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Technical Notes

5-aminolevulinic acid-guided endoscopic biopsy with violet light-emitting diode flashlight in malignant glioma: Technical note

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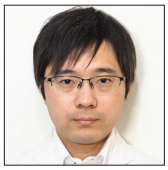

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ABSTRACT

Background: 5-aminolevulinic acid (5-ALA) photodynamic diagnosis (PDD) has enabled better identification of malignant tumor cells and real-time intraoperative guidance. Here, we report a reasonable procedure for 5-ALA-guided endoscopic biopsy with a violet light-emitting diode (LED) flashlight for deep-seated malignant gliomas.

Methods: A 63-year-old man presented with a headache and left upper homonymous quadrantanopia. Imaging studies showed atypical lesions with non-significant and partial contrast enhancement in the right deep temporo-occipital lobe. An endoscopic biopsy was performed under the guidance of 5-ALA PDD with a violet LED flashlight.

Results: The tumor tissues, which were difficult to distinguish from normal brain parenchyma under white light, were positive for 5-ALA fluorescence. The histopathological diagnosis was astrocytoma (the World Health Organization grade 3). The patient underwent adjuvant chemoradiation therapy. Headache and anopia improved, and no recurrence was observed at 12 months follow-up.

Conclusion: This technique of neuroendoscopic biopsy guided by 5-ALA PDD fluorescence with a violet LED flashlight may allow a safe and accurate diagnosis of deep-seated malignant gliomas.

Keywords: 5-aminolevulinic acid, Endoscopic biopsy, Light-emitting diode flashlight, Malignant glioma

INTRODUCTION

The prognosis of malignant gliomas remains poor compared to other malignant tumors in humans.[6,10,18] While safe maximal resection is the first important step in multimodal therapy,[14,15] patients often undergo a less invasive biopsy for an accurate diagnosis and to avoid perioperative complications and neurological deficits. 5-aminolevulinic acid (5-ALA) photodynamic diagnosis (PDD) has enabled the better identification of malignant tumor cells and real-time intraoperative guidance.[4,5,17]

In recent years, surgery combining neuroendoscopy and 5-ALA PDD has been used to remove and biopsy deep-seated lesions.[1,12,13,16,19] However, neuroendoscopy for the intraoperative observation of 5-ALA PDD has been limited to a specific company's product or custom-made

instrument. Here, we describe a more reasonable technique for 5-ALA-guided endoscopic biopsy using a violet light-emitting diode (LED) flashlight for deep-seated malignant gliomas.

MATERIALS AND METHODS

A 63-year-old right-handed man presented with a headache and left upper homonymous quadrantanopia. Magnetic resonance imaging (MRI) revealed a soft-tissue component showing hyperintensity on fluid-attenuated invasion recovery (FLAIR) images of the right deep temporo-occipital lobe. The right medial occipitotemporal gyrus was slightly enhanced along the sulcus with contrast medium on T1-weighted sequences. Magnetic resonance spectroscopy revealed elevated choline and lactate peaks and decreased creatine and N-acetyl aspartate peaks. Given these MRI findings and the patient's medical history, an initial diagnosis of high-grade glioma was made. We considered two alternative approaches for diagnostic biopsy: endoscopic transcortical approach and needle biopsy under neuronavigation and 5-ALA PDD guidance. The endoscopic approach was preferred to decrease the risk of non-diagnostic biopsy and postoperative bleeding.

Operation

The patient received a 20-mg/kg oral dose of 5-ALA dissolved in water three h before surgery. In the supine position under general anesthesia, the head was fixed in Mayfield clamps with over 60° of rotation in the contralateral tumor-side location. A small craniotomy was performed in the right temporal region, and a corticotomy was performed in the non-eloquent cortex of the right middle temporal gyrus. After the direction of approach to the lesion was determined with a neuronavigational system (Brainlab AG, Munich, Germany), we inserted the neuronavigational probe along the inner cylinder of a transparent sheath with a diameter of 10 mm (NeuroPort; Olympus, Tokyo, Japan) using the slight contrast enhancement (CE) on MRI as a target; subsequently, the probe and inner cylinder were removed, and a 4-mm 0° rigid neuroendoscope (EndoArm; Olympus, Tokyo, Japan) was placed along the outer sheath. While the main operator watched the tumor tissue bearing a resemblance to normal parenchyma on the monitor and held the sheath and neuroendoscope, an assistant operator removed the white light attachment and replaced it with a violet LED flashlight [Figure 1], which was set to a maximum zoom mode, delivering an excitation wavelength in the range of 400–405 nm (XML-T6; Holkin, Gifu, Japan). 5-ALA-induced protoporphyrin IX (PpIX) emits red light (635–704 nm) on exposure to violet light (370–440 nm). The 5-ALA PDD fluorescence was observed using a monitor in an otherwise dark room. A filer and a special camera were not used. The white light attachment and violet LED flashlight could be easily exchanged based on the 5-ALA PDD location under the neuronavigational system. While watching the monitor, the indicated tissues were harvested piecemeal using small forceps. After the procedure, the residual tissues were appropriately coagulated with monopolar coagulation and/or tamponaded with hemostatic agents and warm saline irrigation to achieve hemostasis in the sheath.

