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CASE REPORT

Papillary tumor of pineal region with an unusual clinical presentation: Case report and review of the literature

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ABSTRACT

Papillary tumor of the pineal region (PTPR) is a newly described entity, which has been recently included in the World Health Organization classification of central nervous system tumors. We report an unusual presentation of PTPR in a 17-year-old girl, which was extending into the third ventricle, along with a detailed description of morphological and immunohistochemical characteristics of PTPRs. The diagnosis of PTPR was established on immunohistopathological examination.

Key words: Abducens nerve palsy, hydrocephalus, papillary tumor, pineal region

Introduction

Pineal region tumors account for <1% of all intracranial tumors.[1] Primary tumors of the pineal region with papillary features are very rare, and these include papillary pineal parenchymal tumors, papillary ependymoma, choroid plexus papilloma, papillary meningioma and germ cell tumors.[2-5] Recently, papillary tumor of the pineal region (PTPR) was described as a separate entity.[6] The PTPR is one of the rarest tumors occurring in the pineal region, and it has been recognized as a distinct entity in the 2007 World Health Organization classification of central nervous tumors.[7] Based on the immunophenotypic and ultrastructural findings, PTPR has been shown to arise from specialized ependymocytes of the subcommissural organ located in the lining of the posterior commissure and show ependymal differentiation.[6,8] We report a case of PTPR with a unique clinical presentation of long history of 1 year along with bilateral sixth nerve palsy, as such type of presentation in these tumors has not been reported till date to the best of our knowledge.

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Case Report

A 17-year-old girl presented to the outpatient Department of Neurosurgery of our Tertiary Care Institute with chief complaints of recurrent attacks of vertigo for past 1 year, holocranial headache and recurrent projectile vomiting for last 1 month and sub-occipital neck pain and diplopia on lateral gaze for past 20 days. On examination, her vitals were stable. There were bilateral papilledema and bilateral sixth nerve palsy. There was no sensorimotor deficit but neck rigidity was present and patient was able to walk with support. Contrast-enhanced computerized tomography (CECT) revealed a well-defined iso-dense lesion measuring 2.2 cm × 2.1 cm × 2 cm in posterior third ventricular area with third and bilateral lateral ventricular hydrocephalous and periventricular lucency (PVL). Magnetic resonance imaging (MRI) revealed a T1 iso to hypo-intense and T2 iso to hyper-intense lesion with small cystic foci in the pineal area of size 2.7 cm × 2.2 cm × 2.3 cm with tri-ventricle hydrocephalous. The mass was heterogeneously enhancing on gadolinium contrast MRI except for the cystic areas within the tumor. Biochemical and hematological investigations were within the normal limits. The patient underwent a midline sub-occipital craniotomy with infra-tentorial supra-cerebellar approach and total resection of tumor was done. The tumor was gray to pink colored, highly vascular and moderately soft-suckable mass. The tumor was attached to the posterior third-ventricular brain parenchyma with over-lied venous structures. Complete excision of the tumor was done and posterior third ventricle opened. Post-operative period was uneventful and the patient was relieved of her symptoms. However, the bilateral sixth nerve palsies didn't improve. Cerebro-spinal fluid (CSF) analysis revealed no malignant cells and β-human chorionic gonadotropin and alpha-fetoprotein markers were absent in CSF.

After 2 months, patient again presented with complaints of similar headache and recurrent vomiting. On examination, she had persistent papilledema and bilateral sixth nerve palsy as before. Repeat CECT scan of brain was done, which revealed hydrocephalous with PVL. Previous scar site was healthy. Hence, a ventriculo-peritoneal shunting was performed for hydrocephalus and patient was relieved of her symptoms. Patient is on regular follow-up since then and is asymptomatic.

Histopathological Features

Histopathology of the specimen showed a moderately cellular tumor arranged in complex papillary pattern lined by cells with round to oval nuclei, dispersed chromatin, prominent nucleoli and scant to moderate eosinophilic cytoplasm. Increased mitosis (8/10 high power field) with atypical mitosis and areas of necrosis were present. Perivascular rosette pattern was also present. [Figure 1] Immunohistochemistry showed diffuse cytoplasmic positivity for cytokeratin and neuron-specific enolase. Synaptophysin and Glial fibrillary acidic protein (GFAP) were negative. Ki67 proliferation index was 15–20%. Final Health and Physical Education report were high grade PTPR.

