

Papillary tumor of the pineal region with extended clinical and radiologic follow-up

Hakeem J. Shakir^{1,2}, Jingxin Qiu³, Dheerendra Prasad^{1,4}, Laszlo L. Mechtler^{5,6},
Robert A. Fenstermaker^{1,2}

Departments of ¹Neurosurgery, ³Pathology, ⁴Radiation Medicine and ⁵Neuro-oncology, Roswell Park Cancer Institute, ²Department of Neurosurgery, School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, Buffalo, ⁶Dent Neurologic Institute, Amherst, NY, USA

E-mail: Hakeem J. Shakir - hshakir@ubns.com; Jingxin Qiu - jingxin.qiu@roswellpark.org; Dheerendra Prasad - dprasad2@buffalo.edu;
Laszlo L. Mechtler - lmechtler@dentinstitute.com; *Robert A. Fenstermaker - robert.fenstermaker@roswellpark.org

*Corresponding author

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Abstract

Background: Papillary tumor of the pineal region (PTPR) is a rare neoplasm with only anecdotal data to guide the treatment. Results of treatment with surgery, radiation therapy, and chemotherapy have been reported to have varying degrees of success. Here we report a patient with a PTPR, who underwent subtotal resection, gamma knife stereotactic radiosurgery, and adjuvant temozolomide chemotherapy.

Case Description: During 9 years of clinical and radiographic follow-up, the patient has had regression of residual tumor and remains asymptomatic.

Conclusion: When gross total resection of a PTPR is not possible, treatment with gamma knife stereotactic radiosurgery and temozolomide chemotherapy may provide long-term tumor control.

Key Words: Craniotomy, gamma knife, papillary tumor, pineal gland, radiosurgery, temozolomide

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INTRODUCTION

Papillary tumor of the pineal region (PTPR), first described in 2003 by Jouvret *et al.*,^[6] is a rare, but increasingly recognized, pathologic entity. This tumor was classified as a distinct neoplasm in 2007.^[8] Due to its rarity, there are currently no treatment guidelines that are generally agreed upon, although gross total resection appears to be favored when feasible. One retrospective analysis reported that gross total resection and youth were the chief factors associated with prolonged overall survival; however, this study contained limited data regarding radiotherapy and chemotherapy.^[5] The optimal management of cases in which the gross total resection is not possible and for those in which tumors recur despite an apparently complete initial resection has yet to be formally standardized. The case reported here highlights the effective use of combination therapy, including surgery, radiosurgery, and temozolomide chemotherapy, in

a patient who has survived with stable disease for 9 years following diagnosis.

CASE REPORT

This 31-year-old man presented with a 2-year history of headaches, balance problems, intermittent double vision, and a single generalized seizure. Neurologic examination

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demonstrated bilateral papilledema, right hemiparesis, global cognitive impairment, wide-based gait, and slowness to initiate movements. Magnetic resonance imaging (MRI) revealed hydrocephalus and a posterior third ventricular tumor with a volume of 10.9 cm³ [Figure 1]. After the placement of a ventriculoperitoneal shunt, the patient improved clinically, and ventricular size diminished. A stereotactic biopsy was nondiagnostic, so a right parieto-occipital craniotomy with an interhemispheric, transcallosal approach to the tumor was performed. The mass was debulked extensively, but the completeness of resection was limited by the adherence of the tumor capsule to the walls of the third ventricle. Subsequent to the craniotomy for debulking, tissue diagnosis revealing PTPR was confirmed [Figure 2]. Histopathologic analysis of tissue samples obtained from the tumor showed the papillary architecture and columnar and cuboidal epithelia. There were hyalinized blood vessels as well. No evidence of mitosis, necrosis, or vascular proliferation could be seen. Tumor cells were found to be positive for cytokeratin CAM 5.2

Temozolomide was initiated postoperatively, and the patient received 12 cycles over a period of 1-year without the significant complications. Following this regimen, gamma knife stereotactic radiosurgery was performed using a dose of 18 Gy to the 50% isodose surface at the tumor margin. At the time of gamma knife treatment, residual tumor volume measured 4.2 cm³. The treatment provided 100% coverage of the tumor at the prescription dose with 85% selectivity and a gradient index of 2.75. Thereafter, an additional 12 cycles of temozolomide were given for a total of 24 cycles. At the conclusion of chemotherapy, tumor volume measured 3.5 cm³. Subsequently, the patient returned for semiannual MRI scans, which have

shown continued tumor involution [Figure 3]. Nine years after the diagnosis was made, he remains much improved clinically and is gainfully employed without significant neurologic symptoms or findings. The most recent MRI scan obtained 9 years after initial diagnosis demonstrated a residual tumor volume of 1.3 cm³.

