The use of fluorescein sodium in the biopsy and gross-total resection of a tectal plate glioma

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Intravenous administration of fluorescein sodium fluoresces glioma burden tissue and can be visualized using the surgical microscope with a specialized filter. Intraoperative guidance afforded through the use of fluorescein may enhance the fidelity of tissue sampling, and increase the ability to accomplish complete resection of tectal lesions. In this report the authors present the case of a 19-year-old man with a tectal anaplastic pilocytic astrocytoma in which the use of fluorescein sodium and a Zeiss Pentero surgical microscope equipped with a yellow 560 filter enabled safe complete resection. In conjunction with neurosurgical navigation, added intraoperative guidance provided by fluorescein may be beneficial in the resection of brainstem gliomas.

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The quadrigeminal plate, also known as the tectum, is embryonically derived from the alar plate of the neural tube and contains auditory and visual reflex pathways.12 The position of the superior colliculi, inferior colliculi, and the close proximity of the cerebral aqueduct leave this anatomical region susceptible to lesional disruption of visual and auditory pathways as well as interruption of normal CSF flow.12 Patients harboring lesions within the tectal plate commonly present with obstructive hydrocephalus secondary to occlusion of the cerebral aqueduct. Additional common symptoms include headaches, nausea, vomiting, visual abnormalities such as oculomotor palsy and Parinaud syndrome, and imbalance.8

Lesions occupying the tectal plate include pineal-derived lesions, benign hamartomas, low-grade astrocytomas, and, rarely, anaplastic astrocytomas. Tectal plate gliomas comprise approximately 5%8 of all pediatric brainstem gliomas and are represented by pilocytic astrocytoma (36%), fibrillary astrocytoma (21%), oligoastrocytoma (14%), ganglioglioma (7%), and high-grade astrocytoma (7%).21 Management strategies for tectal plate lesions in the pediatric population vary by center and may include tissue diagnosis for contrast-enhancing lesions, through a stereotactic biopsy, endoscopic biopsy, or an open biopsy and resection. Gross-total resection is reserved for tumors that present to the surface of the brainstem and those in which a clear plane can safely be established between the lesion and surrounding eloquent tissue.13

Surgical approaches to the tectum are similar to described techniques for pineal region lesions, and include suboccipital-transtentorial, interhemispheric transtentorial, and supracerebellar-infratentorial approaches12–14. In addition to intraoperative neuronavigation, adjuvant use of fluorescein sodium may increase the fidelity of tissue sampling and aid in the resection of tectal lesions by distinguishing the tumor from the surrounding eloquent tissue in real time.

Fluorescein sodium is a highly fluorescent molecule that is currently FDA approved for use in ophthalmology, and has been reported to assist in the resection of high-grade gliomas.1,2,11,17 Fluorescein extravasates into areas of blood-brain barrier breakdown representative of tumor tissue. The use of fluorescein in glioblastoma resection has been associated with improved rates of tumor resection.2,9,19 Intravenous administration of fluorescein has been demonstrated to be safe, although allergic anaphylactic reactions have been reported.3,4,6 The pharmacokinetics of fluorescein are favorable for intraoperative use, with rapid distribution to tissues within 10 minutes, a plasma half-life of 23.5 minutes, and overall systemic clearance of
500 mg of fluorescein in 2 to 3 days (http://ecatalog.alcon.com/PI/FluoresciteInjection_us_en.pdf).

After intravenous administration, fluorescein sodium fluorescence can be visualized utilizing a surgical microscope equipped with a fluorescent filter system. Specifically, a Zeiss Pentero 900 surgical microscope (Carl Zeiss) outfitted with a yellow 560 long-pass through filter achieves visualization of yellow-green fluorescein-stained tissue in the setting of a normal-appearing background, and allows safe fluorescein-guided microsurgery.

Accordingly, the application of fluorescein sodium to resection of contrast-enhancing lesions in the quadrigeminal plate may confirm the surgical site, confirm acquisition of pathologic tissue, and guide resection. In this paper we report the case of a patient who received 10% fluorescein sodium (Alcon Laboratories) at 3 mg/kg intravenously prior to resection of a contrast-enhancing lesion located within the tectal plate.

Case Report

History and Presentation

A 19-year-old man with a 2-month history of intermittent headaches, double vision, nausea, and vomiting initially presented to his primary care physician, where MRI revealed a 1.7 cm × 1.9–cm contrast-enhancing mass of the midbrain and associated hydrocephalus (Fig. 1). Examination of the patient revealed orientation to name, date, and place, without additional focal neurological deficits. Given the contrast enhancement of the lesion on MRI and the concern for a possible high-grade glioma, a decision was made to operate rather than pursue a more conservative management course.

Operation

The patient underwent endoscopic third ventriculostomy for treatment of hydrocephalus 1 week prior to the planned resection of the tectal lesion. Approximately 1 week later, the patient was consented for intravenous administration of 10% fluorescein sodium prior to surgery via an institutional review board–approved protocol. The patient was placed into the right lateral decubitus position for a right-sided occipital transfentorial approach. Fluorescein sodium (10%) was intravenously administered to the patient at a dose of 3 mg/kg at the time of incision.

