Endoscopic diagnosis of an MRI-occult, low-grade glioma with ependymal dissemination

Konstantinos Margetis, MD, PhD,¹ Prajwal Rajappa, MD,¹ William Cope, BS,² David Pisapia, MD,³ and Mark M. Souweidane, MD¹

Departments of ¹Neurosurgery and ³Pathology and Laboratory Medicine, Weill Cornell Medical College, New York-Presbyterian Hospital; and ²Weill Cornell Medical College, New York, New York

A 21-year-old man presented with triventricular hydrocephalus due to a tectal mass. He underwent an endoscopic third ventriculostomy, and multiple nodules were identified at the floor of the third ventricle intraoperatively. Surgical pathology of one of these lesions demonstrated that the tissue represented a low-grade astrocytoma. The case highlights the existing potential of neuroendoscopy to reveal neuroimaging-occult lesions, in spite of the significant advances of MRI. Furthermore, the combination of the age of the patient, the nonenhancing MRI appearance, and the multifocality of the lesions constitutes a rare and interesting neoplastic presentation within the brain. The constellation of findings likely represents dissemination of a low-grade tectal glioma via the CSF compartment.

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KEY WORDS neuroendoscopy; glioma; astrocytoma; cerebrospinal fluid; third ventricle; neoplasm metastasis; oncology

MAGNETIC resonance imaging has proved to be the imaging modality of choice for the evaluation of intraventricular brain tumors, which have an extensive differential diagnosis.³⁵ However, MRI of the brain often needs to be supplemented with spinal MRI and CSF cytological assessment to provide a complete evaluation of metastatic potential.³⁵

Tectal gliomas are a group of intraventricular tumors defined primarily by their location. Most often, they are low-grade astrocytomas and are considered indolent tumors that can be effectively managed in most cases with CSF diversion surgery and serial neuroimaging alone.³⁴ Their propensity to progress, let alone metastasize, is considered negligible, particularly for those histologically diagnosed as low-grade astrocytomas. Endoscopic third ventriculostomy (ETV) is a preferred method for the treatment of obstructive hydrocephalus for this disease. Herein, we present the case of a lesion that was initially considered to be a typical tectal glioma, but at the time of neuroendoscopy, intraventricular dissemination was recognized.

Case Report

Presentation

A 21-year-old man presented with a 7-year history of headaches. Initially, his headaches were thought to be migrainous, but they progressed in frequency and intensity. Right-sided tinnitus and facial paresthesias ultimately led to brain MRI that revealed a 10 × 11 × 14-mm mass projecting inferiorly from the midbrain tectum (Figs. 1–3). The mass was slightly T2 hyperintense and T1 hypointense with no definite enhancement. There was marked dilation of the third and lateral ventricles with mild periventricular white matter T2 hyperintensity, consistent with transependymal flow of CSF. The radiological findings were thought to be most consistent with a tectal glioma. Sagittal T1-weighted, axial T1-weighted, axial T2-weighted FLAIR, and thin-section sagittal 3D CUBE (GE Healthcare) MRI sequences were obtained. Axial and coronal reformats were also constructed from the CUBE data. Neurological examination revealed left lateral nystagmus, but findings

ABBREVIATION ETV = endoscopic third ventriculostomy.

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FIG. 1. Preoperative axial T2-weighted MR image showing the hyperintense tectal mass.

were otherwise unremarkable. Given the finding of triventricular, noncommunicating hydrocephalus secondary to a mesencephalic mass with imaging characteristics of a tectal glioma, an ETV was planned.

Operation

On initial ventriculoscopic observation, a number of nodules were visualized to be attached on the ependymal surface of the third ventricle (Video 1).

VIDEO 1. Video showing the initial inspection of the third ventricle and recognition of the abnormal nodules, the performance of the ETV, the biopsy of a prominent nodule, and the inspection of the subarachnoid space through the stoma site. Copyright Mark M. Souweidane. Published with permission. [Click here to view with Media Player.](#) [Click here to view with Quicktime.](#)

Morphologically, these were consistent with neoplastic lesions, and, given their multiplicity, most likely appeared to represent metastases (Fig. 4). The ETV was then performed utilizing a blunt biopsy forceps, just at the posterior aspect of the dorsum sellae. The tuber cinereum and the membrane of Liliequist were opened. Then, the largest lesion was biopsied and sent for histological diagnosis (Fig. 5). The ETV stoma was then gradually dilated utilizing a 3-F embolectomy catheter. Clear visualization of the prepontine subarachnoid space through the stoma site indicated no evidence of metastatic seeding.

