Pineal Parenchymal Tumor of Intermediate Differentiation (PPTID): Case Report of an Unusual Malignant Entity

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Abstract

We report a case of a 46-year-old Puerto Rican female presenting with complaints of headaches accompanied by dizziness, and nausea. A brain MRI showed a pineal region mass. Histopathologic evaluation confirmed a Pineal Parenchymal Tumor of Intermediate Differentiation (PPTID), WHO (World Health Organization) grade II. This is an extremely rare malignant neoplasm that accounts for <1% of all intracranial tumors in the adult population. We describe the clinical and imaging findings as well as the histopathologic appearance and immunohistochemical profile of this unusual tumor entity.

Key Words

Pineal Parenchymal Tumor of Intermediate Differentiation; Pineal Parenchymal Tumor; Pineal Tumors

Introduction

Neoplasms originating from the pineal region are very uncommon and account for <1% of all intracranial tumors in the adult population2,3,4 and 3-8% of all intracranial tumors in the pediatric population.1 In adults, only 14-30% of pineal region tumors are of pineal parenchymal origin.5 PPTID are a recently described pineal parenchymal tumor category, and only limited documentation is available regarding their biological behavior and pathological features. We present the case of a 46-year-old Puerto Rican woman diagnosed with PPTID. To our knowledge, this is the first case reported in the Island.

Table 1. Immunohistochemical analyses for tumor phenotype

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Result</th>
<th>Positive</th>
<th>Negative*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Leukocyte Antigen (CD45)</td>
<td>POSITIVE</td>
<td>POSITIVE</td>
<td>NEGATIVE*</td>
</tr>
<tr>
<td>Neuron Specific Enolase (NSE)</td>
<td>POSITIVE</td>
<td>POSITIVE</td>
<td>NEGATIVE*</td>
</tr>
<tr>
<td>Chromogranin A (CHRA)</td>
<td>WEAKLY POSITIVE</td>
<td>POSITIVE</td>
<td>1%</td>
</tr>
<tr>
<td>Synaptophysin (SYN)</td>
<td>POSITIVE</td>
<td>POSITIVE</td>
<td>NEGATIVE*</td>
</tr>
<tr>
<td>Proliferation marker, including G1, S, G2 and M phases (Ki-67)</td>
<td>POSITIVE</td>
<td>POSITIVE</td>
<td>NEGATIVE*</td>
</tr>
<tr>
<td>Gial fibrillary acidic protein (GFAP)</td>
<td>POSITIVE</td>
<td>POSITIVE</td>
<td>NEGATIVE*</td>
</tr>
</tbody>
</table>

*Internal control positive

Clinical Presentation

A 46-year-old female presented with complaints of two-week severe headaches accompanied by dizziness and nausea. A medical history of hypoglycemia, osteoarthritis and osteoporosis was obtained.

A brain MRI showed and enhancing pineal region mass, measuring up to 2.6 cm in diameter displacing the tectum inferiorly and resulting in an effacement of the cerebral aqueduct. Imaging findings as well as the patient age and sex favored an aggressive neoplasm. A head CT scan without contrast showed a large heterogeneous mass in the pineal gland territory measuring 2.6 x 2.8 cm transverse diameter, causing mild obstructive hydrocephalus involving the frontal horns and third ventricles. A stereotactic biopsy was performed and microscopic examination revealed a hypercellular small blue cell tumor without marked atypia, mitosis or necrosis. The histological findings and the immunohistochemical profile corresponded to a PPTID, WHO grade II (see Tables 1 and 2). After the stereotactic biopsy, the patient’s symptoms worsened with agitation, restlessness and cognitive changes; although comprehension and judgment were adequate. Two weeks later, a right paraspinal parietal craniotomy was done for resection of the tumor. The tissue resected in the second biopsy presented the same characteristics of the first biopsy and the pathologic diagnosis remained the same. After tumor resection, the patient showed: upward gaze paresis, agitation, hostility, pallialia, pseudobulbar affect, right eye with left downward gaze, right pupil with minimal anisocoria and left ptosis. There was no reaction to light. The patient was discharged after 36 days of stay and underwent radiotherapy.

Fig. A. MRT with contrast, coronal view. Mass with enhancement in pineal region.

Fig. B. MRT with contrast, sagittal view. Mass with enhancement in pineal region.