Figure 1: Instruments used for the 5-aminolevulinic acid-guided endoscopic biopsy. The white light attachment of the endoscope was removed and replaced with the violet light-emitting diode flashlight.

RESULTS

Pathological findings

Tumor cells showed two intraoperative 5-ALA PDD fluorescence patterns [Figure 2]: (1) strong fluorescence corresponding to slight CE on MRI and (2) vague fluorescence corresponding to non-CE and hyperintense lesions on FLAIR images. These infiltrating cells showed irregularly greater cellularity and nuclear atypia and were immunopositive for glial fibrillary acidic protein, p53, and isocitrate dehydrogenase (IDH)-1. The Ki-67 index was 20% at the hotspots. The tumor was histopathologically diagnosed as an astrocytoma, IDH-mutant, and World Health Organization (WHO) grade 3 (not otherwise specified). The other tissues with no visible fluorescence were divided into two areas in the subcortical parenchyma: (3) non-CE and rim of hyperintense lesions on FLAIR images and (4) non-CE and isointense lesions on FLAIR images, which histopathologically revealed no definite infiltrating tumor cells.

Postoperative course

Because the pathological diagnosis of astrocytoma was grade 3, additional adjuvant therapy was required. The patient underwent concomitant chemoradiotherapy (temozolomide, 60 Gy) and adjuvant temozolomide chemotherapy. Headache and anopia improved, and no tumor recurrence was noted at 12 months follow-up.

