Disputes & Debates: Editors' Choice

Steven Galetta, MD, FAAN, Section Editor

Editors' note: Pilocytic astrocytoma with anaplasia arising from the optic chiasm in a very elderly patient

In reference to the NeuroImage "Pilocytic astrocytoma with anaplasia arising from the optic chiasm in a very elderly patient," Dr. Wasilewski comments that there are few studies and no standard of care guidelines in the treatment of pilocytic astrocytoma in adults. However, bevacizumab, a monoclonal antibody against vascular endothelial growth factor, has shown to be beneficial in case series. Author Hayashi reports on the course of their patient in the NeuroImage, who received radiation and oral temozolomide. He agrees that bevacizumab may be useful in patients with anaplastic pilocytic astrocytoma and microvascular proliferation.

Megan Alcauskas, MD, and Steven Galetta, MD
Neurology® 2018;90:1037. doi:10.1212/WNL.0000000000005594

Reader response: Pilocytic astrocytoma with anaplasia arising from the optic chiasm in a very elderly patient

Andrea Wasilewski (Rochester)
Neurology® 2018;90:1037. doi:10.1212/WNL.0000000000005596

As alluded to by the authors of this NeuroImage,[1] few studies have investigated pilocytic astrocytoma (PA) in adults, given the rarity of these tumors. One study suggested anaplastic PAs have a more aggressive clinical course when compared to juvenile PA with a higher incidence of tumor recurrence (from 30% to 42%) and progression.[2] Specifically, PA with anaplastic features are more aggressive and associated with decreased survival when compared with typical PA.[3] No standard of care exists for treatment of PA, especially in the elderly. Anti-angiogenic treatment, such as bevacizumab (a humanized monoclonal antibody directed against vascular endothelial growth factor), should be considered in patients with recurrent or unresectable PA. The highly vascular nature of these tumors suggests they may be uniquely responsive to bevacizumab and may have a similar response as seen in glioblastoma, including decreased permeability of vasculature and decreased perilesional edema.[4] Case series demonstrated clinical and radiographic improvement as well as disease control with the use of bevacizumab.[5]

1. Hayashi S, Akao N, Nakazato Y, Okamoto K. Pilocytic astrocytoma with anaplasia arising from the optic chiasm in a very elderly patient. Neurology 2017;89:1840.
2. Ellis JA, Waziri A, Balmaceda C, et al. Rapid recurrence and malignant transformation of pilocytic astrocytoma in adult patients. J Neurooncol 2009;95:377–382.
3. Rodriguez F, Scheithauer BW, Burger PC, Jenkins S, Giannini C. Anaplasia in pilocytic astrocytoma predicts aggressive behavior. Am J Surg Pathol 2010;34:147–160.
4. Gilbert MR, Dignam JJ, Armstrong TS, et al. A randomized trial of bevacizumab for newly diagnosed glioblastoma. N Engl J Med 2014;370:699–708.
5. Green R, Woyshner E, Quan J, Pope W, Cloughesy T. Treatment of unresectable adult pilocytic astrocytoma with bevacizumab with or without temozolomide (P01.097). Neurology 2013;80:P01.097.

Author disclosures are available upon request (journal@neurology.org).

Author response: Pilocytic astrocytoma with anaplasia arising from the optic chiasm in a very elderly patient

Shintaro Hayashi (Sawatari, Japan)

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I thank Dr. Wasilewski for the valuable comments on our NeuroImage.[1] Our patient received irradiation (57.6 Gy/32 fractions) and oral temozolomide (100 mg for 5 d/mo for 14 months); however, the tumor gradually extended to the hypothalamus and he was transferred to another hospital for terminal care. We agree with Dr. Wasilewski's comment that alternative regimens for adult patients with anaplastic pilocytic astrocytoma (APA), especially showing recurrent or aggressive nature, are to be explored and established, and antiangiogenic treatment is one of the powerful tools. In our view, alternative treatments, such as bevacizumab, might be justified only when patients with APA show microvascular proliferations, as observed in our patient.[1] We are not fully confident whether tests for BRAF V600E mutant proteins are mandatory, because the gene mutations are found in 6%–8% of extracerebellar pilocytic astrocytomas,[2] as well as in other disorders (e.g., pleomorphic xanthoastrocytoma or ganglioglioma).[3]

