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Case Report

Papillary Tumor of Pineal Region; A Case Report

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Abstract

Background: *Papillary tumor of the pineal region (PTPR) is a rare neuroepithelial tumor that was first classified by the World Health Organization (WHO) in 2003. The diagnosis of this tumor is challenging due to its imaging features, which overlap with those of other pineal region tumors, and due to the paucity of pediatric cases reported in the literature.*

Case Presentation: *We present the case of a 4-year-old male patient who exhibited symptoms including progressive headaches, vomiting, and neurological deficits, such as upward gaze palsy and ataxia. Imaging revealed a pineal mass causing obstructive hydrocephalus, initially suspected to be germinoma. Following the placement of a ventriculoperitoneal shunt, the patient underwent gross total resection (GTR) of the tumor through a posterior fossa approach. Histopathological analysis confirmed PTPR (WHO grade 2/3), with papillary structures and immunohistochemical positivity for S100 and CD56. The patient received adjuvant radiotherapy to the surgical cavity (54 Gy in 1.8 Gy fractions), and no recurrence or neurological deficits were observed at the 6-month follow-up.*

Discussion: *PTPR presents significant diagnostic and therapeutic challenges due to its nonspecific imaging features and critical anatomical location. GTR remains the primary treatment modality, often necessitating adjuvant radiotherapy to reduce the risk of recurrence. This case underscores the significance of multidisciplinary approaches and meticulous radiotherapy planning, particularly in pediatric patients, in achieving a balance between benefits and neurocognitive functions.*

Conclusion: *This report underscores the necessity of considering PTPR in pediatric pineal masses and demonstrates that early diagnosis, surgical resection, and adjuvant radiotherapy can result in improved outcomes. Given the low five-year disease-free survival rate, regular and frequent follow-ups are crucial, with careful attention to every sign, symptom, and imaging change.*

Keywords: *Pediatric CNS, Pineal Tumor, Papillary Tumor of Pineal Region, Pineal Region, Neuro-Oncology.*

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Introduction

Pineal region tumors are considered surgically challenging due to their deep location within the brain, which complicates access, and their proximity to critical neurovascular structures, such as the deep cerebral veins and dorsal midbrain. These challenges are further compounded in pediatric patients. Given the broad spectrum of tumors that can arise in this region, surgical resection or tissue sampling is imperative for precise diagnosis, as different tumor types have distinct prognoses and treatment strategies (Favero et al., 2021).

Papillary tumor of the pineal region (PTPR) is a rare and distinct neuroepithelial tumor that was first introduced into the World Health Organization (WHO) classification of central nervous system (CNS) tumors in 2003 (Jouvet et al., 2003). Prior to its inclusion in the aforementioned classification, it was described under various other tumor categories, including papillary pineocytoma, choroid plexus tumor, meningioma, and ependymoma. PTPR exhibits distinctive histological and immunohistochemical features, distinguishing it from other pineal region tumors. While it is most prevalent in adults, the age range is wide, spanning from 5 to 66 years, with a mean age of 31.5 years, as reported by Fèvre-Montange et al. (2006).

The clinical presentation of PTPR is associated with mass effect on adjacent structures. The most prevalent presentation (accounting for up to 80% of cases) is obstructive hydrocephalus, resulting from compression of the cerebral aqueduct. This leads to symptoms of elevated intracranial pressure, including headache, nausea, vomiting, and papilledema. Other presentations include long-term visual disturbances resulting from tectal plate or colliculus compression and Parinaud syndrome (Poulgrain et al., 2011; Ribeiro et al., 2018; Shakir et al., 2015a). Radiological findings typically include a well-defined, contrast-enhancing mass on MRI, an appearance shared by many other tumors in the area, including other pineal tumors, ependymal tumors, germ cell tumors, and metastatic carcinomas. Given the heterogeneity in management of these tumors, a histopathological confirmation is necessary for diagnosis (Chang et al., 2008; Ribeiro et al., 2018). Immunohistochemical analysis frequently reveals positivity for markers such as keratin (CK), epithelial membrane antigen (EMA), and S100 protein, which are critical diagnostic indicators for PTPR (Hasselblatt et al., 2006; Kuchelmeister et al., 2006).

