Papillary Glioneuronal Tumor:  
A Case Report and Review of the Literature

Susan R. Williams,1* Beth W. Joos,2* Joseph C. Parker,2 and John R. Parker2
1University of Louisville School of Medicine, Louisville, Kentucky
2Department of Pathology, University of Louisville Hospital, Louisville, Kentucky
*The first and second authors made equal contributions to this paper.

Abstract. We report a papillary glioneuronal tumor occurring in the right frontal lobe of a 26-yr-old woman and we review the pertinent literature. Papillary glioneuronal tumor (PGNT) is a rare cerebral neoplasm, identified in approximately 37 cases to date. In 2007, the World Health Organization (WHO) classified the PGNT as a grade I neuronal-glial tumor because of its biphasic neurocytic and glial components and indolent clinical course. Patients commonly present with headaches or seizures, but may be asymptomatic with the mass discovered incidentally upon neuroimaging. Histology demonstrates a pseudopapillary architecture with a single or a pseudostratified layer of glial cells overlying hyalinized vasculature with interpapillary regions of neurocytic or ganglion cells. Peripheral eosinophilic granular bodies, Rosenthal fibers, hemosiderin, and areas of calcification are often noted. The PGNT displays moderate cellularity and is typically devoid of necrosis, microvascular proliferation, and mitoses. Its immunohistochemical profile includes glial fibrillary acidic protein (GFAP)-positive glial cells, synaptophysin-positive interpapillary neurocytes, and MIB-1 labeling in the range of 1-2%.

Keywords: papillary glioneuronal tumor, glial fibrillary acidic protein, synaptophysin-positive neurocytes

Introduction

Papillary glioneuronal tumor (PGNT) is a neoplasm of the cerebral hemispheres described in approximately 37 cases to date. Patients range in age from 4 to 75 yr and present with a variety of symptoms including fever, headaches, seizures, vertigo, vomiting, language disturbances, vision changes, hemiparesis, drowsiness, mood and behavioral changes, and neck pain [1-22]. Some patients may be asymptomatic and have a mass discovered incidentally upon neuroimaging [2,23]. The radiographic images range from a cyst with mural nodular pattern to solid and cystic with ring-like contrast enhancement [24]. Histology shows a pseudopapillary architecture that contains glial cells with scant cytoplasm and round nuclei overlying hyalinized vasculature. Neurocytic-like ganglion cells are seen between the papillary areas [24]. In addition to the cellular constituents, a variety of benign features are peripherally noted, such as eosinophilic granular bodies, Rosenthal fibers, and areas of calcification [2,6-8,12,14,16,19,23]. In 2007, the World Health Organization classified PGNT as a grade I neuronal-glial tumor [25]. The pseudopapillary architecture and variety of cellular constituents set this tumor apart from other mixed glioneuronal tumors.

Case Report

A 26-yr-old woman presented to her physician with complaints of headaches and vomiting beginning after she had her wisdom teeth removed in April,
2007. She reported suffering from migraine headache with vomiting throughout her adult life, but the headaches had become more frequent and consistent, and she was vomiting up to 4 times per week. She noted that nothing alleviated the headaches, and the pain was aggravated by standing and walking. On physical examination, fundoscopic and neurologic evaluations did not reveal any abnormalities. She denied any other health problems and did not use tobacco or alcohol. Her family history was significant for a cerebral aneurysm in her father.

Fig. 1 (left). MRI of the ring-enhancing mass within the right frontal lobe.
Fig. 2 (below). H&E stain (100x) with the characteristic pseudopapillary architecture.
Fig. 3 (below). H&E stain (600x) demonstrating gliovascular papillae with layered astrocytic cells.
Fig. 4 (below). H&E stain (400x) showing mature ganglion cells.
Fig. 5 (below). H&E stain (100x) demonstrating a sheet of tumor with oligodendroglial-like cells.
The patient was referred to the hospital for evaluation and imaging studies. Computerized tomography (CT) of the head, with and without contrast, revealed a 2.2 x 1.5 cm mass in the right frontal lobe, protruding into the right frontal horn. Magnetic resonance imaging (MRI) with contrast characterized the lesion as ring-enhancing (Fig. 1). Areas of calcification were noted. No significant vasogenic edema or hemorrhage was present. Magnetic resonance angiography (MRA) was also performed, and no vascular abnormalities were identified. The patient subsequently underwent a biopsy of the mass.

Histologic sections of the biopsy were stained with H&E and evaluated by light microscopy. The tumor was a neuroglial neoplasm with gliovascular papillae and vascular hyalinization (Fig. 2). Small round cells lined the papillae in single and multiple layers without any evidence of a perivascular pseudorosette formation (Fig. 3). Rare ganglion-like cells were present (Fig. 4), as well as cells that morphologically appeared glial. Solid areas contained neurocytic cells and cells with round nuclei, speckled chromatin, and small nucleoli with clear to eosinophilic cytoplasm (Figs. 5 and 6). Occasional Rosenthal fibers were noted within and adjacent to the tumor (Fig. 7). Scattered hemosiderin, rare mineralization (Fig. 8), and focal hemorrhages were observed. The adjacent neuroglial tissue contained reactive astrocytes, microgliosis, and focal gemistocytes with increased microvascularity. No definite mitoses were seen, but rare apoptotic nuclei were identified.