DISCUSSION

Tumors of the pineal region are rare, accounting for 0.5–1.6% of all intracranial tumors.^[11] Within this rare subset of intracranial tumors, PTPR has emerged as a lesser known, but a more recognizable entity. At present, the literature does not provide a definitive treatment algorithm for PTPR, although the fact that recurrence is common following incomplete resection suggests that aggressive multimodal treatment may be warranted. Various modalities have been employed to treat this particular pineal region neoplasm. Fèvre-Montange *et al.*^[5] conducted a retrospective study, which suggested that gross total surgical resection was the most important factor associated with longer overall survival. This conclusion is supported by case reports as well.^[2,3,7] The literature includes several reports with varying lengths of follow-up and recommendations.^[2-4] Most reports focus on surgical resection followed by radiation therapy with adjuvant chemotherapy.

Little data concerning the combination of radiosurgery and chemotherapy have been reported. One group recently described a patient with PTPR in whom stereotactic radiosurgery was used as the sole treatment, leading to a gradual reduction in tumor size over a 5-year follow-up period.^[10] Similarly, proton beam radiosurgery has been used successfully

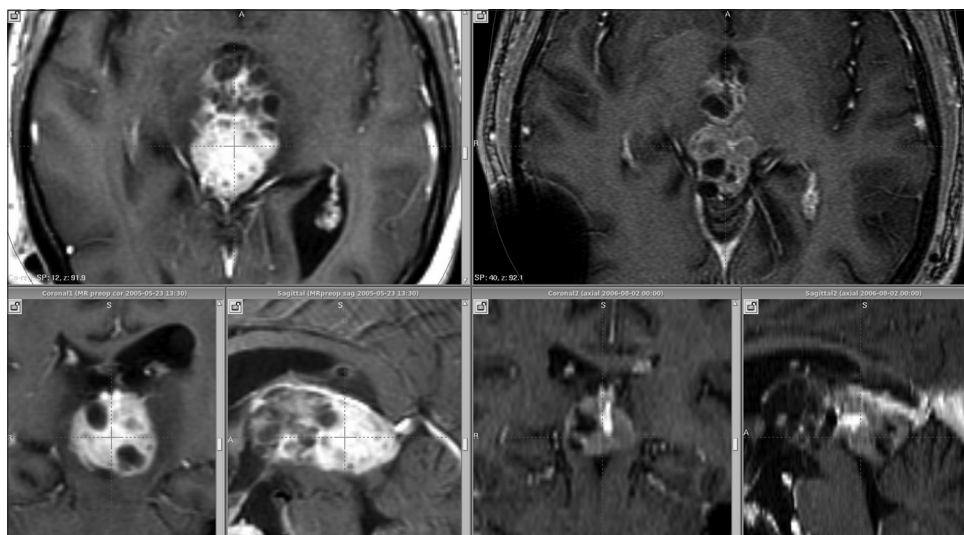


Figure 1: Preoperative T1-weighted axial, coronal, and sagittal images with gadolinium contrast enhancement (left panels, in clockwise direction), and corresponding T1-weighted axial, coronal, and sagittal images obtained on day of gamma knife treatment (right panels, in clockwise direction)

to treat tumor recurrence after apparent gross total resection.^[1] Another report demonstrated a complete response to fractionated radiation therapy without the surgical resection.^[9] In contrast, the authors of a recent retrospective review of a large compilation of cases found no evidence for an effect of either chemotherapy or fractionated radiation therapy.^[4] Instead, gross total resection and young age were the only positive prognostic factors detected.

Our patient experienced a continued slow reduction in tumor volume over 9 years after initial surgical debulking, followed by chemotherapy with temozolomide and gamma knife radiosurgery midway through that regimen. In our patient, gamma knife radiosurgery was performed

between cycles 12 and 13 of a chemotherapy regimen that totaled 24 cycles overall. Therefore, it is not strictly possible to separate the effects of gamma knife therapy from those of temozolomide therapy, with continued tumor volume reduction occurring both before and after gamma knife treatment. It is possible that a similar outcome could have been obtained with the radiosurgery alone, as may be seen with benign tumors such as vestibular schwannoma.

