

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

Tumor papilífero da região pineal: relato de caso e revisão da literatura

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Abstract

Papillary tumor of the pineal region (PTPR) is a neuroectodermal tumor thought to originate from cells of the subcommissural organ. Its oncologic properties are still under investigation, as well as the most suitable therapeutic measures for this type of neoplasm. We report the case of a 36-year-old woman with a 1-year history of headache and intermittent diplopia. The magnetic resonance imaging (MRI) scan showed a heterogeneously enhancing mass in the pineal region that caused an acute hydrocephalus, and an emergency shunt derivation was necessary. One week later, the patient was submitted to subtotal tumor resection, and remained asymptomatic in the post-operative period. In the follow-up, the patient remained asymptomatic; in the imaging control 3.5 years after the surgical resection, local recurrence was identified, and the patient was submitted to a local radiation protocol. Our literature review showed an early clinical onset due to intracranial hypertension signs. Definitive clinical onset might be reached only through a histopathological examination. Gross total resection followed by radiotherapy is the current standard of care. Local recurrence is often observed, with rare dissemination to the cerebral spinal fluid. The natural history of the PTPR remains unknown, as well as the best treatment strategy. Large case series with longer follow-ups are necessary for further conclusions.

Keywords

- pineal gland
- brain tumor
- surgical procedures
- local recurrence

Resumo

O tumor papilífero da região pineal (TPRP) tem origem neuroectodérmica nas células do órgão subcomissural. Suas propriedades oncológicas ainda estão sob investigação, assim como as medidas terapêuticas mais adequadas para este tipo de neoplasma. Relatamos o caso de uma paciente do sexo feminino, de 36 anos, com um histórico de um ano de cefaleia e diplopia intermitente. O exame de imagem de ressonância

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Palavras-chave

- glândula pineal
- tumor cerebral
- tratamento cirúrgico
- recorrência local

magnética (RM) evidenciou massa em topografia da glândula pineal com captação heterogênea ao contraste. Tal lesão tumoral provocou hidrocefalia aguda obstrutiva, com necessidade de derivação de emergência do ventrículo peritoneal. Após 1 semana, a paciente foi submetida a ressecção subtotal do tumor e permaneceu assintomática no período pós-operatório. Durante o acompanhamento, a paciente manteve-se assintomática, com recorrência local da lesão após 3,5 anos, e foi submetida a um protocolo local de radiação. Após revisão da literatura, grande parte dos tumores papilíferos da região pineal tiveram diagnóstico precoce, especialmente devido a sinais de hipertensão intracraniana. Os achados em exames de imagem não são específicos, e o diagnóstico definitivo só pode ser obtido por meio de avaliação histopatológica. Ressecção cirúrgica seguida de radioterapia tem se mostrado a melhor alternativa terapêutica. A recorrência local sido é observada de modo frequente em tumores tratados, mas raramente com disseminação a distância para o líquido cefalorraquiano. A história natural dos tumores papilíferos da região pineal ainda está sob investigação, assim como a melhor estratégia de tratamento. Séries de casos com amostras maiores e acompanhamento mais prolongado são necessárias para que se obtenham conclusões mais consistentes.

Introduction

The pineal region is the site for the occurrence of several unique tumors, each with a distinct biological behavior and, therefore, with a specific treatment and prognosis.^{1–3} Parenchymal neoplasms are the most common finding in this region (that is, pineoblastoma, pineocytoma); however, germ cell tumors, meningiomas, ependymomas and astrocytomas have also been described.^{4,5}

Papillary tumor of the pineal region (PTPR), a rare entity, has been described in the medical literature by Jouvett et al⁶ in 2003, and included in the World Health Organization (WHO) classification of central nervous system (CNS) tumors as of 2007.⁷ Papillary tumor of the pineal region is a neuroectodermal tumor that is thought to originate from cells of the subcommissural organ.⁸ Its oncologic properties are still under investigation, as well as the most suitable therapeutic measures for this type of neoplasm. Since its recognition as a distinct entity, several case reports and case series have addressed the features of PTPR. The present paper describes our experience with a case of PTPR, followed by a review of the literature regarding this rare neoplasm.

