5-aminolevulinic acid–guided resection of bone-invasive meningiomas

TO THE EDITOR: We read with interest the article by Bekelis et al.¹ (Bekelis K, Valdés PA, Erkmen K, et al: Quantitative and qualitative 5-aminolevulinic acid–induced protoporphyrin IX fluorescence in skull base meningiomas. *Neurosurg Focus* 30(5):E8, May 2011).

Hyperostosis associated with intracranial meningiomas is a well-described entity. Al Mefty and his colleagues reported in a large series that hyperostosis associated with meningiomas is caused in up to 96% of cases by tumor invasion of the bone.⁷ Radical resection of these meningiomas can be difficult to achieve because bone infiltration can be hard to recognize.² For this reason, new techniques that make it possible to intraoperatively identify cranial involvement of tumor are welcome. 5-aminolevulinic acid (5-ALA)–guided resection is an emerging technique in neurooncological surgery that has been largely reported to improve the extent of resection and to influence overall survival of patients affected by malignant gliomas. Conversely, the role of fluorescence-guided surgery on meningiomas remains unclear. Few experiences have been published in the literature, and most regard meningiomas without bone invasion; some authors reported in a large series that up to 94% of tumors presented a visible fluorescence.²

We really appreciated the paper by Bekelis et al. in which the authors reported their experience on a case of a sphenoorbital meningioma operated on using 5-ALA-induced fluorescence. Interestingly, the authors compared data of qualitative assessment of visible fluorescence with data of quantitative measurements of protoporphyrin IX (PpIX) with an intraoperative probe for in situ fluorescence detection. In collected samples, the visible fluorescence demonstrated 80% sensitivity in detecting pathology, whereas the intraoperative probe was associated with 100% sensitivity. These are interesting data, appealing images, and a fascinating technique. If we are not wrong, until now only 3 cases have been reported in the literature about fluorescence-guided surgery on bone-invasive meningiomas.^{3,5,6} In all 3 cases the bone invasion was clearly detectable because it was strongly fluorescent at the qualitative assessment. We would like to contribute to this issue with our personal experience on bone-invasive meningiomas with 5-ALA-induced fluorescence even without the assessment of quantitative measurements of PpIX. We operated on 3 cases similar to those presented by Bekelis et al.;¹ all surgeries were guided by neuronavigation (based on MRI in 2 and bone CT scanning in 1

image). In 2 cases they were convexity meningiomas, and in both cases both the tumor and the bone invasion were fluorescent (faint in the first one and strongly fluorescent in the second one) (Fig. 1). In the third case, a sphenoorbital meningioma (Fig. 2), neither the tumor nor the infiltrated bone was fluorescent. Actually, this last was a very unusual situation and was the first description of nonfluorescent bone-invasive meningioma. We would like to emphasize 2 issues on this topic. First, not only intracranial meningiomas but also cranial meningiomas are not always fluorescent under blue-violet light. Some authors have already described possible causes for the absence of 5-ALA fluorescence in meningiomas, and we assume that these are the same reasons for the absence of 5-ALA fluorescence in the bone-infiltrating portion.⁴ In our experience, neuronavigation is a crucial modality in this circumstance. Second, we would highlight that there was in all 3 cases a strict concordance in the fluorescence pattern (positive faint, positive bright, negative) between the cranial and intracranial portions of the meningioma in the same patient. Because of the scarcity of data regarding bone-invasive meningiomas under blue-violet light and because of the potential remarkable role that 5-ALA surgery could play in this challenging field, we hope that this contribution may give rise to larger studies on this issue.

ALESSANDRO DELLA PUPPA, M.D.
RENATO SCIENZA, M.D.
University Hospital of Padova
Padova, Italy

FIG. 1. Convexity bone-invasive meningioma. Microscope images under white light (A and C) and under blue-violet light (B and D). Both the bone invasion (A and B) and the tumor (C and D) were strongly fluorescent.

FIG. 2. Sphenoorbital bone-invasive meningioma. Microscope images under white light (**A and C**) and under blue-violet light (**B and D**). Neither the infiltrated bone (**A and B**) nor the tumor (**C and D**) was fluorescent.

Disclosure

The authors report no conflict of interest.

References

1. Bekelis K, Valdés PA, Erkmen K, Leblond F, Kim A, Wilson BC, et al: Quantitative and qualitative 5-aminolevulinic acid-induced protoporphyrin IX fluorescence in skull base meningiomas. **Neurosurg Focus** 30(5):E8, 2011
2. Bikmaz K, Mrak R, Al-Mefty O: Management of bone-invasive, hyperostotic sphenoid wing meningiomas. **J Neurosurg** 107:905–912, 2007
3. Coluccia D, Fandino J, Fujioka M, Cordovi S, Muroi C, Landolt H: Intraoperative 5-aminolevulinic-acid-induced fluorescence in meningiomas. **Acta Neurochir (Wien)** 152:1711–1719, 2010
4. Hefti M: Comment concerning: Intraoperative 5-aminolevulinic-acid-induced fluorescence in meningiomas, *Acta Neurochir* DOI 10.1007/s00701-010-0708-4. Intratumoral heterogeneity and fluorescence intensity in meningioma after 5-ALA pretreatment. **Acta Neurochir (Wien)** 153:959–960, 2011 (Letter)
5. Kajimoto Y, Kuroiwa T, Miyatake S, Ichioka T, Miyashita M, Tanaka H, et al: Use of 5-aminolevulinic acid in fluorescence guided resection of meningioma with high risk of recurrence. Case report. **J Neurosurg** 106:1070–1074, 2007
6. Morofuji Y, Matsuo T, Hayashi Y, Suyama K, Nagata I: Usefulness of intraoperative photodynamic diagnosis using 5-aminolevulinic acid for meningiomas with cranial invasion: technical case report. **Neurosurgery** 62 (3 Suppl 1):102–104, 2008
7. Pieper DR, Al-Mefty O, Hanada Y, Buechner D: Hyperostosis associated with meningioma of the cranial base: secondary changes or tumor invasion. **Neurosurgery** 44:742–747, 1999

RESPONSE: We would like to thank Dr. Della Puppa and Dr. Scienza for their kind comments on our paper. We read their short report with great interest. We agree that the use of 5-ALA-induced fluorescence appears to be a promising tool that can delineate abnormal pathology, demonstrate invasion, and enable tailoring the extent of tumor resection in order to avoid destruction of normal surrounding tissue.

The authors highlight the potential applications of fluorescence-assisted imaging in anatomically challenging meningioma resections. Some meningiomas, especially those invading bone and those involving the skull base, are difficult to treat because they are close to the cranial nerves, major blood vessels, and air sinuses. The observation of a similar degree of fluorescence in meningiomas and invaded bone, although intuitive, is intriguing. It implies that the bone-invading cells maintain their properties, underlying the importance of complete resection in order to provide the patient with the best chance of cure.

Drs. Della Puppa and Scienza also delineate the limits of visible fluorescence in detecting pathological invasion in some benign tumors. Those limits can be potentially overcome with the use of quantitative techniques that can measure PpIX concentration. The development of intraoperative probes such as the one used in our experience can assist in the detection of pathological tissue in nonvisibly fluorescent areas. Intraoperative in vivo measurement of PpIX concentrations opens the door to real-time delineation of these pathologies with much greater accuracy than visible fluorescence.

KIMON BEKELIS, M.D.
DAVID W. ROBERTS, M.D.
Dartmouth Medical School
Lebanon, NH

Please include this information when citing this paper: DOI: 10.3171/2012.6.FOCUS12236. ©AANS, 2013