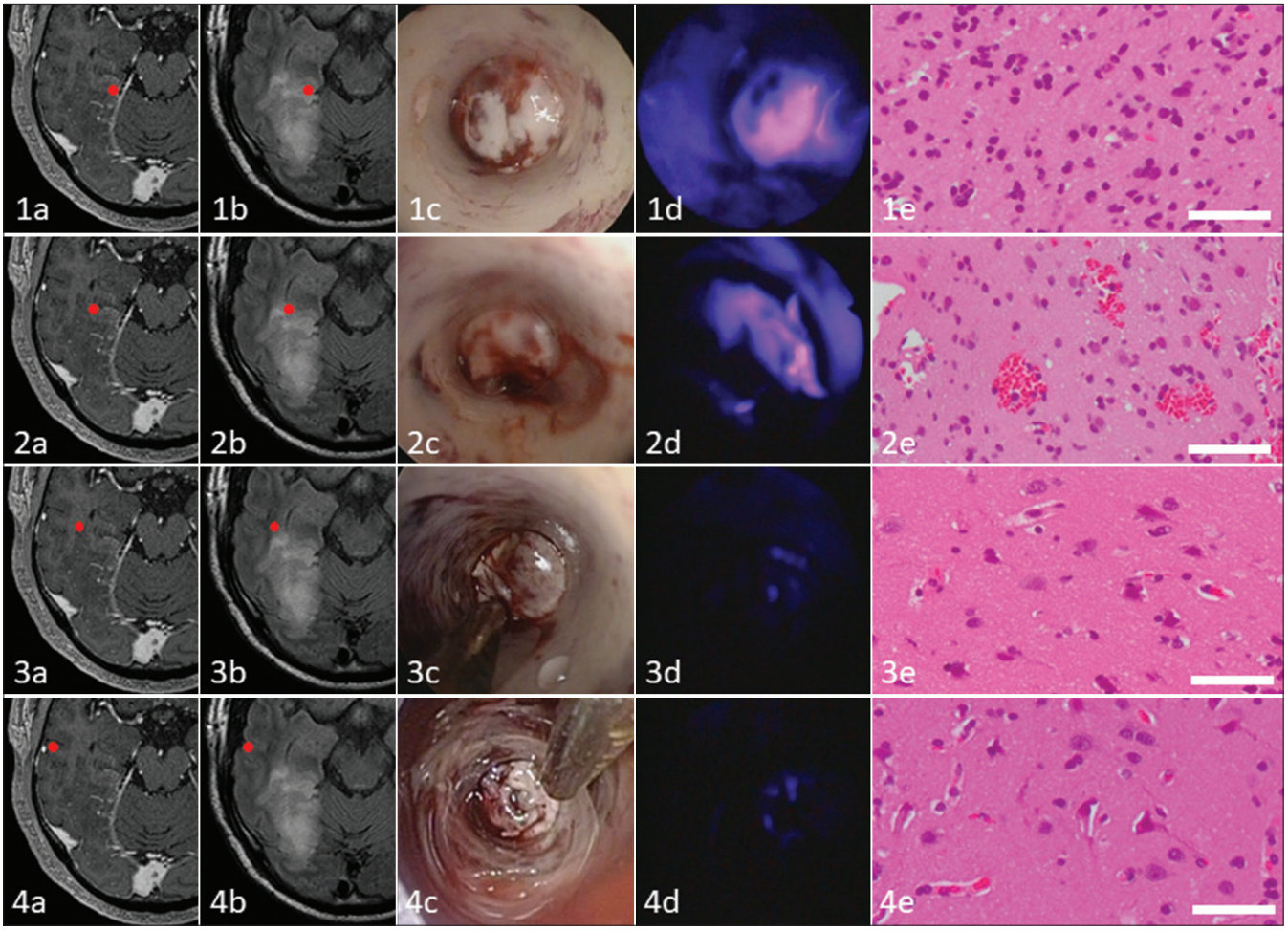

Figure 2: Comparison of indicated intratumoral areas in malignant glioma: Contrast enhancement (CE) on magnetic resonance imaging, fluid-attenuated invasion recovery (FLAIR) image, conventional white light endoscopy, 5-aminolevulinic acid photodynamic diagnosis fluorescence with violet light-emitting diode flashlight, and histopathology. The tissue from inside the (1a) slight CE and (1b) hyperintense on FLAIR depicts (1c) no obvious endoscopic abnormalities, (1d) strong fluorescence, and (1e) corresponding histopathology demonstrates infiltrating anaplastic tumor cells of an astrocytoma, world health organization grade 3. The tissue from inside the (2a) non-CE and (2b) hyperintense on FLAIR shows (2c) no obvious endoscopic abnormalities, reveals (2d) vague fluorescence, and (2e) histopathologically corresponds to infiltrating anaplastic tumor cells of an astrocytoma, grade 3. The tissue from the (3a) non-CE and (3b) rim of hyperintense on FLAIR shows (3c) no obvious endoscopic abnormalities, is (3d) negative for fluorescence, and (3e) histopathologically reveals no definite infiltrating tumor cells. The subcortical tissue from the (4a) non-CE and (4b) isointense on FLAIR shows (4c) no obvious endoscopic abnormalities, is (4d) negative for fluorescence, and (4e) histopathologically reveals no definite infiltrating tumor cells. Bar = 50 μm.

DISCUSSION

We report the novel assistance of a violet LED flashlight during a 5-ALA-guided endoscopic biopsy in a patient with deep-seated malignant glioma.

Although stereotactic surgery is often performed for brain tumor biopsy, blind procedures are associated with a risk of non-diagnostic samples and hemorrhagic complications.[2,7,11] However, neuroendoscopic biopsy enables direct visualization and hemostasis to decrease postoperative intracranial hemorrhage.[20] Neuroendoscopic surgery of deeply located lesions is also difficult due to the absence of anatomic landmarks, but guidance from the neuronavigational system makes it possible. Neuroendoscopic biopsy using a 10-mm sheath is more invasive than stereotactic biopsy due to the damage along the trajectory in the brain parenchyma. Thus, the entry point and trajectory of a neuroendoscopic biopsy must be carefully planned before surgery.

5-ALA is a precursor molecule of PpIX in the heme biosynthetic pathway in the mitochondria and cytoplasm.[5,8,9] 5-ALA administration induces PpIX accumulation in certain types of cells, including cancer cells, making them photosensitive to PDD. 5-ALA PDD, fluorescence-guided resection of malignant gliomas, has become a widely recognized standard

following the report by Stummer *et al*.[17] Recently, neuro endoscopic biopsy and resection under the guidance of 5-ALA for various deep-seated brain tumors has been reported.[1,3,12,13,16,19] 5-ALA is a promising marker for the intraoperative visualization of anaplastic foci in diffusely infiltrating gliomas with non-significant CE findings.[21] According to Choo *et al*., 5-ALA-guided neuroendoscopy helps neurosurgeons identify tumors that are difficult to distinguish from normal brain tissue using white light alone by reinforcing visual information.[1] In our case, red fluorescence under a violet LED flashlight led to a more accurate tumor biopsy, in which the tumor tissue with insignificant and slight CE resembled the normal parenchyma. Because neuroendoscopy for 5-ALA PDD has been limited to a specific company's product or custom-made instrument, we describe the first technical report of a more accessible 5-ALA-guided endoscopic biopsy with a violet LED flashlight for deeply located tumors.

Our technique may offer several advantages over plain tumor biopsy without 5-ALA, including improved diagnostic accuracy and reduced normal brain damage. Contrastingly, our study has some limitations. While using an LED flashlight in our technique was simple and cost-effective, the output power of the light source was relatively low, and the observation was conducted without a filter system for rebound rays, which increased the risk of pseudo-negative and pseudo-positive results, respectively. There was a necessity for dark room observation. Otherwise, our application would be improved by wearing filter glasses or putting an ultrathin filter in front of the usual camera for reflected red light. Furthermore, this procedure requires a combination of two synchronized operators. Nevertheless, we believe that 5-ALA-guided neuroendoscopic visualization with a violet LED flashlight could enhance our surgical experience in deep-seated brain tumor surgery.

CONCLUSION

Neuroendoscopic biopsy of deep-seated malignant gliomas under 5-ALA PDD guidance with a violet LED flashlight allowed for an effective and safe diagnosis of the lesion. Although further research is needed to establish 5-ALA-guided neuroendoscopic surgery with LED flashlights, we believe this technique can be safely and accurately applied to deep brain tumors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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