5-Aminolevulinic Acid and ^{18}F -FET-PET as Metabolic Imaging Tools for Surgery of a Recurrent Skull Base Meningioma

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J Neurol Surg B 2013;74:211–216.

Abstract

Background Metabolic imaging technologies such as 5-aminolevulinic acid (ALA) fluorescence-guided resection and positron-emission tomography (PET) imaging have improved glioma surgery within the last decade. At present, these tools are not routinely used in meningioma surgery.

Objective We present a case of a complex-shaped, recurrent skull base meningioma where 5-ALA fluorescence-guidance and ^{18}F -fluoroethyltyrosine (FET)-PET-imaging facilitated surgical resection.

Material and Methods The patient underwent surgery via a combined transcranial/transnasal endoscopic approach. What was original is that both the microscope and the endoscope were equipped for 5-ALA fluorescence-guided surgery, respectively. Furthermore, preoperative FET-PET imaging was fused with computed tomography (CT) and magnetic resonance imaging (MRI) data for intraoperative navigation. The case richly illustrated the performance of the different modalities.

Conclusions Metabolic imaging tools such as 5-ALA fluorescence-guided resection and navigated FET-PET were helpful for the resection of this complex-shaped, recurrent skull base meningioma. 5-ALA fluorescence was useful to dissect the adherent interface between tumor and brain. Furthermore, it helped to delineate tumor margins in the nasal cavity. FET-PET improved the assessment of bony and dural infiltration. We hypothesize that these imaging technologies may reduce recurrence rates through better visualization of tumor tissue that might be left unintentionally. This has to be verified in larger, prospective trials.

Keywords

- ▶ endoscopic
- ▶ fluorescence-guided resection
- ▶ FET-PET
- ▶ recurrent meningioma
- ▶ skull base

Introduction

Recurrent skull-base meningiomas may be very challenging for surgical resection. In fact, they often display an extended and complex three-dimensional growth pattern. Furthermore, it may be difficult to differentiate recurrent tumor

tissue from scar tissue. Another difficulty is assessing infiltration of the bony skull base.

In glioma surgery, 5-aminolevulinic acid (ALA)-based fluorescence-guided surgery (FGS) and positron emission tomography (PET)-imaging technologies have been shown to improve surgery in clinical trials.^{1–3} In skull base surgery

received

June 19, 2012

accepted after revision

January 22, 2013

published online

April 1, 2013

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Stuttgart · New York

DOI <http://dx.doi.org/10.1055/s-0033-1342918>.
ISSN 2193-6331.

Fig. 1 Magnetic resonance imaging, T1 with gadolinium. The images show a recurrent olfactory groove meningioma with extension into the nasal cavity. Tumor, scar tissue, and fluid retention in the paranasal sinuses are difficult to assess.

and especially for meningiomas, those molecular imaging tools have not been largely studied yet.⁴ There are some reports about PET imaging for planning in stereotactic radiotherapy.^{5,6} Some case series reported about FGS of meningioma or pituitary adenoma with 5-ALA.^{7,8}

In the present article, we present a case of a recurrent olfactory groove meningioma with invasion into the upper nasal cavity. The exact extension of the lesion was difficult to judge on preoperative computed tomography (CT) and magnetic resonance imaging (MRI). Therefore, the patient underwent preoperative PET using the radiolabeled amino acid ¹⁸F-fluoroethyltyrosine (FET), which was fused with CT and MRI for preoperative planning and intraoperative navigation. Furthermore, we used 5-ALA for fluorescence-guided resection. What was original is that we used an operating microscope and an endoscope equipped for 5-ALA fluorescence detection during a combined transcranial/endoscopic-endonasal approach. We review the relevant literature and thoroughly discuss technical details.

Illustrative Case

A 65-year-old woman with an olfactory groove meningioma resected in 1996 presented with a huge recurrence. In 1996, a multiple sclerosis (MS) and an olfactory groove meningioma were diagnosed due to a right-sided loss of vision. The meningioma (World Health Organization [WHO] Grade 1) was resected via a transcranial route. Despite the known MS,

she did not undergo follow-up imaging after 1996. Only in 2012 did she undergo a new CT and MRI because of persisting headaches. Clinical examination showed a well-orientated patient with no alteration of her mental status; she was blind on the right side and had anosmia. The images revealed a local left-dominated recurrence of the olfactory groove meningioma with possible expansion into the nasal cavity and the paranasal sinuses (►Fig. 1). However, the exact extension of the lesion was difficult to judge on MRI and CT, especially considering bony invasion, infiltration of the mucosa, and retention within the paranasal sinuses. The intranasal tumor portion presented a growth pattern with a different MRI morphology as compared with the intracranial tumor portion. Additionally, no significant osseous defect was seen in CT imaging. Therefore, the intranasal mass was initially diagnosed as a possible mucosal reaction by the neuroradiologists.