Discussion

The normal pineal gland secretes melatonin and is located in the supratentorial midline, above the superior colliculi and below the vein of Galen. Tumors of the pineal region account for <1% of intracranial neoplasms in adults. Ninety-six cases of PTPR have been reported in the literature so far.[9,10] These tumors can occur across wide age range, but mostly, they occur from 3rd to 5th decade though our patient belonged to 2nd decade of life.[11] Our patient presented with symptoms for 1-year duration whereas the duration of symptoms mentioned in the literature for PTPRs has been 3–4 months.[6] Also, bilateral sixth nerve palsy presentation in our case has not been reported previously in PTPRs.

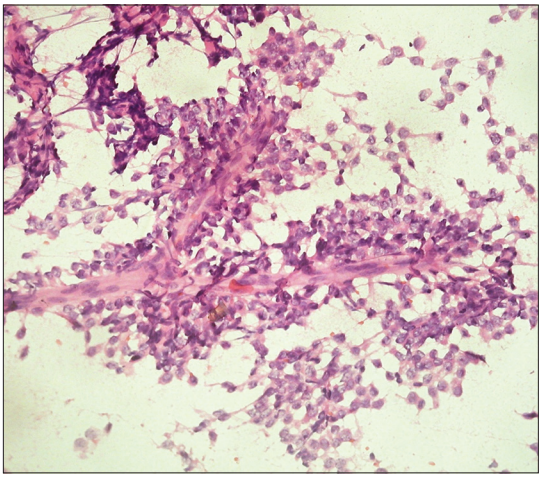

Figure 1: Histopathology slide shows papillae with fibrovascular core lined by tumor cells with round to oval nuclei, vesicular chromatin, prominent nucleoli and scant eosinophilic cytoplasm. (Hematoxylin and eosin, ×20)

The clinicopathological behavior of PTPR is not well established. PTPR is a neuropathologic description of the tumor manifested by papillary features, rosettes and pseudorosettes.[7] PTPR is characterized by an epithelial-like growth pattern in which the vessels are covered with multiple layers of tumor cells forming perivascular pseudorosettes, similar to our case.[11] The immunohistochemical characteristics of PTPR include widespread immunoreactivity for cytokeratin, neuron-specific enolase and S-100 protein, focal immunoreactivity for vimentin and complete absence of immunoreactivity for GFAP as was seen in our case.[4] The morphologic and immunohistochemical characteristics of PTPRs are very similar to papillary ependymomas and choroid plexus papillomas but PTPRs can be distinguished from these tumors by the absence of immunoreactivity to epithelial membrane antigen, membranous inwardly rectifying potassium channel (Kir 7.1) and cytoplasmic staniocalin-1 and by the presence of distinct microtubule associated protein-2 (microtubule-associated protein-2) immunoreactivity.[12] Mitosis was frequent in our case, and Ki67 index was also high (15%). Similar high proliferation index (13%) was also reported by Fèvre-Montange *et al*.[13] However, most of the cases reported in the literature have mentioned low proliferation index (<5%) in these tumors.[7,9]

Papillary tumor of pineal region appear to have well-differentiated secretory functions that may predispose to the secretion of proteins and glycoproteins. The secretory inclusions of PTPR have been noted to contain proteins and glycoproteins.[6] Concentration of proteins in the small cystic spaces seen in these masses may explain the intrinsic hyperintensity on T1-weighted sequences, which is characteristic for PTPRs contrary to our case in which, T1-weighted MRI showed iso to hypo-intense mass.[14] The limited MR imaging reports of PTPRs in the literature have described a heterogeneous enhancing mass centered in the pineal region.[6] Like other masses in this location, obstructive hydrocephalus is a common secondary finding, as was seen in our case.[1] Characteristic radiological features of PTPRs include solid and cystic tumor, T1-weighted and T2-weighted hypointensity, contrast enhancement and presence of associated hydrocephalus. Differentiation of this tumor from other tumors of pineal region is necessary as natural history, and behaviour of this tumor is not yet clear and has reported high recurrence rate of this tumors. Radiological differential diagnosis of the mass lesion in this region includes germinoma, pineocytoma, pineoblastoma, and teratoma. The points for differentiation between these lesions from PTPR are given in Table 1.[15] T1 hyperintensity and higher perfusion values may help in differentiating PTPR from other pineal region tumors. From the available literature, these tumors appear well-defined and usually <4 cm in size.[16]

These features may help differentiating these tumors from pineoblastoma and glioma, which are, usually, infiltrative and larger in size.