Case Report

A 36-year-old woman with a 1-year history of headache and intermittent diplopia was under investigation at our institution. The neurologic exam was unremarkable. The magnetic resonance imaging (MRI) scan showed a 2.0 × 1.5 × 1.0-cm, heterogeneously-enhancing mass at the pineal topography. The lesion was hyperintense in T1, with multiple small cysts inside the tumor and a close relationship with both internal cerebral veins (►Fig. 1). One week later, the patient was recruited through the elective surgery schedule; however, she did not attend the hospital.

Two weeks later, the patient was admitted to the emergency department with progressive deterioration of her level of consciousness. A computed tomography (CT) scan demonstrated complete obstruction of the cerebral aqueduct and the onset of acute hydrocephalus. The patient was taken to the operating room for a ventricle derivation, with complete resolution of the symptoms of hydrocephalus. One week after the emergency surgery, the patient underwent a subtotal tumor resection through a supracerebellar infratentorial approach, as the lesion infiltrated the superior segment of the midbrain (►Fig. 2). The postoperative period was uneventful, with early hospital discharge. During follow-up, she remained asymptomatic. The MRI scan showed regrowth 3.5 years after the surgery (►Fig. 3). She was then submitted to adjuvant radiotherapy with local irradiation. The tumor remained stable after irradiation.

Histopathologic Findings

A microscopic examination of the lesion revealed a proliferation of polygonal epithelioid cells arranged in a predominantly papillary pattern, surrounding broad fibrovascular cores. The nuclei were round to oval, with finely speckled chromatin and little pleomorphism. The immunohistochemistry was performed. The neoplastic cells stained diffusely positive for cytokeratin 35 β H11. Focal S-100 staining and scattered glial fibrillary acidic protein (GFAP) reactivity were noted. The Ki-67 proliferative index was estimated as 10%. Other markers, such as the epithelial membrane antigen (EMA), the placental alkaline phosphatase (PLAP), synaptophysin and neurofilament were negative (►Table 1).

Discussion

Tumors of the pineal region account for less than 1% of brain tumors in Europe and North America.⁹ Despite their rarity, a plethora of different entities can be found at this site.⁹

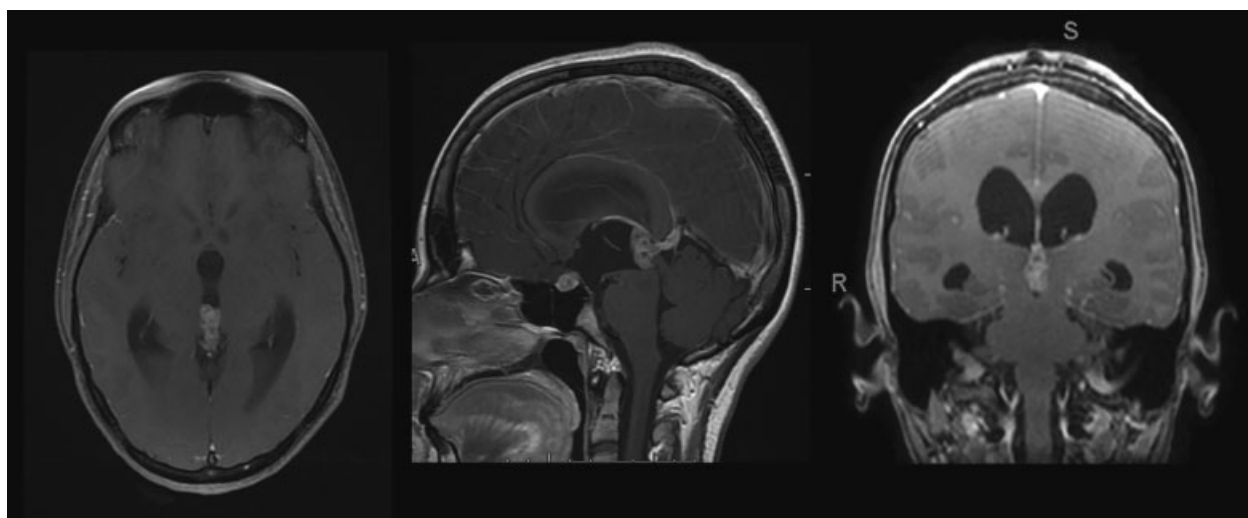


Fig. 1 Heterogeneous pineal mass with multiple cysts within a solid enhanced component in T1 postcontrast image.