Additional FET-PET imaging was performed and helped to better define the tumor target volume, which extended into the nose through a small bony defect. A fused dataset of CT, MRI, and FET-PET imaging was used for intraoperative navigation (Brainlab AG, Feldkirchen, Germany) (►Fig. 2).

Surgery

Informed consent with special regard to the off-label use of ALA and FET-PET was obtained from the patient. 5-ALA

Fig. 2 Screenshot of the intraoperative navigation system with image fusion of ^{18}F -fluoroethyltyrosine (FET)-positron emission tomography (PET), magnetic resonance imaging (MRI), and computed tomography (CT). Tumor infiltration of the skull base may not clearly be assessed with conventional MRI and CT. FET-PET showed no link between the tumor mass at the skull base and the nasal cavity, indicating that the skull base was not infiltrated by the tumor. Intraoperatively resected bone was 5-aminolaevulinic acid (ALA) negative and histopathological work-up found no tumor.

(20 mg/kg body weight) was given orally 3 hours prior to surgery in accordance with the routine protocol for gliomas in our department. Image fusion of thin-slice CT with fiducials, MRI, and FET-PET was performed using a Brainlab Workstation (iPlan[®], Brainlab AG). At induction of anesthesia, cefazolin, dexamethasone, and mannitol were administered. The patient was installed in a supine position. The head was fixed in a Mayfield-holder and was slightly flexed and rotated to her right side. After calibration of the neuronavigation system (Brainlab AG), the nostrils were prepared with oxazoline swabs, the face prepared with β -isadonna and covered in a sterile fashion. The former bicoronal incision was reopened and the skin flap retracted. A new smaller and lower-lying craniotomy was performed. Under the microscope (OPMI

Pentero, Zeiss, Oberkochen, Germany) the dura was opened and firm fibrous attachments were released. The tumor was debulked and dissected in a circumferential fashion. Frozen sections confirmed a meningioma relapse with no features of higher grade. Alternating white and ultraviolet (UV) light facilitated dissection of the tumor-brain interface. Tumor tissue was characterized by a vivid reddish fluorescence signal. Dural resection limits were checked with navigated CT/MRI and FET-PET images. After total resection of the cranial part, the endoscopic-endonasal resection was started. After partial resection of the posterior nasal septum and left middle turbinectomy, we used a four-handed technique (*JFC and PJS*) with a 12-degree-angled fluorescence endoscope system (Tricam SL II, PDD camera, D-Light, Karl Storz,

Fig. 3 Endoscopic view of the left nasal cavity. White light mode (left) and ultraviolet (UV) light mode (right). Note the grapelike meningioma tissue growing out of the sphenoid sinus. Tumor tissue displays reddish 5-aminolaevulinic acid (ALA) fluorescence (*). Note faint autofluorescence of the septal (^) and lateral mucosa (**). Note: In reality, the fluorescence intensity appears much more intense to the surgeon than may be reproduced in this image. Optimal detection requires a dark operating room.

Fig. 4 Microscopic view of the bony skull base defect from above. Microscope and endoscope were used in their different white-light (WL) and ultraviolet (UV) light modes, respectively, to assess residual tumor infiltration. (A) Microscopic WL and endoscopic WL mode. (B) Microscopic UV mode and endoscopic WL mode. (C) Microscopic UV mode without any endoscope light. (D) Microscopic UV and endoscopic UV mode. Note that in the microscopic UV light mode (C) the deep operating field is completely dark; it could be hypothesized that this may represent a false-negative result. With the additional UV light of the endoscope (D) the bone shows only slight autofluorescence. Some of this bone was removed and inspected under microscopic UV and WL mode (E and F). Note that there was no fluorescence. This corresponds to the hypometabolic area in the ^{18}F -FET-positron emission tomography (PET) (cf. Fig. 2). Histopathological work-up found no tumor.

