including topics such as whole brain radiation therapy, surgery, stereotactic radiosurgery, chemotherapy, prophylactic anticonvulsants, steroids, and instances of multiple brain metastases.
as surgery, radiation, and chemotherapy. The methods and style used here are adapted from and similar to other guidelines projects endorsed by the AANS and CNS. Each section was developed with recognition of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist items. By way of definition, this systematic review and subsequent set of guidelines defines brain metastases as solid metastases to the brain from systemic cancer. The definition excludes leptomeningeal metastatic disease.

METHODS

The objectives of these guidelines are to establish the best evidence-based management of metastatic brain tumors in terms of whole brain radiation therapy, surgery, stereotactic radiosurgery, chemotherapy, prophylactic anticonvulsants, steroids, and instances of multiple brain metastases. Because management of these tumors remains imperfect, it was also recommended that information on promising emerging therapies be assessed in the same manner to determine the possible application of these findings. Authors with expertise in the management of metastatic brain tumors were recruited for this writing. They assessed the question from the previously published guidelines, modified them if deemed appropriate, and added questions to allow for assessment of new literature if they determined that to be necessary.

A wide-ranging literature search strategy was undertaken to identify all citations relevant to the management of metastatic brain tumors. The MEDLINE (utilizing the PubMed or Ovid interface) and Embase® electronic databases were searched with additional data being gleaned from the Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials. The date range was from October 2008 through December 2015 for questions that were unchanged from the guidelines published in 2010. For new questions or questions modified significantly from the 2010 publication, the date range for the searches was chosen to be January 1990 through December 2015. The eligibility (inclusion/exclusion) criteria to screen the citations for each of the questions were determined ahead of time for each section by the respective writing group.

RESULTS

Studies that met the eligibility criteria were subject to more detailed scrutiny. Their data were extracted by one reviewer and the extracted information was checked by one or more other reviewers. Evidence tables, reporting the extracted study information and evidence classification, were generated for all of the included studies. The evidence classifications for each manuscript chosen as informative for these guidelines were then used to create recommendations. The strength of the recommendations was graded according to the AANS/CNS guideline development methodology. Detailed information on this is available at https://www.cns.org/guidelines/guideline-procedures-policies/guideline-development-methodology. Thus, the class of evidence assigned to each study was based on study design (ie, class I, II, or III). The strength of the recommendations made (ie, level 1, 2, or 3) was directly linked to the evidence classification and took into account aspects of study quality and whether or not the plan was accomplished, not just study design.

Of note, one topic from the previous set of guidelines, retreatment of brain metastases, was not included as the authors deemed there was no new meaningful data beyond anecdote and case series. Additionally, this topic had yielded only on level 3 recommendation in the original set of guidelines. The authorship also pursued the possibility of writing a section on the management of radiation necrosis. After review of selected manuscripts from 1253 citations that resulted from the search, it became clear that there was no uniform definition of radiation necrosis for this disease type and data could only be gleaned from case series of patients treated with a wide variety of tumor types and treatment paradigms. Thus, this topic section was abandoned for the purposes of this set of guidelines.

Upon completion of all sections, there were 19 questions considered overall yielding 9 level 1 recommendations, 6 level 2 recommendations, 23 level 3 recommendation, and 9 instances in which data were deemed insufficient to make a recommendation. The completed evidence-based clinical practice guidelines for the management of metastatic brain tumors were then presented to the Joint Guidelines Review Committee of the AANS/CNS for peer review and revision prior to submission for publication.

DISCUSSION

This series of guidelines was constructed to assess the clinically relevant evidence for the management of metastatic brain tumors through 2015 in order to set benchmarks regarding the quality of knowledge on this topic while also highlighting important key areas for future research. Only by designing future investigations in a high-quality manner that recognizes and overcomes prior weaknesses noted in these guidelines will advancement toward a remedy for this disease be achieved. The recommendations provided are set forth for conscientious use by the practicing physician who must take into account all of the unique individual conditions in the therapy of a given person during his or her illness. The recommendations are not meant to resolve every issue or controversy in the management of this disease. Planned updates for this set of guidelines will be provided in approximately 5 years with additional updates dependent upon emergence of important scientific and therapeutic advances.

Disclosures

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Potential Conflicts of Interest

The Brain Metastases Guideline Update Task Force members were required to report all possible conflicts of interest (COIs) prior to beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Review Committee, including potential COIs that are unrelated to
the topic of the guideline. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination. The CNS Guidelines Committee and Guideline Task Force Chair are given latitude to approve nominations of task force members with possible conflicts and address this by restricting the writing and reviewing privileges of that person to topics unrelated to the possible COIs. The authors of this paper have the following relationships to disclose: Dr Olson-American Cancer Society, Takeda, Arbor Pharmaceuticals; Dr Ryken-Medtronic Inc, Arbor Pharmaceuticals LLC, K2M Spine Inc. The COI findings are provided in detail in the companion introduction and methods manuscript (https://www.cns.org/guidelines-treatment-adults-metastatic-brain-tumors/chapter_1).

Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a multidisciplinary physician volunteer task force and serves as an educational tool designed to provide an accurate review of the subject matter covered. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a competent physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

REFERENCES


Neurosurgery Speaks! Audio abstracts available for this article at www.neurosurgery-online.com.

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