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Case Report

Papillary tumor of the pineal region in pediatric patient – A case report

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ABSTRACT

Background: Papillary tumor of the pineal region (PTPR) represents a rare and histologically distinct subgroup of tumors originating in the pineal region. Few pediatric cases have been reported so far in the literature; therefore, clinical data are scarce.

Case Description: We describe a case of PTPR in a 9-year-old girl who presented with a 5-month history of excessive appetite and weight gain. The patient underwent neuroimaging procedures and total gross surgical resection with postoperative adjuvant local radiotherapy, which from our experience was the best treatment choice as an attempt to avoid local recurrence. During 78-month follow-up, the patient from our study manifested no disease recurrence.

Conclusion: PTPR should be included in the differential diagnosis of pineal region masses.

Keywords: Central nervous system, Children, Immunohistochemistry, Papillary tumor of the pineal region, Pineal region

INTRODUCTION

Tumors of the pineal region account for about 3–11% of all brain tumors in childhood. Papillary tumor of the pineal region (PTPR) is a rare neuroepithelial tumor originating in this area.[9,11] Since it is first description in 2003 (Jouvet *et al.*) and inclusion in the 2007 World Health Organization (WHO) classification of tumors of the nervous system, several pediatric cases of the PTPR were described up to date.[2,4,6,21,27]

PTPR affects mostly young adults in the third decade of life.[14] Children account for only 16–19% of PTPR cases.[6] It originates from specialized cytokeratin-positive and nestin-positive ependymal cells derived from the subcommissural organ. Due to similar morphological features of PTPR with a number of other papillary-like tumors of the pineal region, immunohistochemical analysis is crucial to its distinction.[12,17,24] We describe a case of PTRP in a 9-year-old girl with clinical and neuroradiological follow-up.

CASE DESCRIPTION

A 9-year-old girl presented with a 5-month history of excessive appetite and weight gain. Patient's mother noticed 2–3 weeks before admission, an adjustment of patient's head during specific activities (i.e., watching television). One week before admission, the patient suffered from mild frontal headache, and manifested blurred vision as well as broad-based gait. On the day before admission to hospital, diplopia occurred. Physical and neurological examination was unremarkable except for unstable gait and diplopia in all directions. Initially bilateral papilledema was found; therefore, neuroimaging was performed. Brain magnetic resonance imaging (MRI) revealed a triventricular hypertensive hydrocephalus due to heterogeneously-enhanced and space-occupying lesion 3.3 × 3 cm in diameter with limited cystic and hemorrhagic components in the pineal region. The tumor was localized; extended temporarily from the roof of the fourth ventricle (filling the cerebral aqueduct) with infiltration of the mesencephalon tectum and separation of the cerebral peduncles. Diffusion restriction and T2-hyperintense signal indicated tumor hypercellularity [Figure 1].

The initial treatment option was to perform an endoscopic third ventriculostomy to treat hydrocephalus and to simultaneously obtain a tumor specimen for histopathological analysis, which revealed a PTPR. A median suboccipital craniotomy was preformed 14 days later; the pineal region was reached through a supracerebellar-infratentorial approach, followed by complete resection of the tumor.

The definitive histopathological analysis revealed tumor tissue composed of papillary formations and cellular tumor with ependymal-like differentiation. Eosinophilic columnar or elongated cells were present in papillary areas around the vessels, while in ependymal-like areas gliovascular rosettes and tubes were noticed. The nuclei of tumor cells were round to oval, while atypical nuclei were only occasionally present. Mitotic activity ranges from 4 to 10/10 HPF, while Ki67 values range up to 8%. Microvascular proliferation was not present. Large foci of necrosis were without pseudopalisades of the surrounding tumor cells. Tumor tissue was diffusely immunopositive for AE1/AE3, CK18, neuron-specific enolase (NSE), S100, and vimentin, but was only sporadically positive for synaptophysin. Nuclear INI1 expression was present in tumor cells. Neu-N was not seen. Neurofilament protein was evaluated with the aim of exclusion of pineocytomas, and it was negative. Chromogranin as marker of pinealoblastoma (PB) was negative. Epithelial membrane antigen (EMA) and glial fibrillary acidic protein (GFAP) immunostain were negative. Therefore, histological diagnosis of the tumor was PTPR [Figure 2]. Marked mitotic activity corresponded to Grade 3. Tumor markers such as alpha-fetoprotein and beta-human chorionic gonadotropin in serum and cerebrospinal fluid were within the normal range.