Tuttlingen, Germany). The nasal tumor portion was macroscopically very different from the intracranial portion (►Fig. 3). It was less fibrous and had a glossy aspect. Frozen section confirmed meningioma with the same characteristics as the intracranial portion. 5-ALA fluorescence was helpful in distinguishing tumor tissue from swollen nasal mucosa. After gross total resection of the intranasal tumor, the optic nerve on the left side was decompressed. Finally, the infiltration of the bony skull base was inspected from above and below with 5-ALA-based fluorescence with the microscope and the endoscope, respectively (►Figs. 4 and 5). There was no significant 5-ALA fluorescence, and the FET-PET-based navigation indicated that resection had achieved metabolically inactive regions. The defect was closed in a sandwich-technique with TachoSil (Takeda, Zurich, Switzerland) and fibrin glue. The postoperative course was uneventful, and the patient was discharged on postoperative day 5.

Discussion

Pre-Operative and Intra-Operative ^{18}F -FET-PET-Based Imaging

The clinical situation of this patient was unusual. She underwent surgery in 1996 and there were no follow-up images until 2012. At presentation she had a huge recurrent tumor. The assessment of the exact tumor extension was difficult in several instances: differentiation between scar and tumor, margins of pathological dura, infiltration of the bony skull base, and differentiation between tumor, swollen mucosa, and fluid retention in the paranasal sinuses. Our initial experiences indicate that additional information from FET-PET may help to better delineate tumor extension before surgery, especially with regard to the extension into the nasal cavities. Although the spatial resolution of PET is limited compared with that of CT and MRI, the possibility

Fig. 5 Endoscopic view of the bony skull base defect from below (left: microscopic and endoscopic white-light [WL] mode, right: endoscopic ultraviolet [UV] mode). Note the 5-aminolaevulinic acid (ALA)-negative fluorescence indicating no residual tumor infiltration. This was confirmed by a biopsy.

of navigating FET-PET images fused to CT and MRI datasets increased information during surgery. It was especially helpful in assessing bony and dural infiltration intraoperatively. Although PET with radiolabeled amino acids has become a regularly used metabolic imaging tool in glioma surgery, its clinical adoption for meningioma surgery lags behind.^{1,4,9} So far, PET has been applied for planning stereotactic radiotherapy of complex-shaped skull base meningiomas using the amino acid ¹¹C-L-methionine or the somatostatin receptor ligand ⁶⁸Ga-DOTATOC.^{5,6} As demonstrated in the present case, FET-PET imaging may be helpful in surgery of recurrent complex-shaped skull base meningiomas.

From Endoscope-Assisted Microsurgery to Fluorescence Endoscope-Assisted Microsurgery

Unlike in glioma surgery, 5-ALA-based fluorescence-guided resection is not yet routinely established in meningioma surgery.^{3,10} However, several case reports and case series reported a good potential of this technology for meningioma surgery.^{8,11} Coluccia et al found a fluorescence rate of 94% in their surgical series of 33 meningiomas.⁸ In the present case, it was especially useful to dissect the plane between tumor and adjacent brain, which was adherent in this case of recurrence. Furthermore, in the nasal cavity, 5-ALA fluorescence helped to easily distinguish tumor tissue from swollen mucosa. This allowed for a straightforward dissection and prevented unnecessary mucosa resection.

As previously reported, we observed a high variability of the signal intensity of 5-ALA fluorescence within the tumor.¹² This is in part due to tissue properties, but may also be explained by the characteristics of light emission and detection. In fact, the operating microscope has a much longer distance between light source-target-detector. In contrast, the endoscope has a “torch-effect” enabling the induction and detection of fluorescence signals within much shorter distances. This may enable detection of lower signal intensities as compared with the microscope. In our opinion, there is a place for fluorescence endoscope-assisted microsurgery, especially in deep operating fields.

Combined Transcranial/Endonasal Endoscopic Approach

The combined approach offered excellent control of the operative field in the present case. In fact, a pure endonasal approach would not have allowed easy access to the lateral intracranial parts. Furthermore, closure of the osteodural defect was easier from above. On the other hand, a pure transcranial approach would only have allowed restricted access to the intranasal portion of the tumor.

Conclusion

Metabolic imaging tools such as 5-ALA fluorescence-guided resection and navigated FET-PET were helpful for the resection of this complex-shaped recurrent skull base meningioma. 5-ALA fluorescence was useful for dissecting the adherent interface between tumor and brain. Furthermore, it helped to delineate tumor margins in the nasal cavity. FET-PET improved assessment of bony and dural infiltration. Whether the presented metabolic imaging tools that were helpful intraoperatively may ameliorate patient outcome and reduce recurrence rates remains to be tested in larger clinical trials.

Disclosure

None of the authors has any personal or institutional financial interest in the materials and devices described in this article.

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