

Case Report

Papillary Tumor of the Pineal Region: A Case Report and Literature Review

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To cite this article:

Peng Lilin, Zhong Lijuan, Yang Bo, Lu Yuanzhi. Papillary Tumor of the Pineal Region: A Case Report and Literature Review. *American Journal of Clinical and Experimental Medicine*. Vol. 11, No. 2, 2023, pp. 29-32. doi: 10.11648/j.ajcem.20231102.11

Received: February 7, 2023; **Accepted:** March 1, 2023; **Published:** March 20, 2023

Abstract: Pineal tumors of the pineal region (PTPR) are rare neuroepithelial tumors of the central nervous system, and their clinical features often lack specificity, so it is always difficult to make a definite diagnosis before surgery, and the treatment is mainly based on complete surgical resection. We report the case of a 21-year-old male who presented with intermittent dizziness and headache with vomiting for more than 2 months. The imaging revealed a mass in the region of the pineal region with obstructive hydrocephalus. After the hospitalization, the patient underwent a microscopic excision of the pineal mass, and the tissue was sent for histopathological examination and available immunohistochemical tests, which resulted in a definitive diagnosis of a papillary tumor of the pineal region. He had undergone several radiation treatments during his hospitalization and remained recurrence-free until the latest follow-up visit. This article highlights the similarities between this case and the PTPR described in WHO 2021 in terms of clinical presentation, imaging, and histopathological features. Therefore, this case report completes the sample database of PTPRs. By reviewing the literature related to PTPRs, we hope that this report will be helpful to improve the understanding of clinicians and pathologists about this rare tumor. However, more relevant studies are needed to clarify the pathogenesis, prognosis, and optimal treatment options to achieve early diagnosis, early treatment, and improved prognosis.

Keywords: Papillary Tumor of the Pineal Region, PTPR, Pineal Parenchymal Tumor, Diagnosis

1. Introduction

Pineal parenchymal tumors are neuroepithelial tumors originating from the epithelial and mesenchymal cells of the pineal region and account for less than 1% of all primitive central nervous system (CNS) tumors and 15% to 30% of pineal tumors [1-2]. These tumors are uncommon, and among them, papillary tumors of the pineal region (PTPR) are even rarer, with an incidence of approximately 1% in adult intracranial tumors [3]. As a neuroepithelial tumor, papillary tumors of the pineal region were originally described by Jouve et al. in 2003 [4] and were included in the 2007 World Health Organization (WHO) classification of tumors of the central nervous system [5]. PTPRs are characterized by a combination of papillary structures and solid regions with morphological features of epithelial-like

cells and strong immunoreactivity to cytokeratin [6]. However, the pathogenesis of PTPRs has not been fully elucidated, and some studies prompt the possibility of an association with the loss of chromosome 10 and the gain of chromosomes 4 and 9 [7-8], where the genetic alterations of PTEN have been described [9]. Epidemiological data on these rare tumors are limited, and the published reports suggest that they can occur in both children and adults without gender preference [10]. Notably, the limited prognostic data indicate a high frequency of local recurrence of PTPRs and the possibility of spinal dissemination [11]. Moreover, surgical resection and the increased mitotic and proliferative indices were strongly correlated with the prognosis of PTPRs [12].

2. Case Presentation

2.1. Clinical Information

The patient, a 21-year-old male, was admitted to the hospital with intermittent dizziness, headache, and vomiting for approximately 2 months. There was neither an obvious trigger nor an abnormal family history, and no enlargement of superficial lymph nodes was noted during the physical examination. After admission and completion of ancillary examination such as hematology and imaging, the results showed that the concentration of Ferritin (558.02 ng/ml) was elevated and the concentration of β -human chorionic gonadotropin (β -HCG) was normal (0.26 mIU/ml). The cranial CT and MRI showed an occupying lesion in the pineal region, occlusion of the midbrain aqueduct, fluid in the superior ventricular system, and demyelinating changes in the white matter of the cerebrum around the bilateral ventricles and of the cerebrum in the hemi-oval center (Figure 1); in addition, cranial vascular CTA showed bilateral embryonic posterior cerebral arteries and a small A1 segment of the left anterior cerebral artery. After discussion, the patient was preoperatively diagnosed with a germ cell tumor, and the tumor was subsequently removed from the posterior ventricle under the microscope. Intraoperatively, the tumor was observed to be located in the posterior part of the third

ventricles, grayish red in color, soft, adherent to the surrounding tissues, and rich in blood supply, and the midbrain conduit was opened after the lesion was removed. Postoperative histopathological examination clarified that the patient was diagnosed with PTPR.