1. Hayashi S, Akao N, Nakazato Y, Okamoto K. Pilocytic astrocytoma with anaplasia arising from the optic chiasm in a very elderly patient. Neurology 2017;89:1840.
2. Tanboon J, Williams EA, Louis DN. The diagnostic use of immunohistochemical surrogates for signature molecular genetic alterations in gliomas. J Neuropathol Exp Neurol 2016;75:4–18.
3. Shindler G, Capper D, Meyer J, et al. Analysis of BRAF V600E mutation in 1,320 nervous system tumors reveals high mutation frequencies in pleomorphic xanthoastrocytoma, ganglioglioma and extra-cerebellar pilocytic astrocytoma. Acta Neuropathol 2011;121:397–405.

Editors' note: ELAPSS score for prediction of risk of growth of unruptured intracranial aneurysms

In "ELAPSS score for prediction of risk of growth of unruptured intracranial aneurysms," the authors established a 6-predictor risk score for aneurysm growth. In their study, they defined significant aneurysm growth as greater than 1 mm. Dr. Willey discusses the possibility of measurement error and bias as a result of this methodology. He also questions whether the readers were blinded, how aneurysm ruptures were treated statistically, and how ELAPSS compares to other existing classification systems. The authors did not respond.

Megan Alcauskas, MD, and Steven Galetta, MD

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Reader response: ELAPSS score for prediction of risk of growth of unruptured intracranial aneurysms

Joshua Z. Willey (New York)

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In the article by Backes et al.,[1] the primary outcome was defined as greater than 1 mm growth as measured at local sites. The use of this cutoff was not referenced and a 1 mm change could be subject to potential measurement error. Furthermore, if different imaging modalities in one patient (magnetic resonance angiography vs CT angiography) were used to measure growth,

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their results could also lead to measurement error. An additional source of error and bias is if the physician carrying out the measurement was aware of the prior size. In that instance, the interpreting physician may judge an aneurysm that is larger to be more likely to grow, thereby biasing measurement. The potential sources of measurement error and bias may affect the results; it would be helpful to know if there was a blinded central reading center.

In the analysis, it was also unclear how aneurysm rupture was treated statistically. It appears that a stable aneurysm in 2 scans before rupture was treated as not having grown. Would this patient be treated as censored in survival analysis and not contribute information on aneurysm growth? Aneurysm rupture is a clinical outcome indicating a change in the aneurysm more serious than a 1 mm growth and with similar risk factors. The estimates, which had a large standard error, were heavily weighted toward size and location, which are well-known risk factors. To interpret the clinical and additive utility of ELAPSS, a statistical comparison to a traditional score with receiver operating characteristics or net reclassification would help. In other words, how much better was patient risk stratified with ELAPSS compared to a simple classification (e.g., posterior circulation and size greater than 7 mm)?

1. Backes D, Rinkel GJE, Greving JP, et al. ELAPSS score for prediction of risk of growth of unruptured intracranial aneurysms. Neurology 2017;88:1600–1606.

CORRECTION

Multiparametric MRI changes persist beyond recovery in concussed adolescent hockey players

Neurology® 2017;90:1039. doi:10.1212/WNL.0000000000004909

In the data supplement for article "Multiparametric MRI changes persist beyond recovery in concussed adolescent hockey players" by K.Y. Manning et al.,[1] there is an error in the "MRI Acquisition" section on page 4. The first sentence should read "All MRI data were acquired using a 32-channel human head coil" rather than "64-channel coil" as originally published. The authors regret the error.

Reference

1. Manning KY, Schranz A, Bartha R, et al. Multiparametric MRI changes persist beyond recovery in concussed adolescent hockey players. Neurology 2017;89:2157–2166.

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