Postoperative, vertical supranuclear gaze palsy, convergence deficit, and dilated pupils (Parinaud's syndrome) were noticed what led to mild gait instability. The patient also had need for cortisol supplementation. Postoperative MRI of brain and total spinal cord found no residual tumor or signs of leptomeningeal dissemination [Figure 3]. The patient was evaluated comprehensively (neurosurgical, oncological, and neuroradioterapeutic) and local photon radiotherapy was performed in cumulative dosage of 50.4Gy, applied in 28 fractions 1.8. Further MRI (most recent follow-up 78 months after surgery) found no residual mass or recurrence of disease. So far the patient is well with mild residual Parinaud syndrome and without need for cortisol supplementation.

DISCUSSION

Primary tumors of the pineal region with papillary features are very rare.[2] The new WHO 2021 classification

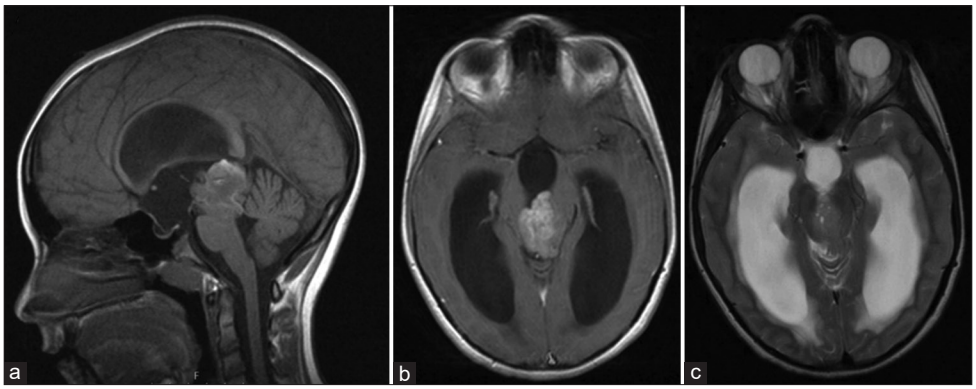

Figure 1: Preoperative magnetic resonance imaging (MRI). T1 contrast-enhanced midsagittal MRI displays a tumor mass located in the pineal region, demonstrating heterogeneous post contrast opacification, signs of hemorrhage, and cystic areas (a and b). T2-weighted axial MRI reveals tumor hypercellularity, a ballooned third ventricle and enlarged lateral ventricles-signs of hydrocephalus (c).