The patient was discharged from the hospital after finishing postoperative combination chemotherapy and was in good general condition with normal laboratory parameters. We advised him to review regularly at the outpatient clinic, and the last telephone follow-up was in February 2023 (Table 1). Until February 2023, the tumor markers were normal and MRI did not show any evidence of recurrence.

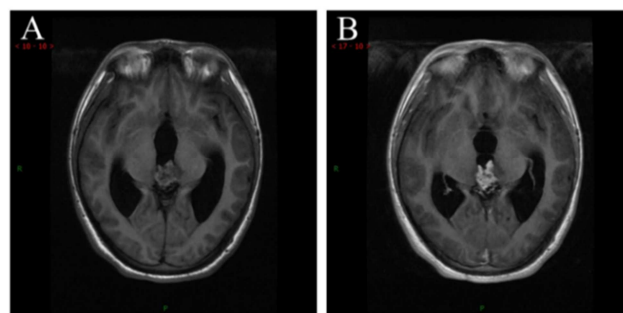


Figure 1. MRI of papillary tumor of the pineal region. (A) shows the MRI plain T1-weighted image (T1WI); (B) shows the enhanced scan image.

Table 1. Timeline.

Time	Clinical process
January 01, 2021	First symptoms: intermittent dizziness and headache with vomiting
March 1, 2021	Cranial MRI: the pineal region is occupied, consider germ cell tumor
March 2, 2021	Hospitalization
March 4, 2021	Laboratory tests: Ferritin: 558.02ng/mL, β -HCG: 0.26mIU/ml
March 5, 2021	CT cranial vessels: the pineal region and the pars intermedia of the midbrain aqueduct are occupied, bilateral embryonic posterior cerebral arteries
March 9, 2021	Cranial MRI: the pineal region is occupied, consider germ cell tumor, size about 2.4*2.0*2.5 cm
March 13, 2021	After discussion with the neurosurgery team, elective surgery treatment was performed
March 15, 2021	Surgical treatment
April 1, 2021	Refining the radiotherapy plan
April 7, 2021	Start radiotherapy
May 16, 2021	Finish radiotherapy
May 18, 2021	Discharge from hospital
February 03, 2023	Latest follow-up

2.2. Histological and Immunohistochemical Characteristics

After adequate fixation with 10% neutral formalin, the tissue appeared off-white or gray-red, with moderate hardness, and a size of approximately $2.0 \times 2.0 \times 2.3$ cm. Microscopically, the tumor tissue was mainly composed of cuboidal or columnar epithelial-like cells with clear cytological boundaries. The cytoplasm was eosinophilic and partially translucent, and the nuclei were round to ovoid, with obvious heterogeneity and speckled chromatin. However, defined nuclear fission images are less commonly seen. Equally significantly, the tumor tissue was principally arranged in a papillary, micropapillary, or solid lamellar pattern, with locally visible pseudo-rose nodes, as well as invasion of the brain parenchyma (Figure 2).

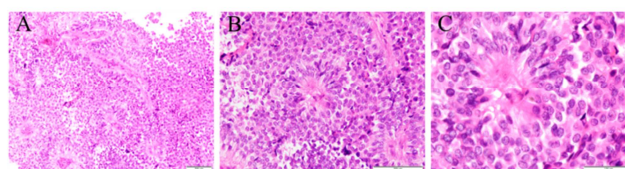


Figure 2. Light microscopy and immunohistochemical features of papillary tumor of the pineal region. (A) PTPR with a striking papillary structure. (B) The vessels are surrounded by layers of large, acidophilic columnar cells. (C) The nuclei are round to oval and the chromatin is stippled (hematoxylin-eosin staining, original magnification: A $\times 10$; B $\times 20$; C $\times 40$).