A right parietooccipital craniotomy and occipital transfentorial corridor exposed the posterior superior brainstem. The superior colliculi were moderately swollen and avascular. A midline incision was made at the geometrical center of the lesion between the superior colliculi. Subsequently, the yellow 560 filter was employed and the lesion was found to be highly fluorescent (Fig. 2A and B). Resection of the mass was achieved with neurosurgical navigation in conjunction with intraoperative fluorescent guidance (Fig. 2C and D). Residual fluorescein-stained tissue allowed for verification of complete resection, and no visible fluorescent tissue remained within the resection cavity (Fig. 2D). Total operative time was 4 hours 3 minutes, and was without complication.

Postoperative Course

Postoperatively, the patient was found to have symptoms consistent with Parinaud syndrome and bilateral ophthalmoplegia. Throughout his hospital course, his ocular symptoms resolved significantly, and he was discharged to rehabilitation on postoperative Day 10 with a moderate upgaze palsy. Three months postoperatively, the patient continues to demonstrate improvement of his Parinaud syndrome compared with his postsurgical baseline. Postoperative MRI of the brain demonstrated gross-total resection of the lesion in the immediate postoperative period (Fig. 3) as well as on surveillance MRI 2 months later. Consequently, a clinical decision was made to conservatively monitor the patient without treatment with chemotherapy and/or radiation.

Pathological Examination

Formalin-fixed, paraffin-embedded sections acquired from this patient illustrate the pathological diagnosis of

![Fig. 1. Preoperative MRI illustrating a 1.7 cm × 1.9–cm mass located in the tectal plate. Axial (A) and sagittal (B) T1-weighted postcontrast images are shown.](image1)

![Fig. 2. Intraoperative images obtained using a Zeiss Pentero 900 microscope equipped with a yellow 560 filter. Microsurgical photograph of the tectal lesion under white light (A) and with the yellow 560 filter engaged (B) from initial stages of tumor resection. A microsurgical mirror was used to examine the resection cavity for residual tissue. Residual tissue located in the proximal borders of the resection cavity was identified and removed (C). Final inspection of the resection cavity indicated no residual tumor tissue (D). Figure is available in color online only.](image2)
an anaplastic pilocytic astrocytoma. The mitotic activity was globally increased, with multiple foci having a range of 4–7 mitotic figures per 10 high-power fields, as well as several microscopic fields containing multiple mitotic figures (as high as 5 per high-power field). Increased single-cell necrosis was also noted. Ki 67 labeling was variably increased but was focally measured as high as 17%. Additionally, large fragments of global tumor necrosis and florid glomeruloid vascular proliferations were observed (Fig. 4).

Discussion

Fluorescein Sodium: Safety and Application

Recent evidence suggests the safe application of fluorescein sodium in malignant glioma and can be applied to lesions of the tectal plate, where safe entry and identification of the gliotic plane are necessary. Administration of 10% fluorescein sodium at a dose of 3 mg/kg after the induction of anesthesia, but prior to surgical incision, was not associated with adverse events and provided adequate fluorescence of the lesion without associated staining of the surrounding normal parenchyma. Furthermore, fluorescein-stained tissue was consistent with neurosurgical navigation, and provided the surgical team with intraoperative microsurgical guidance during tumor resection. This minimized normal tissue manipulation, and facilitated microsurgical dissection of the lesion from the surrounding parenchyma.

With the Zeiss yellow 560 filter, it was relatively easy to visualize the discretely fluorescein tumor tissue. Fluorescein staining was found by the operating surgeons to be advantageous during the course of the surgery, and provided intraoperative identification of residual tumor tissue. Utilizing a microsurgical mirror (Fig. 2C), identification of residual fluorescent tissue within the resection cavity facilitated complete resection and was verified on postoperative MRI (Fig. 3).

Anaplastic Pilocytic Astrocytoma

Pilocytic astrocytomas are generally regarded as benign tumors (WHO Grade I), usually occurring in pediatric and young adult populations. Typically, these tumors are located within the posterior fossa, and treatment ranges from radiographic surveillance to resection. Although generally considered an indolent disease, aggressive histopathological features, subtotal resection, and brainstem lesions are linked to worse prognosis.

Histopathological diagnosis of pilocytic astrocytoma is important, as identification of anaplastic features may influence treatment algorithms. Although relatively rare, the presence of malignant features within pilocytic astrocytomas is associated with a more aggressive disease course. Anaplastic pilocytic astrocytoma differs from typical pilocytic astrocytoma and these tumors exhibit increased mitotic figures, necrosis, and endothelial proliferations. Presence of these features is associated with a decrease in overall and progression-free survival when compared with typical pilocytic astrocytoma. Given the rarity of this tumor, limited research exists defining the postoperative treatment of anaplastic pilocytic astrocytoma, although reports suggest response to early temozolomide chemotherapy.

In patients with a brainstem tumor, safe maximal resection may prove beneficial in the overall prognosis of patients. Adjuvant use of fluorescein may increase surgical identification of tumor tissue for histopathological analysis and impact the ability to achieve maximal safe resection.

Our clinical case presentation illustrates the safety and utility of fluorescein sodium in the identification and resection of quadrigeminal lesions. In combination with neurosurgical navigation, the additional intraoperative guidance afforded by fluorescein may ultimately impact patient treatment and prognosis by facilitating the more specific resection of pathological tissue in such a highly eloquent area. Additional studies are warranted to fully investigate the utility of fluorescein sodium in the resection of brainstem lesions.

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Disclosures
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