Myxopapillary Ependymoma With Pleuropulmonary Metastases and High Plasma Glial Fibrillary Acidic Protein Levels

Introduction

Myxopapillary ependymoma is a rare glial tumor with almost exclusive localization in the distal spinal cord (intraspinal variant) or the sacrococcygeal subcutaneous tissue (extraspinal variant).\(^1\) The average age at manifestation has been reported to be approximately 36 years. The overall incidence is approximately 0.08 per 100,000 persons per year for males and 0.05 per 100,000 persons per year for females. Myxopapillary ependymoma typically lacks histopathologic signs of malignancy and corresponds to WHO grade 1.\(^1\)

In this article, we report a rare case of extraspinal myxopapillary ependymoma with multiple pleuropulmonary metastases detected 24 years after initial diagnosis. The case is of interest for two reasons. First, distant metastases of myxopapillary ependymoma are exceedingly rare.\(^2\) Second, we found high levels of glial fibrillary acidic protein (GFAP) in the blood plasma of our patient, which corroborated the notion that this protein may be a useful circulating biomarker for selected glioma cases.\(^3\)\(^-\)\(^4\)

Case Report

In 1987, a 35-year-old woman presented with unilateral drop foot that had persisted for 2 years and a small indolent tumor over the coccygeal bone. The tumor grew slowly over the next 2 years until it was totally resected in 1989 with a size of 6.5 \(\times\) 5.5 \(\times\) 4 cm. Intraoperatively, the tumor was found to be located subcutaneously and seemed to have contact to the dural sack in the area of the tip of the coccygeal bone. The bone was not infiltrated. Histologic diagnosis was myxopapillary ependymoma (WHO grade 1). Six years later, the patient had to undergo a second total surgical resection as a result of the local recurrence. Again, histology showed myxopapillary ependymoma without signs of malignancy and with tumor-free resection borders. In April 2009, multiple tumors of both lungs were coincidentally detected during preoperative evaluation for a GI procedure. Computed tomography images showed multiple pleuropulmonary tumor masses, and some of them were fairly large (Fig 1A, asterisks) with compression of the right atrium (Fig 1A, arrow) and compression atelectasis of the left inferior pulmonary lobe (Fig 1B, arrow indicates atelectasis; asterisk indicates tumor). The patient was asymptomatic at this time. A transthoracic biopsy of one of the tumor masses was performed. Histopathologically, there were the typical features of myxopapillary ependymoma with cuboidal to elongated tumor cells radially arranged around microcysts filled with myxoid material (Fig 2A; hematoxylin and eosin; original magnification \(\times\) 100). We found no detectable mitotic activity and no signs of anaplasia. Immunohistochemistry showed strong expression of GFAP in virtually all tumor cells (Fig 2B; anti-GFAP; original magnification \(\times\) 200). A surgical resection of the pulmonary tumor masses was not feasible as a result of diffuse pleural and pericardial involvement. Dose-dense temozolomide (100 mg/m\(^2\) weekdays for 12 weeks) and imatinib (400 mg/d for 4 months) showed no measurable clinical benefits. However, with sorafenib (600 mg/d), tumor stabilization was observed for 9 months and had to be stopped because of peripheral neuropathy. Pazopanib was started at 400 mg/d, and has been well tolerated. At the time of publication, the patient was alive and under treatment with pazopanib because radiologic follow-up did not show clear disease progression for 6 months.

We have determined GFAP concentration in blood plasma samples from this patient collected at 14 months (4.34 ng/mL), 16...
months (7.23 ng/mL), and 26 months (8.17 ng/mL) after detection of the pleuropulmonary metastases. The analyses were performed by using a commercially available enzyme-linked immunosorbent assay kit according to the instructions of the manufacturer (Biovendor, Brno, Czech Republic). All investigations were approved by the local ethics committee.

**Discussion**

Distant metastasis of myxopapillary ependymoma is rare and has been suggested to occur more frequently in extraspinal (subcutaneous sacrococcygeal) than in intraspinal cases.1,5 The metastatic potential of myxopapillary ependymoma is surprising given the characteristic benign histopathology. In our patient, the rather large thoracic tumor masses detected incidentally 24 years after first diagnosis and their slow growth suggested that distant spread has occurred early in the disease course. Because of the widespread pleurapulmonary tumor manifestations, we had to initiate experimental drug therapy that did not show high efficacy in halting tumor growth. Early detection of the metastases may have allowed more effective therapy like surgical metastasectomy or radiotherapy.

It is interesting to note that we detected high levels of GFAP in the blood plasma of our patient. To the best of our knowledge, this was the first documented case of low-grade glioma with detectable circulating GFAP concentrations. GFAP is an intermediate filament of astrocytes and is typically expressed in glial tumors including myxopapillary ependymoma. GFAP is usually not found in the blood of healthy individuals. However, two previous studies have found increased levels of circulating GFAP in a fraction of glioblastoma patients.3-4 It is thought that intratumoral necrosis and disruption of the blood-brain barrier leads to the release of GFAP from tumor cells into the blood in glioblastoma. In low-grade gliomas located in the brain, the intact blood-brain barrier may prevent the release of GFAP into the circulation. We feel that the relatively high levels of plasma GFAP found in our patient were most likely associated with tumor manifestations outside of the CNS. The increasing concentrations of GFAP in the blood of our patient may have reflected slow tumor growth. Additional studies are needed to validate the correlation of the plasma GFAP concentration with tumor growth in glial tumors, including myxopapillary ependymoma, and whether it may serve as useful biomarker for patient follow-up.

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**AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

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**REFERENCES**


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