The immunohistochemistry was: AE1/AE3(+), Vim(+), GFAP(partial +), S-100(partial +), CD56(+), SSTR(partial +), Nestin(partial +), H3K27me3(+), EMA(-), PR(-), NeuN(-), Olig-2(-), Syn(-), CgA(-), CEA(-), H3K27m(-), PTEN (-),

Ki-67 (5%) (Figure 3).

The patient was eventually diagnosed with a papillary tumor in the pineal region (WHO grade II to III).

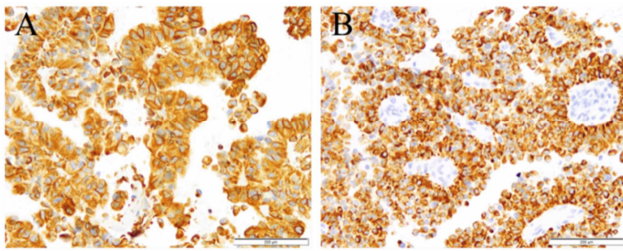


Figure 3. Immunohistochemical test results of papillary tumor of the pineal region. Tumor tissue is diffusely positive for vimentin (A) and AE1/AE2 (B) (EnVision, original magnification: A, B $\times 20$).

3. Discussion

The biological and clinical behavior of PTPR is alterable. Most of them correspond to WHO grade II and the more aggressive ones may correspond to grade III, but no usable histological grading criteria have been proposed to define them precisely [5, 13]. At the time of presentation, patients experience the highest frequency of elevated intracranial pressure, while other symptoms are relatively common, including Parinon syndrome, ataxia, and isolated diplopia [14]. Radiographically, PTPRs generally show clear boundaries, mild lobulation, focal cystic lesions, and enhanced heterogeneity of the mass, usually accompanied by obstructive hydrocephalus [15-16]. They seem to be difficult to distinguish from other intracranial tumors, especially pineocytomas [15, 17]. Nevertheless, a portion of previous PTPR-related reports described high signal in non-contrast T1-weighted sequences [18-19], which may be a result of the high concentration of secreted material in the small cystic spaces and may contribute to the diagnosis of PTPR [20]. In contrast, no hyperintensity signal was found in other cases [21-22], including ours, suggesting a difference in radiographic presentation among the lesions.

It is well known that PTPRs is characterized by papillary formations and an epithelial growth pattern [10]. These epithelial-like tumor cells are chiefly cuboidal and columnar with eosinophilic or somewhat hyaline cytoplasm. Besides, this solid tumor usually exhibits ventricular tubular-like differentiation, with blood vessels frequently covered by large, pale-to-eosinophilic columnar cell layers in papillary areas. Further immunohistochemistry demonstrates that these tumor cells are strongly reactive to cytokeratin, specifically to cytokeratin 18 (CK18) [23] as well as varying degrees of expression of neuron-specific enolase (NSE), wave proteins, glial pro-fibrillary acidic protein (GFAP), and S-100. The diagnosis of this tumor is always complex due to its similarity to other primary or secondary papillary lesions in the pineal region, including pineal parenchymal tumors, papillary ependymoma, choroid plexus papillomas, germ cell tumors with papillary features, and metastatic papillary carcinoma [24].

The clinical course of PTPRs is often complicated by frequent local recurrences, leading to a continuing controversy about the optimal treatment of PTPRs. Whether surgery, radiation, or chemotherapy is applied individually or combinedly, research has revealed that PTPR is unavoidably prone to recurrence [23]. However, a large study showed that chemotherapy did not seem to affect overall survival (OS) or progression-free survival (PFS) [11]. Currently, the definitive treatment for patients with PTPRs involves mainly surgical resection in combination with radiotherapy [9]. Unfortunately, the outcome of these patients remains poor and even fatal, with a 5-year OS of 73% and a 10-year of 58% [25]. Therefore, what we still need is to continue exploring new potential therapeutic targets to prolong PFS.

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