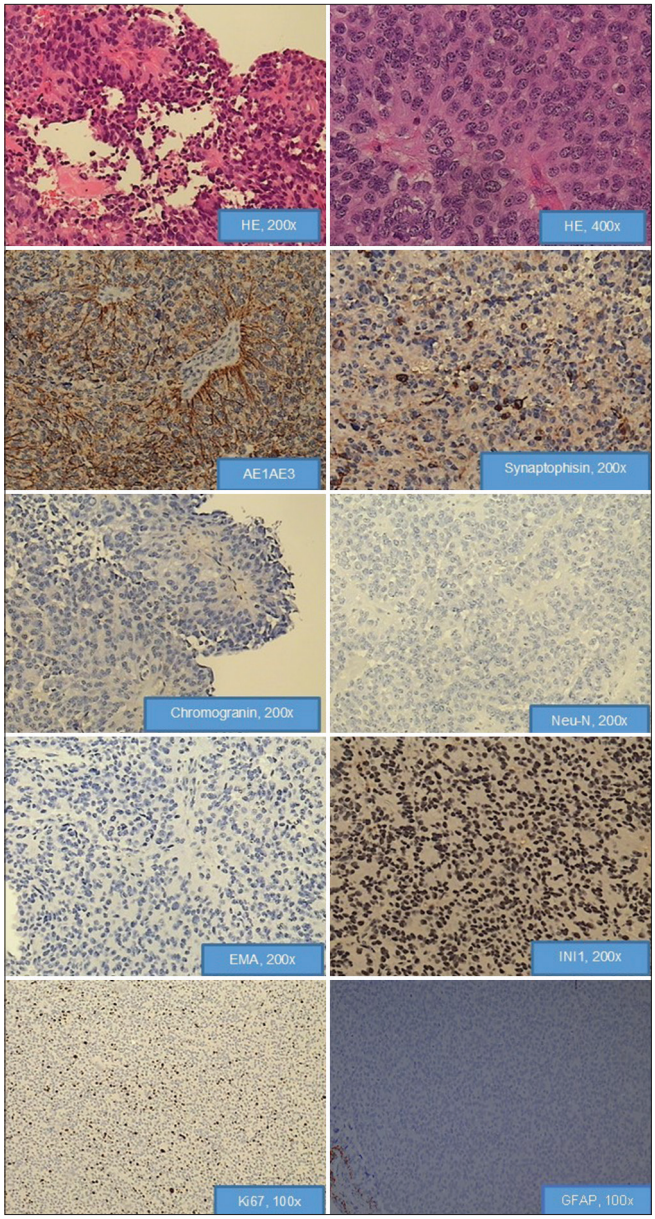

Figure 2: Hematoxylin and eosin-stained sections of paraffin embedded tissue show tumor tissue composed of papillary formations and cellular tumor with ependymal-like differentiation. Eosinophilic columnar or elongated cells are present in papillary areas around the vessels, while in ependymal-like areas gliovascular rosettes and tubes are noticed. The nuclei of tumor cells are round to oval, while atypical nuclei are only occasionally present. Microvascular proliferation is not present. Large foci of necrosis are without pseudopalisades of the surrounding tumor cells. Tumor tissue is diffusely immunopositive for AE1/AE3, sporadically positive for synaptophysin neuron-specific enolase, negative for chromogranin, Neu-N, and Epithelial membrane antigen. Nuclear INI1 expression is present in tumor cells. Mitotic activity ranges from 4 to 10 per 10 HPF, while Ki67 values range from 2% to 8%. Tumor showed complete absence of immunoreactivity for glial fibrillary acidic protein.

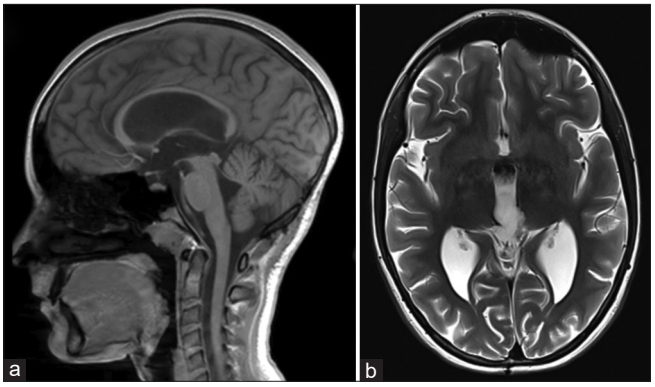

Figure 3: Postoperative magnetic resonance imaging (MRI). T1-weighted mid-sagittal (a) and T2-weighted axial (b) MRI scans show no signs of residual/recurrent tumor mass or hydrocephalus.

of tumors of the central nervous system (fifth edition) differentiates five histotypes of pineal parenchymal tumors including pineocytoma, pineal parenchymal tumors of intermediate differentiation, PTPR, PB, and desmoplastic myxoid tumor of the pineal region, SMARCB1-mutant. Arabic (rather than Roman) numerals are utilized for grading within the types.[28] The term "PTPR" is based on the histopathological description of a tumor characterized by a papillary pattern, rosettes, and pseudorosettes.[22] Microscopic evaluation often demonstrates a lesion with papillary areas lined by epithelioid tumors with eosinophilic cytoplasm, and numerous cells exhibiting clear or vacuolated cytoplasm.[36] Since first description of PTPR, growing awareness familiarized pathologists with the presentation of PTPR and increased recognition as well as revision demands. The literature data regarding immunohistochemistry, thus, are rising presenting more additional features to reflect and accentuate this rare entity in more profound manner from overlapping diagnoses. However, immunohistochemical diagnosis is not always feasible.[31] Comprehensively, the immunohistochemical characteristics of PTPR include variable immunoreactivity for cytokeratin (AE1/3 and CK18 as most associated, and KL1, CAM5.2 in addition), S-100, NSE, and vimentin as well as complete absence of immunoreactivity for GFAP. Since PTPR is frequently misdiagnosed as ependymoma or choroid plexus papilloma, it is important to point the GFAP staining out in their distinction (negative in case of PTPR as was shown in our case).[1,8,14,19,23,30] Furthermore, positive immunohistochemical stains for microtubule associated protein 2 could be found as well as for synaptophysin (negative in papilloma), even for EMA and anti-NeuN. In addition, positivity of membranous Kir7.1 or cytoplasmic stanniocalcin-1 and transthyretin could be noticed, however, usually are absent in PTPR and seen in choroid plexus tumors.[10,30,36] Nevertheless, high N-CAM (CD56)