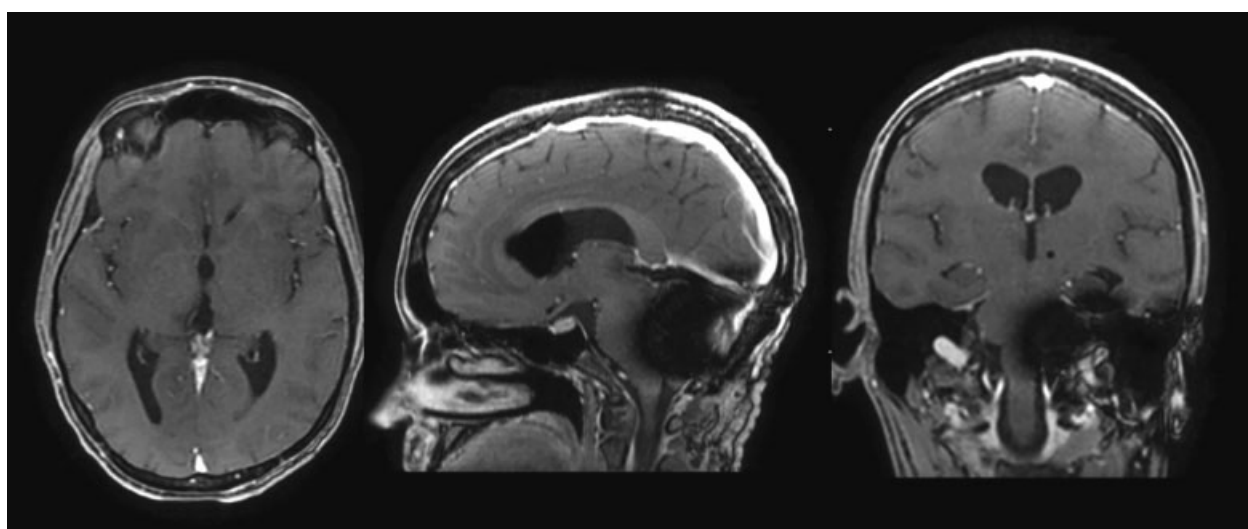


Fig. 2 Axial, sagittal and coronal T1 postcontrast image demonstrating subtotal resection of the pineal mass.