Postoperative brain MRI did not show any complications. However, some abnormalities in the fourth ventricle and in the right lateral ventricle were considered to be ad-

FIG. 2. Preoperative sagittal T1-weighted MR image showing the slightly hypointense tectal mass.

ditional lesions. A spine MRI searching for metastatic disease was negative.

Pathology

The neuropathologist's diagnosis was diffuse astrocytoma (WHO Grade II). More specifically, the pathology report stated that the tumor consisted of mildly pleomorphic neoplastic glial cells with subependymal spread of neoplastic cells (Fig. 6a and b). The immunohistochemical profile of the neoplastic cells showed positive staining for GFAP (Fig. 6c), focal positivity for P53, a Ki 67 proliferation index of < 1% (Fig. 6d), and negative staining for mutated *BRAF* (V600E), *IDH1* (R132H), synaptophysin, and NeuN.

FIG. 3. Preoperative sagittal T2-weighted MR image. The third ventricular floor does not have any clear pathological abnormality.

FIG. 4. Intraoperative image showing the abnormal nodules at the floor of the third ventricle. The most prominent nodule is located between the mammillary bodies (M.B.).

FIG. 5. Intraoperative image showing the biopsy and ETV sites.

Postoperative Course

The patient was asymptomatic on follow-up, and MRI performed 4 months postoperatively did not show any changes in the lesion. The subcentimeter lesions along the dorsal aspect of the pons and medulla, as well as the ependymal floor of the right occipital horn, were also stable.

Nine months postoperatively, the patient remained asymptomatic; he had graduated from college and was pursuing the career of his choice. The MRI study at this point showed no appreciable change in the presumed tectal glioma. There was a low likelihood of a subtle increase in the size of the nonenhancing FLAIR/T2 signal abnormality along the floor of the right occipital horn, while the other multiple nonenhancing FLAIR/T2 signal abnormalities were unchanged in size. Repeat spine MRI failed to detect any metastases. The patient continues to undergo follow-up with serial MRI, according to the recommendations of the multidisciplinary pediatric tumor board.

Discussion

The direct visualization afforded by neuroendoscopy was introduced in 1910, when Victor Darwin Lespinasse performed the first endoscopic procedure, which was a choroid plexus cauterization.¹² Despite the current impressive advance of neuroimaging modalities, the direct visualization allowed by neuroendoscopy has been shown to reveal, on rare occurrence, pathology that does not appear on neuroimaging. We acknowledge that this is not the only example in which neuroendoscopy reveals pathology that is MRI occult. Germinomas of the third ventricular wall have been diagnosed with neuroendoscopy in the absence of MRI findings, suggesting that neuroendoscopy might be more sensitive than MRI in the detection of small intraventricular lesions.^{28,36} Both of these cases raise the possibility of using endoscopy as an added measure of meta-

static potential. There is an increasing use of simultaneous endoscopic tumor biopsy of pineal region tumors.²³ At a minimum, we believe it may be of importance that a relative comment be made in operative records of all patients with intraventricular tumors if endoscopy is performed.

The metastatic potential of high-grade gliomas is well documented,^{1,3,4,6,7,10,13,14,19–21,24,25,30–32} even to extraneural locations.¹¹ The metastatic potential of pilocytic astrocytomas^{5,9,18} and oligoastrocytomas^{16,33} has also been described. Metastasis by a low-grade, nonpilocytic astrocytoma has been rarely reported in the literature, although the first report was in 1930.²⁹ A literature review yielded 18 cases of metastatic, low-grade gliomas that were not juvenile pilocytic astrocytoma (Table 1). The majority refer to pediatric patients, but 5 cases were observed in adult patients.^{15,17,27,29} Notably, in the sole case in which MRI appearance of a satellite lesion is reported, the metastasis was enhancing, unlike those seen in our case.¹⁷

The pathological process presented in this case could theoretically represent multiple, synchronous primary astrocytomas. However, the degree of multiplicity in conjunction with the exclusive intraventricular ependymal localization of these lesions renders this possibility less likely than a scenario in which these lesions represent seeding through the CSF. In this latter scenario, however, the fact that the metastases are localized to the ventricular system and are not seen within the spine or the intracranial subarachnoid space raises the question of how CSF seeding becomes regionally restricted. The impairment of normal CSF flow as a consequence of the patient's noncommunicating hydrocephalus may play a role. An additional factor may be related to subtle differences in tumor microenvironment that permit growth of tumorlets in some areas of the CNS but not others. The limited nature of the specimen that was sent for histological analysis precluded more definitive exclusion of a higher grade component within the tumor. Nevertheless, given the degree of gross similar-

FIG. 6. Morphological and immunohistochemical features of the low-grade astrocytic neoplasm. **a:** The neoplasm is astrocytic in morphology and exhibits subependymal spread of tumor cells. **b:** Cellular atypia and occasional Rosenthal fibers are appreciated. **c:** The tumor cells are strongly positive for glial fibrillary acidic protein. **d:** The Ki 67 proliferation is less than 1%. Original magnification $\times 200$ (a); $\times 400$ (b–d).