expression was described in PTPR, distinguishing it from choroid plexus tumors.[13,35] Most of the cases reported in the literature have mentioned low proliferation index (<5%) in these tumors.[21,27] However, proliferation index may be as high as 13–15%.[30] Evaluating mitotic and proliferation index were important in grading of PTPR as Grade 2 (mitotic count <2–3, Ki67 2–3%) or 3 (mitotic count ≥3, Ki67≥10%), implicating possible prognosis and malignant/recurrence potential.[26] Methylation profiling studies are moreover helpful in discriminating PTPR from other tumor entities in indistinctive cases (in addition to immunohistology and proliferation index), onward categorizing PTPR into prognostic subgroups regarding progression-free survival as well as providing PB subtypes.[6,4,18,28] Molecular alterations of PTPRs revealed PTEN mutation and PI3K alteration.[26,30] Methylation profiling was not available in our case. Genetic background by hybridization methods including chromosomal aberrations has been discussed in few adult reports, yet not clearly determined.[30,35] PTPRs seem slightly more observed in female adult and pediatric patients.[30,34] PTPR is a rare neoplasm, especially in children. More than 30 cases have been reported in pediatric population (0–18 years) so far.[1-3,5-7,10,14-16,19,20,25,29,30,32,33,37,38,40] Our patient has to date the longest period of follow-up and without recurrence in comparison with other reported pediatric cases treated surgically alone or surgically with adjuvant radiotherapy. Pathogenesis, prognosis as well as behavior remain undetermined. The limited MRI reports of PTPRs in the literature have described a heterogeneous enhancing mass centered in the pineal region, solid and cystic tumor, T1-weighted and T2-weighted hypointensity, contrast-enhancement, and presence of associated obstructive hydrocephalus, as was seen in our case.[2,21] Total tumor resection seems the optimal treatment guideline,[19,30] whereas following radiotherapy is preferable,[1,8,26,28,30] as was done in our patient. Gross total resection is the only clinical factor associated with good survival and absence of recurrence, contrary to incomplete resection, and a mitotic index higher than five per 10 high power fields. The malignant potential, as well as effect of radiotherapy and chemotherapy on disease progression, requests further investigation. The 5-year overall survival and progression-free survival in the largest series of PTPRs are 73% and 27%, respectively.[1,2,12,14,21,32] Expansion of PTPRs typically results in clinical symptoms associated with obstructive hydrocephalus, as seen in our case. Recurrences have been reported, though we have not observed any local recurrence in the presented case so far.[8,30] PTPR generally exhibits propensity for local recurrence.[10] Prognostic value of histopathologic features in biological behavior was evaluated and showed inconsistency. However, marked mitotic and proliferative activity, as found in our case, may be associated with worse prognosis and shorter progression-free survival.[12,18,26,30,40] PTPR diagnosed at a younger age did not exhibit more aggressive behavior.[30,32] Data with respect to long-term prognosis in pediatric patients are scarce, particularly in recurrence-free survival despite the elevated mitotic and proliferation index. Recurrence even 9 years after treatment has been mentioned in the literature.[30,31] Overall, the prognosis of PTPR is favorable, with a 36-month survival rate of 83.5%.[4] Longer disease-free interval is correlated to better overall survival at 36 months.[39] Still, meeting the diagnostic criteria for PTPR including differentiation, histological profile, and grading remains demanding and insufficiently addressed with nebulous criteria between Grades 2 and 3, thus course unpredictable.

CONSCLUSION

The PTPR is a rare tumor that must be included in the differential diagnosis of pineal region masses. Regarding treatment options, as we have demonstrated in our case study, local radiotherapy could be provided after gross total resection with the aim to avoid local recurrence. However, long-term follow-up is required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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