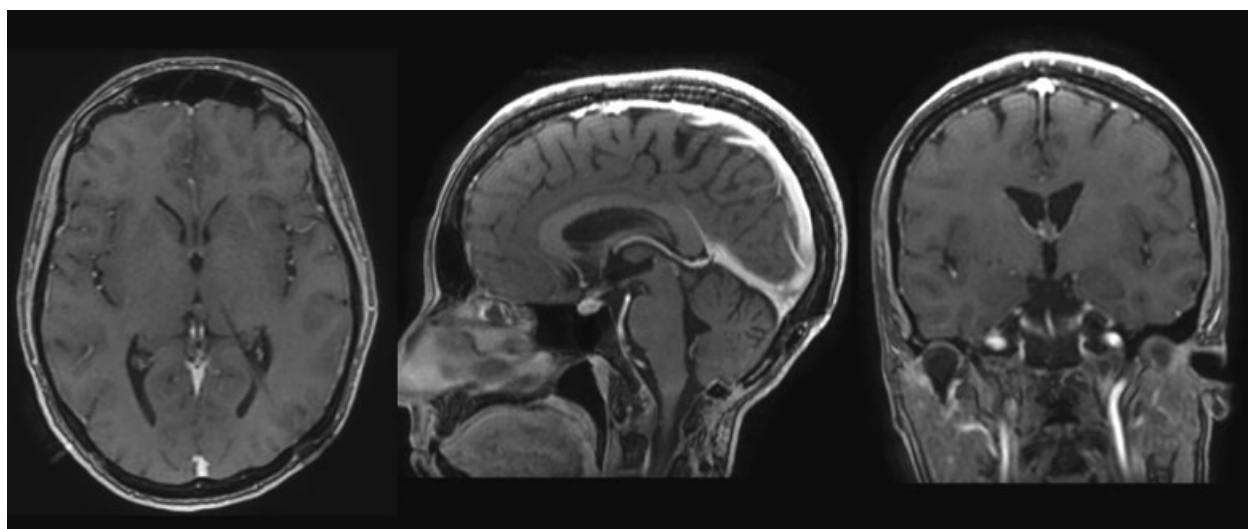


Fig. 3 Axial, sagittal and coronal T1 postcontrast image demonstrating local recurrence of the PTPR, measuring 2.1×1.3 cm, especially in the posterior part of the III ventricle.

Table 1 Immunohistochemical characteristics of the neoplasm

Cytokeratin 35βH11	+ ^a
EMA	—
PLAP	—
GFAP	+ ^b
Synaptophysin	—
S-100	+ ^c
Neurofilament	—
Ki-67	+ ^d

Abbreviations: —, negative immunoreactivity; EMA, epithelial membrane antigen; PLAP, placental alkaline phosphatase; GFAP, glial fibrillary acidic protein; +^a, positive immunoreactivity; +^b, Weak immunoreactivity; +^c, Focal expression of S-100; +^d, Ki-67 index was estimated as 10%.

Histopathological examination following tumor biopsy or resection is required to achieve a definitive diagnosis. Our patient developed the typical clinical presentation of a pineal tumor, with visual disturbance and headache as initial symptoms, eventually complicated by an acute hydrocephalus that required an urgent shunt procedure.

Most papers advocate surgical removal as the main therapeutic measure for PTPR,^{2,3,10–18} however, the proper adjuvant therapy and its efficacy remain unknown. Our patient underwent surgery as the initial treatment, and local radiation at recurrence, and remains with a good functional outcome.

Clinical Presentation

The pineal gland produces and secretes melatonin.^{1,2} Symptoms from tumors located in the pineal region are, however, related to its mass effect against adjacent structures. In the literature, the most common clinical presentation is cerebral aqueduct occlusion and consequent hydrocephalous. Therefore, in ~ 80% of case reports patients exhibited signs of increased intracranial pressure, such as bilateral papilledema, abducens nerve palsy, morning headache or vomiting without nausea. Long-term visual disturbances were also often described, which may be attributed to compression of the mesencephalic tectal area or of the superior colliculus. Parinaud syndrome was described in less than 10% of the cases, and it might be misdiagnosed in an emergency situation of acute hydrocephalus.^{1–3,6–8,10–68}

Regarding its biological behavior, PTPR shows a high propensity toward local recurrence, but only rarely disseminates to the spine. Hong et al¹⁵ reported tumor dissemination to the spinal cord at the level of L3. Kim et al³⁷ described the case of a 39-year-old woman with secondary implants at the pituitary stalk and bilateral internal acoustic canals. Moreover, Nowicka et al⁶⁵ evidenced cerebral spinal fluid (CSF) dissemination of PTPR to the subependymal region of the frontal horns and the stem of the lateral ventricles. Therefore, the authors have encouraged an MRI scan of the whole cerebrospinal axis after the histopathologic diagnosis. More accurate case series with longer follow-ups are necessary to determine the accurate natural history of the PTPR.