Gross total resection (GTR) is the optimal approach for achieving symptom relief and long-term disease control. However, complete resection may present a challenge in pediatric patients due to the proximity of the tumor to critical structures, such as the vein of Galen and the quadrigeminal plate (Azab et al., 2014; Dagnew et al., 2007). In circumstances where GTR is not feasible, subtotal resection (STR) is often accompanied by adjuvant radiotherapy to mitigate the probability of recurrence (Dagnew et al., 2007; Fèvre-Montange et al., 2006; Yamaki et al., 2019a). The role of adjuvant radiotherapy after GTR remains to be delineated; however, given the high recurrence rate, it is probable that the majority of patients will undergo radiotherapy postoperatively (Lancia et al., 2020). However, the utilization of radiotherapy in pediatric patients necessitates a meticulous approach, with the objective of mitigating the potential for long-term consequences on neurocognitive function and developmental outcomes (Major et al., 2022).

While PTPR generally carries an intermediate prognosis, recurrence is not uncommon, particularly in cases of incomplete resection. The 5-year overall survival and progression-free survival rates are estimated to be 73% and 27%, respectively (Fèvre-Montange et al., 2006).

This report presents a case of PTPR in a pediatric patient, emphasizing the unique challenges in clinical management and reviewing available literature on outcomes and therapeutic strategies in the pediatric population.

Case Presentation

History

A 5-year-old male patient exhibited symptoms including progressive headaches, generalized weakness, poor appetite, and vomiting over a period of one month, accompanied by neurological findings such as impaired upward gaze, nystagmus, and ataxia.

Imaging Findings

A CT scan performed at the emergency department following the patient's clinical deterioration revealed a 30 * 20 mm well-defined, heterogenous pineal region mass with engulfed calcification, causing dilatation of the third and lateral ventricles, suggesting pineal germinoma.

Contrast-enhanced MRI (**Figure 1**) revealed a 30 * 20 * 23 mm mass at the pineal region, iso-intense in T1, T2, and FLAIR sequences, restricted in diffusion, and vividly enhancing post-contrast, resulting in moderate hydrocephalus in the third and lateral ventricles with periventricular effusion. These findings are consistent with a diagnosis of pineal germinoma. A comprehensive neuraxis MRI revealed no additional lesions.

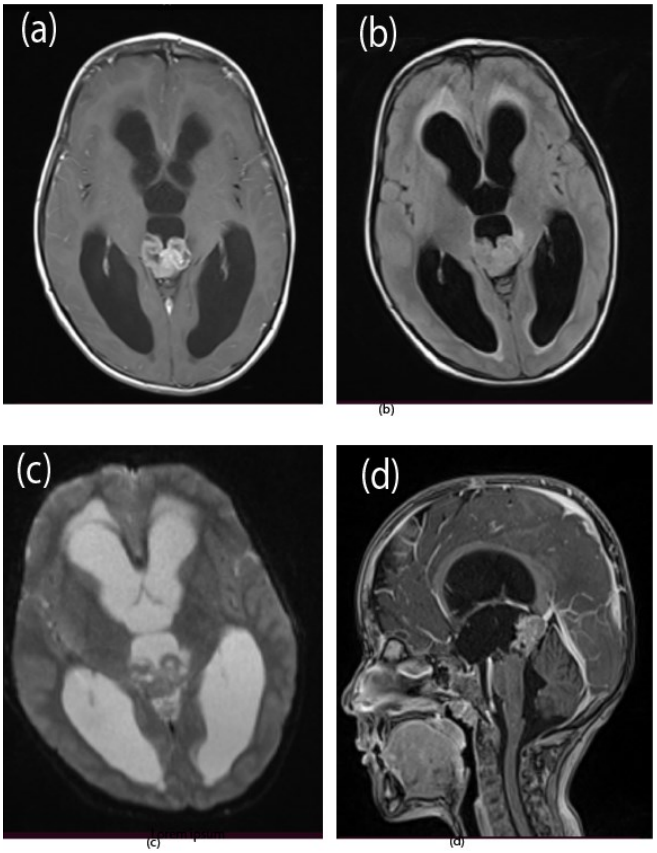

Figure 1. Pre-Operative MRI, (a): T1 Post Contrast, (b) FLAIR, (c) Diffusion Weighted Series, (d) Sagittal View T1 Post Contrast.