Fig. C. Sxew of tumor. Piaemorphic cells with vague nuclei and eosinophilic cytoplasm (H&E, X40).

Fig. D. PPTID. Presence of I-differentiated cells, nuclear enlargement and pleomorphism. Massive are not identified in this field (H&E, X20).

Fig. E. PPTID. Scattered tumor cells with giant nuclei, marked pleomorphism and ill-defined rosettes. Only one mitosis is identified in this field (H&E, X40).

Fig. F. PPTID Ki-67 proliferation index is 1% (CD20).

Fig. G. PPTID tumor cells are positive for synaptophysin (X40).

Fig. H. PPTID tumor cells are negative for GFAP (internal control positive, X40).

Fig. I. PPTID tumor cells are strongly positive for NSE (X40).

Fig. J. PPTID. All tumor cells are strongly positive for NF protein (X40).

Table 2. Pineal Parenchymal Tumor Grading Classification

<table>
<thead>
<tr>
<th>Grade</th>
<th>WHO Criteria</th>
<th>Jouvet Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I (Pineocytoma)</td>
<td>Low cellularity</td>
<td>No mitosis</td>
</tr>
<tr>
<td>Grade II (PPTID)</td>
<td>Pilocytic astrocytomas rosettes</td>
<td>6 mitoses/10 fields</td>
</tr>
<tr>
<td>Grade III (PPTID)</td>
<td>Moderate to high cellularity</td>
<td>6 mitoses/10 fields with negative or weak NF staining</td>
</tr>
</tbody>
</table>

Discussion

PPTIDs can appear as either diffused or lobulated tumors.2,3 PPTIDs occur at all ages but present a peak incidence in early adults, with a mean of 38 years of age.1 A slight female preponderance has been observed.6 Clinical findings include a combination of hydrocephalus, compression of the tectal plate, Parinaud’s Syndrome, ataxia and diplia.1,2,7 Interestingly, most of these neurological findings were presented in our patient, with the exception of ataxia and diplia. Our patient was also a middle age female. Currently, there is no specific imaging finding that can help distinguish a PPTID from other masses in the pineal region or other pineal parenchymal tumors.1 The histopathological evaluation is essential for the proper diagnosis.1 In this particular case, MRI spectroscopy along with brain CT scan allowed to favor a neoplasm of parenchymal origin in the pineal region.

Tumor grading criteria depends on the amount of mitotic figures present and immunoreactivity for neurofilament protein (NF); prognosis is not affected either by anaplastic features nor calcifications.8 It is very important to stress that the grading of a PPTID can be very challenging due to an intratumoral variation in grade. When it comes to our case, the tumor corresponded to a hypercellular small blue cell lesion without marked atypia, necrosis and <5 mitoses in 10 high-power field. PPTIDs immunohistochemical profile shows positivity for synaptophysin and NSE,2,3,7-9 in addition, variable labeling can be expected for: NF, chromogranin A, retinal S antigen and S-100.10 As seen in our case, the immunohistochemical profile was positive for synaptophysin, NSE, NF and chromogranin A; the GFAP labeling was negative. Also, for a grade II tumor, Burger et al. (2012) states a Ki-67 of 3-7%. In our case, Ki-67 immunolabeling was at 1%. It is important to note that Ki-67 is not a conclusive criterion for grading (see Table 1 and eFigure 2). These findings along with the histopathological evaluation are consistent with a PPTID classified as a grade II according to the most recent criteria.6,9

Treatment for PPTIs varies from surgery to radiotherapy and chemotherapy. There is no optimal treatment for patients with a PPTID. Nevertheless, tumor resection is generally recommended as an initial treatment at the largest possible extent in all PPTIs.1,3 In our case, the patient underwent radiation therapy since there were no clear indications of benefit from chemotherapy.

Conclusion

1. PPTIDs are extremely rare intracranial malignant entities of pineal parenchymal origin that can show a transition between pineocytoma and areas of intermediate differentiation, or a biphasic pattern with pinceocytoma admixed with pineoblastoma.

2. Classic clinical findings in this lesion relates to hydrocephalus and Parinaud’s Syndrome.

3. Tumor grading and therefore prognosis can be challenging to estimate due to an intratumoral variation in grade exhibited by this neoplastic process.

4. It is important to recognize the histopathological features presented by this malignant lesion since a correct diagnosis secures a better prognosis and survival with the appropriate therapy.