Orally administered 5-aminolevulinic acid (5-ALA)–induced fluorescence has been commonly used in glioma surgery in recent years.5–7 One randomized controlled multicenter Phase III study has shown that its use is associated with increased extent of resection and prolongation of progression-free survival in patients with malignant gliomas.5 The 5-ALA passes through the intact blood-brain barrier and is metabolized intracellularly by tumor cells to form the fluorescent molecule protoporphyrin IX.2,6 We present a case of 5-ALA–induced fluorescence in a primary CNS lymphoma (PCNSL) located in the fourth ventricle. To the best of our knowledge this is the first demonstration of a 5-aminolevulinic acid–induced fluorescence pattern in primary CNS lymphoma.

Key Words • 5-aminolevulinic acid • brain tumor • fluorescence • lymphoma • oncology

Case Report

History and Examination. This 66-year-old man with an 8-year history of chronic lymphocytic leukemia presented to our neurosurgical department for evaluation of progressive gait disturbances and diplopia. Physical examination revealed mild left hemiparesis and dysmetria, an unstable wide gait, and a positive Romberg test. Complete blood count tests showed 156,000 leukocytes and 76% lymphocytes, which were unchanged from complete blood count results in the previous years. Brain MRI sequences revealed an exophytic 13 × 12–mm intraaxial mass located on the left side of the floor of the fourth ventricle. The tumor was hypointense on T1- and T2-weighted sequences and showed a homogeneous enhancement after contrast injection. The tumor was associated with edema involving the cerebellar peduncle andpons (Fig. 1). Diffusion-weighted MRI sequences showed mild fluid restriction. Whole-body CT as well as PET-CT scans showed no systemic involvement.

Operation. Tumor resection took place after oral administration of 5-ALA according to a previously described protocol.5 Via a suboccipital midline approach, the tumor was identified on the left side of the floor of the fourth ventricle (Fig. 2 left). Blue-light illumination of the tumor revealed the typical red fluorescence under a 440-nm ultraviolet (UV) light source (violet-blue light, an optical component of the OPMI Pentero microscope; Carl Zeiss AG) (Fig. 2 right). The fluoresced tumor tissue was resected in a piecemeal fashion after identification and preservation of the pontine cranial nerves. The intensity of fluorescence gradually diminished over distance from the main tumor bulk, suggesting an infiltrating zone in the floor of the ventricle.
**Histopathological Findings.** Histopathological examination of the tumor revealed sheets of large anaplastic and pleomorphic tumor cells with a B-cell immune phenotype and a high proliferation index, findings that were compatible with a large B-cell CNS lymphoma (Fig. 3). The patient was referred for further oncological treatment for his disease.

**Discussion**

Accumulation of photosensitive protoporphyrin IX in glioma cells is observed after oral administration of 5-ALA. This phenomenon has been used in recent years to identify infiltrating glioma, to discriminate between normal and tumor tissue, and to improve the extent of tumor resection in gliomas. The use of 5-ALA–based fluorescence has been recently described in brain metastases and meningiomas. There is one report describing a stereotactic biopsy specimen of a deep-seated lesion in the thalamus that showed 5-ALA–induced fluorescence and was found to be a large B-cell lymphoma.

In the present report, the preoperative MRI results suggested an intraaxial tumor reminiscent of a high-grade glioma. The open resective approach to this tumor allowed us to observe the macroscopic appearance of 5-ALA–induced fluorescence in PCNSL. Interestingly, the fluorescence UV light microscope correlated with the tumor extension and infiltration as demonstrated by the MRI FLAIR sequence.

In this report we show for the first time the fluorescence pattern of PCNSLs in the brain. This observation may be of importance considering the recent published report indicating a survival advantage when PCNSL is resected rather than biopsied. It appears that intraoperative tools to enhance resection may apply to lymphoma in a similar way to what has been shown in glioma surgery. The knowledge that this phenomenon of tumor fluorescence is not exclusive to high-grade glioma, but may occur in the same pattern in PCNSLs, should be taken into account during tumor resection and, as previously noted, cannot assist in differentiating among various tumor types.

**Disclosure**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Grossman, Ram. Acquisition of data: Grossman, Nossek, Raz. Analysis and interpretation of data: Grossman. Drafting the article: Grossman, Ram. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Grossman. Administrative/technical/material support: Grossman, Nossek. Study supervision: Grossman, Ram.
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Manuscript submitted June 1, 2013.
Accepted September 17, 2013.

Please include this information when citing this paper: published online October 18, 2013; DOI: 10.3171/2013.9.JNS131076.
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