Surgical Intervention

Subsequent to the imaging diagnosis, the patient underwent ventriculoperitoneal shunt placement surgery to alleviate the hydrocephalus. Once the patient's condition stabilized, he underwent laboratory investigations focusing on germ cell tumor markers. All the panels returned to normal, including the tumor markers and CSF cytology.

Following further neurosurgical consultations and extensive discussion in MDT, the decision was made to proceed with open surgery aiming for GTR. The surgical procedure was performed via an incision in the midline of the posterior fossa, with the dura opened through a left infratentorial suprasellar approach, and the tumor was completely excised.

Postoperative Course

The patient exhibited a smooth postoperative recovery, regaining the majority of his basic activities by the tenth day after the operation. A post-operative MRI revealed the absence of the pineal gland and the absence of a space-occupying lesion. The patient also had a ventriculoperitoneal shunt placed in the right lateral ventricle, with the tip positioned in the ventral horn.

Histopathological Examination

A histopathological examination was conducted, which revealed the following findings:

Due to the absence of stereotactic biopsy and the tumor location, the preoperative biopsy was not performed. The initial histopathological report indicated the presence of multiple papillary structures lined by multiple layers of cuboidal cells, moderate nuclear atypia, scattered mitoses, and foci of necrosis. No microvascular proliferation was observed. Subsequent immunohistochemistry panel testing revealed strong diffuse positivity for S100 and CD56, along with punctate positivity for AE1/3. Conversely, GFAP, PLAP, OCT 3/4, chromogranin, and synaptophysin were negative. Ki-67 labeling index revealed an approximate value of 15-20%. These findings collectively indicate a diagnosis of papillary tumor of the pineal region, classified as World Health Organization (WHO) grade 2-3.

To ensure the accuracy of the diagnosis, a second opinion was sought from an independent laboratory. This second evaluation involved a review of both slides and a repetition of the IHC panel. The results of this second evaluation were consistent with those of the initial evaluation, confirming the initial diagnosis.

Radiotherapy

The patient was scheduled to receive postoperative adjuvant radiotherapy. One month after surgery, he underwent conventional external beam radiotherapy (EBRT). The treatment was simulated in a supine position with thermoplastic mask fixation. A CT series with 2.5 mm slice thickness was acquired, and the target volume was delineated as the surgical cavity on fused MRI series with the addition of 1.0 cm extra margin, constrained by anatomical barriers. The prescribed dose was 54 Gy in 1.8 Gy daily fractions. The planning was performed utilizing a full-arc VMAT technique. Special attention was given to organs at risk, including both hippocampi. The radiation treatment course proceeded without incident, with the exception of acute toxicity manifested as nausea. This adverse effect was addressed through the administration of a short-term corticosteroid. Concurrent or adjuvant chemotherapy was not offered.

The patient has been under follow-up since the completion of radiotherapy, with MRI imaging conducted periodically (**Figure 2**). After eight months of treatment, no recurrence or abnormal MRI signals were observed, and the patient was found to be fully active with no neurological abnormalities.