TABLE 1. Literature review of CSF seeding cases from low-grade, non–juvenile pilocytic astrocytoma, gliomas

Authors & Year	Age at Diagnosis of Metastasis (yrs), Sex	Pathology	Site of Primary Tumor	Site of Metastasis
Russell & Cairns, 1930	28, M	Fibrillary astrocytoma	Thalamus	Spinal cord
Polmeteer & Kernohan, 1947	18, not stated	Fibrillary astrocytoma	Midbrain	Widespread
	15, not stated	Protoplasmic astrocytoma	Corpus callosum	Widespread
	32, not stated	Protoplasmic astrocytoma	3rd ventricle	Widespread
Civitello et al., 1988	3, not stated	Fibrillary astrocytoma	Cervical cord	Basal cisterns, tentorium, chiasm, hypothalamus, spinal cord
	3.5, not stated	Fibrillary astrocytoma	Cervical cord	Basal cisterns, tentorium
	6, not stated	Fibrillary astrocytoma	Cervical cord	Cerebral white matter, vermis, spinal cord
Pollack et al., 1994	7, M	Microcystic astrocytoma	4th ventricle	Basal cisterns & supratentorial ventricular system
Gajjar et al., 1995	5/12, M	Astrocytoma	Hypothalamus	Spinal cord, ventricle, cerebellum
	5, M	Astrocytoma	Hypothalamus	Spinal cord, ventricle, cerebellum
	5, F	Astrocytoma	Spinal cord	Cerebral hemisphere, cerebellum
	13, M	Astrocytoma	Spinal cord	Cerebral hemisphere, spinal cord, cerebellum
	20, F	Astrocytoma	Pons	Cerebral hemisphere, spinal cord
Akar et al., 2000	8, M	Astrocytoma	Suprasellar	Basal cisterns, sacral spinal canal
Hukin et al., 2002	2.9, not stated	Fibrillary astrocytoma	Diencephalon	Spine
	15.8, not stated	Fibrillary astrocytoma	Diencephalon	Intracranial & spinal cord
	22.8, not stated	Fibrillary astrocytoma	Brainstem	Intracranial & spinal cord (all lesions were enhancing on MRI)
Moon et al., 2012	16, M	Fibrillary astrocytoma	Pons	Left cerebellopontine angle, leptomeningeal disease of entire spine

ity between the sampled lesion and those left behind as well as the absence of enhancing lesions on imaging, it is probable that the histology seen in the sampled lesion is representative of the entirety of the multifocal process. Moreover, the stability of the remaining intraventricular lesions during follow-up also suggests that they are low grade in nature. While further genetic and molecular studies could not be conducted on the limited tissue and would have been interesting from a research perspective, it is unlikely that they would have been clinically significant, in terms of changing the management of the patient at this stage.

Conclusions

This case suggests that low-grade tectal astrocytomas may rarely have the potential for metastasis through the CSF pathways. More importantly, the current case highlights that direct visualization by neuroendoscopy remains relevant, even in the current era of advanced neuroimaging. It was the neuroendoscopy procedure that enabled us to visualize and diagnose the small ependymal lesions that eluded MRI diagnosis.

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Author Contributions

Conception and design: Souweidane, Margetis, Rajappa, Pisapia. Acquisition of data: Margetis, Pisapia. Analysis and interpretation of data: Margetis. Drafting the article: Margetis, Rajappa, Cope.

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: Souweidane. Study supervision: Margetis.

Supplemental Information

Videos

Video 1, Media Player. http://mfile.akamai.com/21490/wmv/digitalwbc.download.akamai.com/21492/wm.digitalsource-national/peds14-444_video_1.asx.

Video 1, Quicktime. http://mfile.akamai.com/21488/mov/digitalwbc.download.akamai.com/21492/qt.digitalsource-global/peds14-444_video_1.mov.

Correspondence

Mark M. Souweidane, Department of Neurosurgery, Weill Cornell Medical College, New York-Presbyterian Hospital, 525 E. 68th St., Box 99, New York, NY 10065. email: mmsouwei@med.cornell.edu.