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Case study

# Papillary tumor of the pineal region with synchronous suprasellar focus and novel cytogenetic features☆,☆☆

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**Summary** Papillary tumor of the pineal region (PTPR) is an uncommon neoplasm with variable biologic behavior. Cytogenetic and molecular diagnostic studies are rare, yielding no definitive genetic signature. We report a case of PTPR with a multicentric presentation and unusual cytogenetic features. A 25-year-old man presented with headache, disconjugate gaze, and confusion. Mass lesions in the pineal and suprasellar regions, with identical imaging characteristics, were identified. The former extended partially into the fourth ventricle. It showed typical PTPR histology and losses of chromosomes 3, 7, 10, 14, 18, and Y with gains of chromosomes 3, 8, and 9. Seventeen months postsurgery, the patient is stable without disease progression after radiation therapy. Synchronous mass lesions at presentation and losses of chromosomes 3, 7, 14, 18, and Y are unusual features, adding to the available data and underscoring the biologic and genetic variability associated with these neoplasms.


## 1. Introduction

Papillary tumor of the pineal region (PTPR) was originally described in 2003 by Jouvet et al [1] and was codified in the 2007 World Health Organization *Classification of Tumours of the Central Nervous System* [2]. Its typical location in the posterior aspect of the third ventricle near the posterior commissure and its histologic, immunohistochemical, and ultrastructural similarities to the specialized ependymal cells of the subcommissural organ suggest a histogenetic origin from this structure [1,3,4]. Gene expression studies support this hypothesis [5]. Because of variable biologic behavior and lack of consistent criteria to predict outcome, PTPR has been assigned World Health Organization grades 2 to 3 [2]. Cytogenetic and molecular diagnostic studies are rare [6,7], with additional data needed

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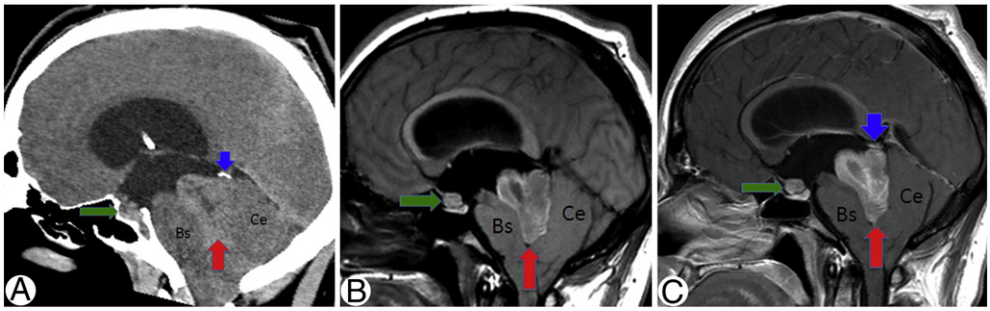


**Fig. 1** Radiographic features (red arrow, pineal and peripineal region mass lesion; blue arrow, pineal calcification; green arrow, suprasellar mass lesion). A, Sagittal noncontrast computed tomography shows a mass lesion involving the pineal and peripineal region, aqueduct, fourth ventricle, and posterior third ventricle as well as a suprasellar mass. Both lesions are hyperdense on the noncontrast computed tomography examination. B, Both lesions are heterogeneously hyperintense on sagittal precontrast T1 magnetic resonance imaging. C, Both lesions show minimal heterogeneous contrast enhancement on sagittal postcontrast T1 magnetic resonance imaging study. Bs, brainstem; Ce, cerebellum.

to yield a definitive genetic signature. We report a case of PTPR with a bifocal presentation and hitherto unreported cytogenetic features.

## 2. Case report

The patient is a 25-year-old man with no significant past medical history who presented with a 1-year history of headaches, worse in the morning and with recumbent position. He also reported blurry vision and diplopia with rightward gaze, which created driving problems. A severe episode of dizziness finally led to an emergency department visit, where no other neurologic signs were identified. An initial computerized tomography scan revealed massive hydrocephalus because of obstruction of the fourth ventricle and posterior aspect of the third ventricle (Fig. 1A). Magnetic resonance imaging studies demonstrated a 4.5 × 2.5-cm, minimally enhancing, heterogeneous lesion involving the pineal and peripineal region, the aqueduct, and extending into the third and fourth ventricles, with obstruction of cerebrospinal fluid (CSF) outflow resulting in dilatation of the proximal lateral and third ventricles (Fig. 1B and C). The lesion was hyperintense on precontrast T1 images and showed prominent gradient susceptibility suggestive of hemorrhagic changes. On the T2 sequence, the lesion was heterogeneous, with hyperintense and isointense components. A separate 1.1-cm mass with identical imaging features was identified along the anterior floor of the third ventricle in the chiasmatic/infundibular recess, with no intrasellar extension or connection to the pituitary gland. Mild cerebellar tonsillar herniation was present. No abnormal leptomeningeal enhancement was identified. No intramedullary or spinal leptomeningeal signal abnormality was seen. The radiologic differential diagnosis for these findings included pineal ependymoma with metastatic spread, metastases with hemorrhage, germinoma, and meningioma. A ventricular drain was placed, and CSF was sampled for cytopathologic evaluation; it was acellular. Resection of the larger mass in the fourth and posterior third ventricles was undertaken, but intraoperative hemorrhage precluded total removal. The pathologic specimen consisted of multiple irregular fragments of tan to dark brown tissue measuring 1.7 × 1.4 × 0.4 cm in aggregate.

Light microscopic examination (Fig. 2) showed the neoplasm to be composed of papillary structures reminiscent of the pseudorosettes of an ependymoma (Fig. 2A), with a loose, epithelioid population of cells among the papillae. The cells demonstrated bland cytologic features (Fig. 2B). Mitotic figures were rare; the Ki-67 proliferation index was 3%. No vascular proliferation or necrosis was seen. Immunohistochemically, the neoplasm was positive for pancytokeratin and cytokeratin 8/18 with a peculiar paranuclear pattern of dense positivity in many cells (Fig. 2C). CD56 (neural cell adhesion molecule) and CD99 were also positive in a membranous pattern (Fig. 2D). Synaptophysin was positive. Epithelial membrane antigen and glial fibrillary acidic protein were entirely negative, the former without any intracytoplasmic dot-like positivity. Stains for TTF-1 and CK7 were negative. Collagen type IV highlighted a multichannel vascular architecture in the papillary structures (Fig. 2E). The diagnosis of PTPR was made based on these findings.

Approximately 1 month after surgery, the patient chose to pursue treatment options at another institution. A second subtotal resection of the residual pineal region mass was carried out, again with intraoperative hemorrhage limiting full resection. Cytogenetic analysis of the resection material from the second surgery revealed a primary clone, which was hypodiploid and characterized by losses of chromosomes 3, 7, 10, and 14 (Fig. 3A), and the presence of a duplicated primary clone additionally characterized by gains of chromosomes 3, 8, 9, and loss of a Y and chromosome 18 (Fig. 3B). Both the primary and duplicated clones were further characterized by a derivative chromosome 5 with additional material translocated to 5q22. The patient subsequently received radiation treatment to the tumor. Now, 17 months after his initial presentation, he is stable without disease progression. Both tumors have shown considerable shrinkage, with the suprasellar lesion barely detectable by magnetic resonance imaging. No leptomeningeal or spinal dissemination has been identified.