At present, treatment for PTPR involves a multispecialty approach with reliance upon maximum safe surgical resection and either fractionated radiation therapy or stereotactic radiosurgery.^[2,3,5] The role of adjuvant chemotherapy is not well defined, and further study is warranted. Our case highlights the ability of combination therapy to provide the long-term tumor control when complete surgical resection is not feasible.

CONCLUSION

This report describes the long-term result of multimodal treatment in a single patient with PTPR. Following subtotal resection, gamma knife stereotactic radiosurgery, and temozolomide chemotherapy, this patient has experienced a continued slow decrease in tumor volume over time, even well after the conclusion of treatment. As additional cases are reported, the role of adjuvant therapies like stereotactic radiosurgery may become clearer. In the meantime, gamma knife radiosurgery, with or without temozolomide chemotherapy, should be considered as an option for the treatment of residual disease following subtotal resection of PTPR.

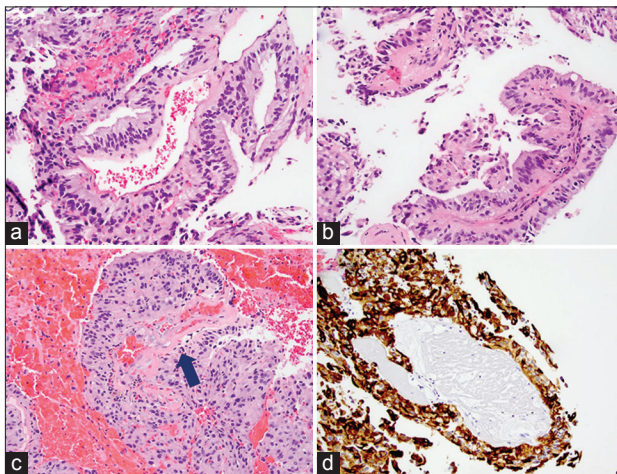


Figure 2: Representative H and E images ($\times 200$) of the tumor showing papillary architecture and columnar and cuboidal epithelial histology (a-c). There are hyalinized blood vessels (c, arrow) as well. There is no evidence of mitosis, necrosis, or vascular proliferation. Tumor cells are positive for cytokeratin CAM 5.2 (d, $\times 200$)

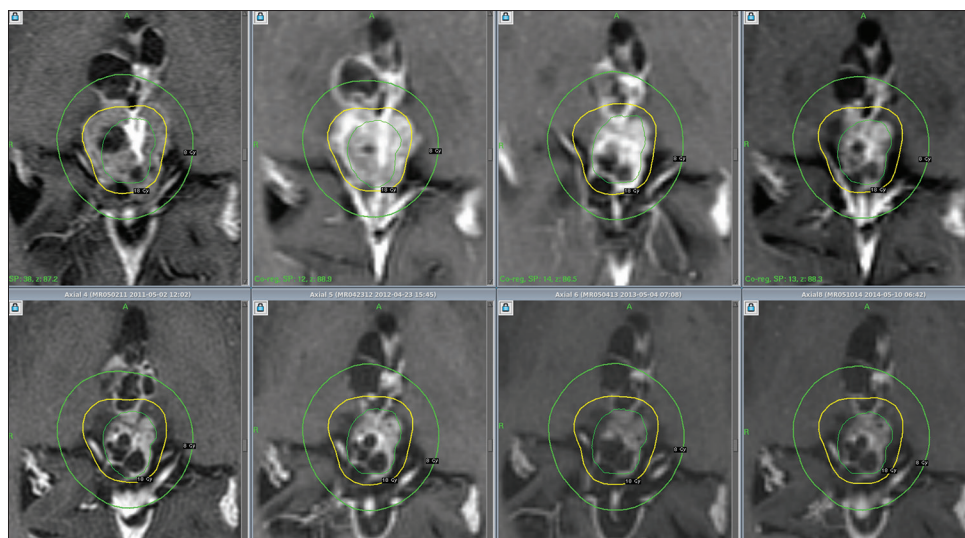


Figure 3: Serial T1-weighted coronal images beginning with day of gamma knife treatment and ending with current year (9 years after diagnosis) (upper set of images, left to right), and corresponding tumor volumes (lower set of images, also left to right) determined following co-registration of diagnostic images using Leksell GammaPlan 10 (Elekta, Henderson, NV, USA), with superimposition of the treatment plan on later image sets

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Conflicts of interest

There are no conflicts of interest.

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