The proper differentiation of papillary tumors has management implications because treatment response of PTPRs is less well-documented than other tumors in the pineal region.[4,6,12] Surgical resection, followed by radiotherapy is the preferred treatment.[16] The prognosis for PTPR is also not well understood. An understanding of the biologic behavior of PTPR is evolving as more cases are documented, and frequent local recurrence of PTPRs have been described, though we have not observed any local recurrence in our case.[6,17] Thus, gross total resection is probably the only clinical factor associated with good survival and absence of recurrence.[17] The malignant potential of PTPRs is also not established and has to be monitored by follow-up examination. The effect of radiotherapy and chemotherapy on disease progression also needs to be investigated, but radiotherapy is, usually, given after a local recurrence. The 5 year estimates for overall survival and progression-free survival in one of the largest series of PTPRs published by Jouvet *et al.* were 73% and 27%, respectively.[4,6] Main clinical and radiological data of patients of PTPR in reviewed articles are summarized in Table 2.[15]

Conclusion

Our case report on PTPR is unique in the sense that it the first case in the literature to present with such a long history of symptoms for almost 1 year along with bilateral sixth nerve palsy. Also, PTPR closely mimics other primary tumors of the pineal region like choroid plexus papilloma and papillary ependymoma and hence every tumor tissue of pineal region should be subjected to immunohistochemistry to differentiate

Table 1: Comparison of imaging findings of papillary tumor of the pineal region with other common pineal region tumors

Imaging findings	PTPR	Germinoma	Pineocytoma	Pineoblastoma	Embryonal cell carcinoma
T1 Intensity	Hyperintense	Isointense to hypointense	Isointense to hypointense	Iso/hypointense	Foci of hyperintensity due to protein/blood/fat
Cystic spaces	+	–	+/–	+/–	+
Enhancement	Strong heterogenous	Strong homogenous	Peripheral rim enhancement	Well to moderate heterogenous	Strong heterogenous
Calcification	+/-	Central; engulfed pineal gland	Exploded, peripheral Ca++	Exploded, peripheral Ca++	+
CBV	Elevated	Elevated	–	–	–
Margins	Well defined	Well defined	Well defined	Ill defined, infiltrative	Variable
Plain CT	Hyper/ Isodense	Hyperdense	Isodense to hypodense	Hyperdense	Hyper/Isodense
Size	2-4 cms	>3 cms	<3 cms	=3 cms	=3 cms
Age	6-66 years	10-12 years		3 years	10-20 years

+ – Present; – – Absent; +/– – Present in some cases; Ca++ – Calcifications; CBV – Cerebral blood volume; PTPR – Papillary tumor of the pineal region

Table 2: Summary of review of literature on papillary tumor of the pineal region describing natural history and imaging findings

Author	Year	*n*	Age	Sex	Recurrence	T1 hyperintensity	Size	Cystic changes
Shibahara J, *et al.*	2004	1	29 y	F	–	–	<3 cms	–
Fevre-Montage M, *et al.*	2006	31	5 to 66 y	14M; 17 F	Yes	–	–	–
Kawahara, *et al.*	2007	1	48	F	No	–	–	–
Dagnew E, *et al.*	2007	3	37-55 y	F	No	–	–	–
Bosco T, *et al.*	2008	1	22 y	M	–	–	–	–
Inoue T, *et al.*	2008	1	43	M	–	–	–	Yes
Chang AH, *et al.*	2008	4	27-50	F	–	Yes	–	Yes
Fevre-Montage M, *et al.*	2008	1	42	F	–	–	–	–
Buffenoir K, *et al.*	2008	1	13	M	No	–	–	–
Cerase A, *et al.*	2009	1	56	M	No	Yes	–	–
Sato TS- 11, *et al.*	2009	1	18	M	Yes	Yes	<3 cms	–
Nakamura H, *et al.*	2009	1	11	M	No	Isointense	–	–
Yano H, *et al.*	2009	1	17	M	Yes	–	<3 cms	–

Negative – -; Male – M; Female – F; *n* – Number of patients in study; PTPR – Papillary tumor of the pineal region

between these closely related tumors to manage them accordingly.

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