

Choroid Plexus Papilloma in the Fourth Ventricle Associated with Pheochromocytoma: A Case Report

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Abstract

We report for the first time a case of choroid plexus papilloma (CPP) of the fourth ventricle associated with adrenal pheochromocytoma. A large tumor was found in the fourth ventricle of a 24-year-old man who presented with symptoms of increased intracranial pressure due to obstructive hydrocephalus. A systemic search revealed that the patient also had an asymptomatic left adrenal tumor. Both tumors were resected. The pathological diagnosis of the brain tumor was CPP and that of the adrenal tumor was pheochromocytoma, both of which showed no pathological signs of malignancy. Genetic testing for von Hippel–Lindau disease was negative. There have been no reports of cases of CPP associated with pheochromocytoma. In this report, we discuss the relationship between both tumors.

Keywords: choroid plexus papilloma, pheochromocytoma, von Hippel–Lindau disease

Introduction

Choroid plexus papillomas (CPPs) are tumors that originate from the epithelium of choroid plexus and account for 0.4–0.6% of all brain tumors.¹⁾ It is very rare for CPP to be associated with tumors of other organs. Pheochromocytoma is a neuroendocrine tumor that arises primarily from the adrenal medulla and results in the overproduction of catecholamines. Pheochromocytoma is associated with several familial tumor syndromes and can be complicated by intracranial tumors,²⁾ but its association with CPP has not been mentioned in the past. We report a case of CPP arising in the fourth ventricle associated with pheochromocytoma in a young adult male.

Case Report

A previously healthy 24-year-old man presented with symptoms of morning headache and vomiting

for six months. The patient did not have any significant past history or family history. A careful neurological examination revealed no apparent symptoms. Head computed tomography (CT) showed enlargement of the ventricles and a tumor-like lesion, 3.5-cm in diameter with marked calcification in the fourth ventricle (Fig. 1A). In addition, an abdominal CT scan taken for systemic search to rule out the possibility of metastatic tumor indicated a left adrenal tumor (Fig. 1F). The levels of 24-hour urinary noradrenaline and normetanephrine were markedly elevated at 658.3 µg/day and 3.96 mg/day, respectively. These findings suggested that the tumor was an asymptomatic pheochromocytoma. On head magnetic resonance (MR) images, the tumor-like lesion was homogeneously enhanced with well-defined borders and mild perifocal edema (Fig. 1B–1D). Cerebral angiography showed only slight tumor staining from the left posterior inferior cerebellar artery (Fig. 1E). Because of the symptoms due to hydrocephalus, priority was given to the removal of the tumor in the fourth ventricle by suboccipital craniotomy with careful blood pressure control during surgery. The tumor was mainly a solid, intraventricular tumor with attachment to the choroid plexus, and hemostatic manipulation was not

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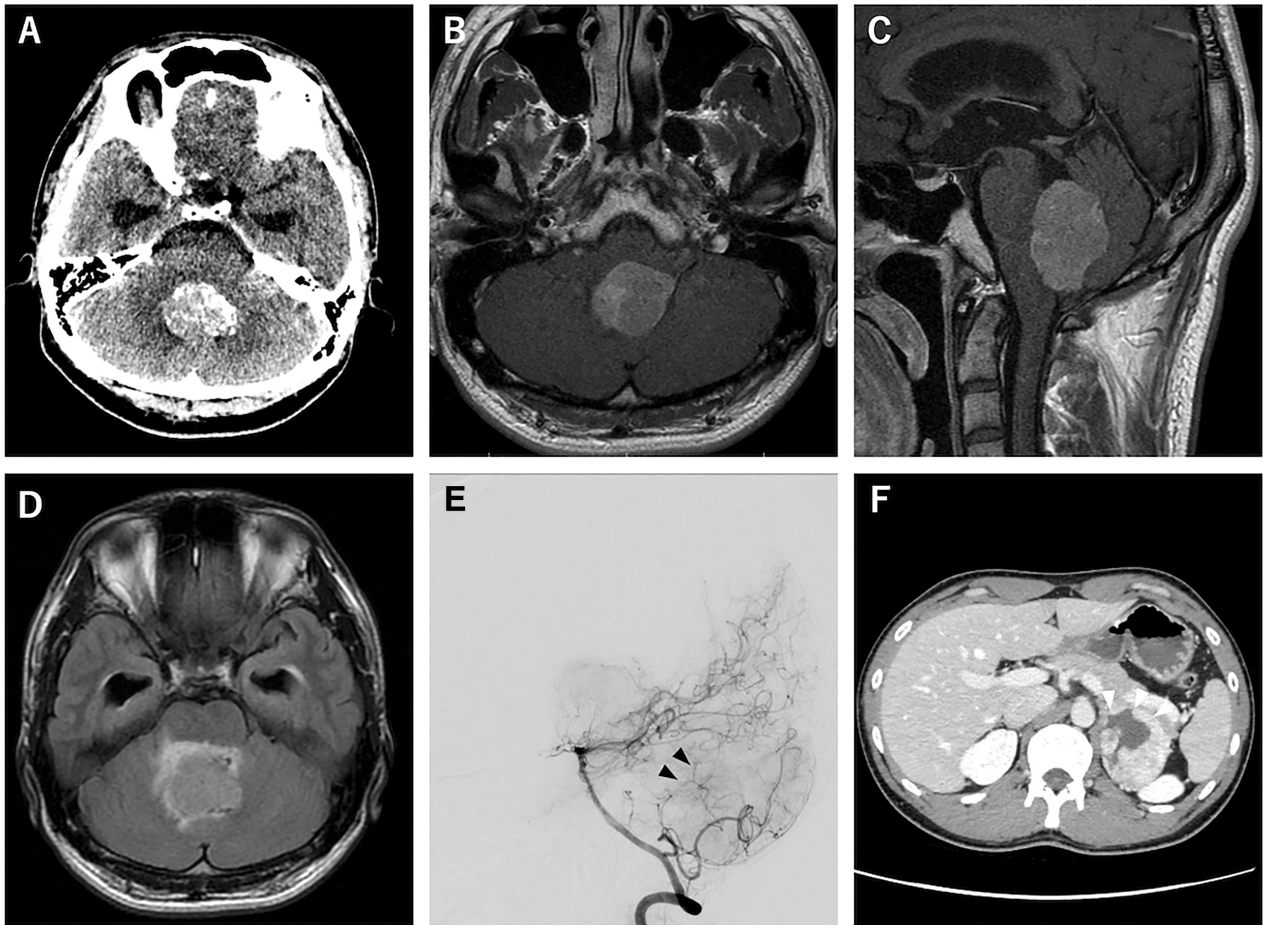