Imaging

The differential diagnosis of pineal tumors by imaging methods is vast. A heterogeneous enhancing mass with some cystic component might be representative of a great variety of CNS neoplasms, such as pineal parenchymal tumors, ependymal tumors, germ cell tumors and even metastatic carcinomas. The intensity of the PTPR is variable in MRI weighting images.^{1,4,26} Tumor size usually ranges from 2 to 3 cm, and the volume ranges from 10 to 14 cm.³

Histopathology

Papillary tumors of the pineal region are epithelial-like neoplasms arranged in papillary or solid architecture. In papillary areas, fibrovascular cores are broad, and may have multiple capillaries with a pseudoangiomatous appearance. These vessels are covered by a multilayered large columnar epithelium with a pale eosinophilic cytoplasm. In more solid areas, the cytoplasm may become clear or vacuolated, harboring an eosinophilic periodic acid-Schiff positive intracytoplasmic mass.

The nuclei are round to oval and basally situated. Chromatin is finely stippled, and small nucleoli may be seen. Some tumor cells feature anisonucleosis, hyperchromasia and multinucleation – these changes are thought to be more reactive in nature rather than reflecting a more aggressive biological behavior. Perivascular pseudorosettes, true rosettes, tubules and canals have been reported, and are more prominent in areas with solid architecture. This should warrant a differential diagnosis with ependymoma. Mitotic figures are variable, ranging from none to frequent. Necrosis is a common finding.^{6,35,69,70}

Careful evaluation of the immunophenotype is pivotal to the diagnosis of PTPR. Strong reactivity for a broad spectrum of cytokeratins (Cam 5.2, AE1/AE3, CK8, and CK18), especially CK18, appears to be the most distinctive feature of this neoplasm. Staining for S100, neural cell adhesion molecule (NCAM), neuron-specific enolase and transthyretin is frequent. Immunoreactivity for GFAP, synaptophysin, chromogranin and neural antigens is usually absent, although some cases may exhibit focal, weak staining. Ki67 staining is variable, and the correlation with the biological behavior has not been established. Some authors advocate that a higher proliferative activity is found in younger patients.¹²

Although there are well-defined diagnostic criteria for PTPR, divergent findings in the literature and the low number of cases have deterred the establishment of a histologic grading scale that correlates with the prognosis. Therefore, systematic review studies are needed so that evidence-based conclusions regarding PTPR can be drawn.

Treatment

The therapeutic planning for PTPR is guided by effective treatments for other pineal tumors and by the opinion of experts. Most papers agree that tumor resection should be the first step in the treatment protocols. The actual need and efficacy of adjuvant therapy remain unknown. Surgical resection followed by local radiation was the most employed strategy to manage this type of tumor.

Freve-Montange et al¹² published one of the largest series in the current literature, reporting 31 cases of PTPR. Adjuvant radiotherapy was used in 40% (12/30) of these patients, with a mean survival of 57.4 months. Recurrent tumors were treated with radiotherapy alone.

Dagnew et al,¹ in 2007, reported 3 illustrative cases of PTPR treated by partial surgical resection followed by stereotactic radiosurgery (SRS) 1 month after surgical resection. In the last follow-up, the patients had remained with a good functional status 50 months after the treatment.

Cardenas et al²⁵ and Kim et al³⁷ used gamma-knife radiosurgery without surgical resection, and both of their patients presented early recurrence and needed additional therapy. Adjuvant platinum-based and temozolomide chemotherapy in addition to radiotherapy were the main treatments chosen in the studies retrieved, especially in cases of recurrence or evidence of CSF dissemination.

Conclusion

Papillary tumor of the pineal region must be included in the differential diagnosis of pineal masses. The definitive diagnosis relies on the histopathological evaluation. Gross total resection followed by radiotherapy is the current standard of care in most studies. The precise biological behavior of PTPR is not determined; local recurrence is common after the first treatment, and rare cases of CSF dissemination have been described. Large case series with longer follow-ups are necessary in order to draw further conclusions.

Conflict of Interests

The authors have none to declare.

Funding Information

The authors have none to declare.

Ethical Statement

We confirm that this study is original, never before published, and it is not under consideration by any other journal. This research is in compliance with ethical standards, and informed consent was obtained from all individual participants included in the study.

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The authors have none to make.

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