Immunohistochemical stains were performed using an automated system, LSAB2, and included synaptophysin (dilution 1:300; Dako), NeuN...
(dilution 1:100; Zymed), Neurofilament (dilution 1:50; Cell Marque), GFAP (dilution 1:400; Dako), MIB-1 (dilution 1:50; Dako), and p53 (dilution 1:100; Dako). The tumor had scattered cells in the solid areas that were positive with synaptophysin (Fig. 9) and NeuN. There were many GFAP-positive cells. The MIB-1 antibody labeled fewer than 1.0% of the neoplastic nuclei, and rare cells labeled weakly with p53 antibody.

The patient subsequently underwent a right frontal craniotomy and stereotactic volumetric resection of the tumor. A second tissue sample was obtained from the tumor resection and stained with H&E. This tissue similarly revealed the discrete gliovascular papillae with vascular hyalinization and biphasic neuronal and glial cells. The second tumor specimen was rich in ganglion cells and displayed more eosinophilic granular bodies. Rare tumor cells showed nucleomegaly.

A postoperative CT scan of the head without contrast displayed a small postoperative hemorrhage with encephalomalacia; however, no mass effect or midline shift was evident. The patient had a favorable postoperative follow-up and will have further imaging studies performed as part of routine follow-up.

Discussion

Papillary glioneuronal tumor (PGNT) is a cerebral neoplasm with some similarities to other neuroglial neoplasms; however, it has a distinctive papillary morphology. It has been labeled “mixed” due to its biphasic neurocytic and glial components. “Ganglioid cells,” ganglion cells, and neurocytes comprise its neural component, while astrocytes and oligodendrocyte-like cells represent its glial elements [24].

The clinical presentation of a PGNT may include fever, headaches, seizures, vertigo, vomiting, language disturbances, vision changes, hemiparesis, drowsiness, mood and behavioral changes, or neck pain, with the most common symptoms being seizure and headache [1-22,24]. Papillary glioneuronal tumor was first described in 1998 in a series of 9 cases of brain tumors in patients ranging from 11 to 52 yr [2]. Although the mean presentation age is 26 yr, cases have been reported in patients from age 4 to 75 yr [3,9,26]. Due to the rarity of this neoplasm, no epidemiologic data regarding the incidence or gender predilection have been described.

Overall, the PGNT resides in the cerebrum, often adjacent to the lateral ventricle [24]. However, there was one case in which the tumor was intraventricular with connection to the choroid plexus [22]. Some cases have neuroimaging with a cystic mural nodule pattern similar to the radiographic appearance of a ganglioglioma. Other cases, including our case, have shown a ring-like contrast enhancement [24]. Of the 37 total cases reported, most displayed a cystic mass [1,2,7,11,12,14,17-20,21,23,26], while others were documented as cystic with a mural nodule [5,6,9,10,13-15] or as having areas of peripheral or rim enhancement [2,3,6,8,9,11,16,20,26,27]. The lesion may have areas that are focally calcified [2,7,8,14,16] with edema surrounding the tumor, but mass effect has generally been mild [5,28].

The characteristics of this mass upon histologic analysis and immunohistochemistry have yielded a unique glioneuronal tumor. Common findings among all of the reported tumors are the biphasic glial and neural elements, pseudopapillae, and positivity for GFAP [24]. As a variant of a ganglioglioma, it may display interpapillary neurocytic and ganglion-appearing cells within the tumor. Glial elements stain positively for GFAP and S100 [1-9,12-16,18,19,21-23,27,29]. However, in contrast to gangliogliomas, which often display perivascular lymphocytes, PGNT typically contains a perivascular glial element in a pseudopapillary arrangement. The majority of cases, including our case, show hyalinized vessels lined by cuboidal glial (GFAP positive) cells. Rosenthal fibers were identified in our case as well as many reported cases [2,4,6,12,19,23], and eosinophilic granular bodies were seen in 7 of the 9 original cases [2]. These are usually situated at the periphery. In one case, cells adjacent to the GFAP positive cells were labeled with Olig2 antibody. Olig 2 is a transcription factor associated with oligodendrocytes, supporting the possibility of oligodendrogial origins of this tumor [29]. MIB-1 labeling rates are usually in the range of 1.0-2.0%. No unique genetic features have been reported.
Of critical importance is the prognosis in this newly described tumor variant. The original 9 cases indicated no short-term recurrences of tumor after surgery alone [3]. Postoperative recurrence was noted at 6 mo in one case after partial resection of the tumor and postoperative radiochemotherapy [7], while another case had multifocal recurrence after gross total resection at 4 yr, but with resolution after 18 mo of radiation and chemotherapy [27]. Because most of the tumors exhibit low grade phenotypes such as Rosenthal fibers, eosinophilic granular bodies, and moderate cellularity, without necrosis or mitoses, it appears hopeful that surgery may be curative. The longest follow-up period noted has been 19 yr without recurrence [8].

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References