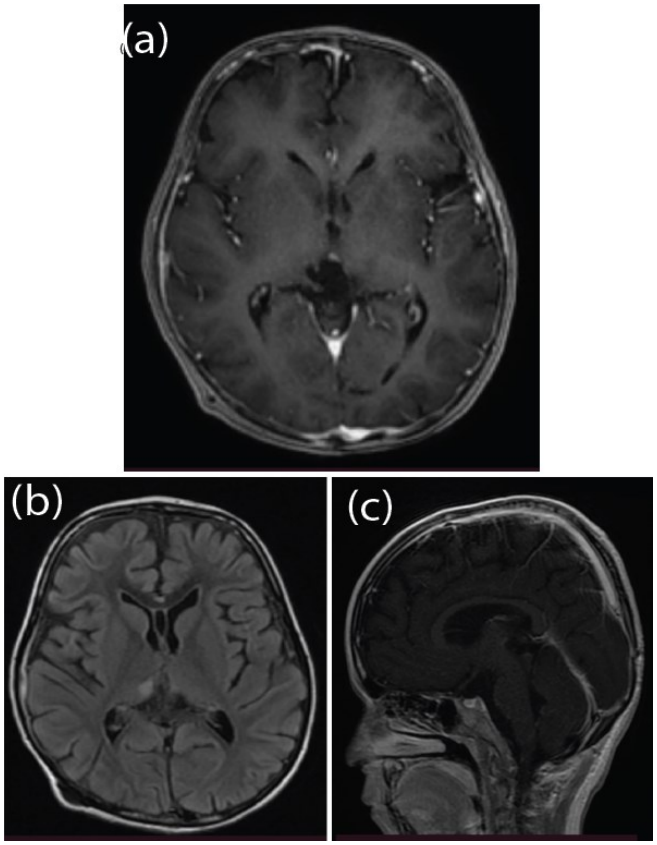

Figure 2. Eight Months Post Treatment MRI; (a) T1 Post-Contrast, (b) FLAIR, (c) Sagittal T1 Post-Contrast

Discussion

PTPR, being an uncommon neoplasm, poses a considerable diagnostic challenge due to its location, as it can be mistaken for more prevalent pediatric brain neoplasms, particularly central nervous system germinomas. In such cases, surgical intervention is often limited to diagnostic biopsy, with chemotherapy and radiotherapy serving as the primary treatment approaches (Osorio & Allen, 2015). The absence of unique imaging characteristics that distinguish PTPR from other tumors in the region poses a significant diagnostic challenge. Its variable T1 and T2 enhancement patterns have been observed to overlap with those of several other tumors, including germinomas, ependymomas, pineal parenchymal tumors, and metastases (Chang et al., 2008; Ribeiro et al., 2018; Smith et al., 2010; Vandergriff et al., 2012).

Despite the tumor's radiological resemblance to germ cell tumors, open surgery was opted for with the aim of achieving gross total excision. This approach was justified by the following factors: the tumor's unicentric and respectable nature, negative germ cell tumor markers, a neuraxis MRI showing no abnormalities, and the inaccessibility of stereotactic biopsy. It is widely acknowledged that complete surgical removal is the most significant prognostic factor and is associated with enhanced disease-free survival. Other prognostic features include the tumor size and mitotic index (represented by Ki-67) (Heim et al., 2014; Mobark et al., 2022; Yamaki et al., 2019b).

Given the high recurrence rate associated with PTPR, the recommendation is often for adjuvant radiotherapy, even after GTR (Lancia et al., 2020). However, the existing body of literature does not provide sufficient data to determine the most appropriate radiotherapy technique or modality. Conventionally, fractionated radiotherapy, stereotactic radiosurgery, and stereotactic radiotherapy are all employed in extant literature. The treatment volumes also vary, encompassing local, whole ventricular, whole cranial, and craniospinal irradiation (Edson et al., 2015; Fauchon et al., 2013; Kim et al., 2010; Shakir et al., 2015b). A notable study by Fèvre-Montange et al. (2006) reported a mean survival of 57.4 months for patients undergoing conventionally fractionated EBRT for resected PTPR cases, with most patients experiencing recurrence within five years. In this particular instance, the patient underwent external beam radiotherapy (EBRT) to the surgical bed with 1 cm expansion for the CTV, constrained by anatomical barriers. Meticulous attention was paid to organs at risk, including the hippocampi, to minimize long-term neurocognitive sequelae. The total dose of 54 Gy was administered in 1.8 Gy fractions. The absence of data concerning the benefits of larger treatment volumes and the potential neurocognitive toxicity associated with them, particularly in this age group, justified the utilization of the aforementioned treatment technique. It is noteworthy that no concurrent chemotherapy was administered in this case, due to the limited efficacy of chemotherapy in PTPR (Fauchon et al., 2013; West et al., 2015).

The study's limitations include its relatively brief follow-up period, and the absence of long-term neurocognitive assessments related to surgical and radiation interventions. We intend to continue monitoring the case and present updates in future reports.

Conclusion

Papillary tumor of the pineal region (PTPR) poses significant diagnostic and therapeutic challenges, particularly in pediatric patients. Gross total resection (GTR) is paramount for enhancing prognosis, while adjuvant radiotherapy is frequently imperative due to the tumor's high recurrence rate. This case underscores the necessity for meticulous surgical and radiotherapy planning to optimize tumor control while minimizing neurocognitive risks, particularly in younger patients. While the short-term prognosis appears favorable, it is imperative to emphasize the necessity of regular and frequent follow-ups, with meticulous observation of every sign, symptom, and imaging change, given the relatively low five-year disease-free survival rate.

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