Fig. 1 Preoperative images. (A) The head CT shows marked calcification of the tumor. (B and C) Gadolinium contrast-enhanced T1-weighted images show a homogeneously contrasted tumor in the fourth ventricle. (D) FLAIR image shows mild perifocal edema. (E) Cerebral angiography shows a slight tumor staining from the posterior inferior cerebellar artery (black arrowheads). (F) The abdominal CT shows a contrast-enhancing tumor in the left adrenal gland (white arrowheads). CT: computed tomography, FLAIR: fluid-attenuated inversion recovery.

difficult. A majority of the tumor was removed except for a portion on the cerebellar side with prominent calcification, and patency of the Sylvian aqueduct was confirmed after removal. Postoperative images showed minimal, calcified residual tumor on the cerebellar side (Fig. 2A–2C), and ventricle size was normalized.

After surgery, the patient's symptoms improved, and he was discharged one month after the surgery. However, one month later, the hydrocephalus recurred with consciousness disturbance, headache, and vomiting, and an external ventricular drainage was performed. Subsequent MR images showed no re-enlargement of the tumor, suggesting postoperative adhesive hydrocephalus. Subsequently, a laparoscopic resection of the left adrenal tumor was performed under external ventricular drainage

management, and the tumor was completely removed. Then, endoscopic third ventriculostomy was performed. The hydrocephalus improved after surgery and the patient was discharged. More than three years have passed without recurrence of either tumor.

Histopathological analysis showed that the tumor in the fourth ventricle consisted of cylindrical or cuboidal tumor cells arranged in a papillary fashion with vascular connective tissue as the stroma (Fig. 3A). There was little nuclear atypia and no evidence of mitosis or necrosis. The tumor stained positive for S-100 protein, vimentin, prealbumin, and AE1/AE3, and negative for p53 (Fig. 3B–3E and 3G). The Ki-67 labeling index was 1.4% (Fig. 3F). Based on these findings, the tumor was diagnosed as CPP. On the other hand, the adrenal tumor was

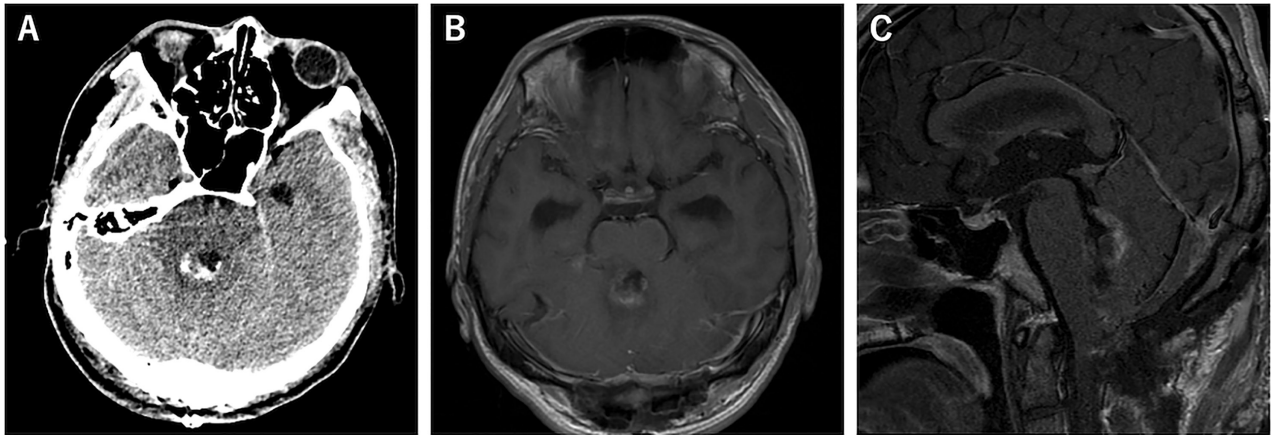


Fig. 2 Postoperative images. (A–C) The tumor has been removed except for a calcified, residual tumor on the cerebellar side.

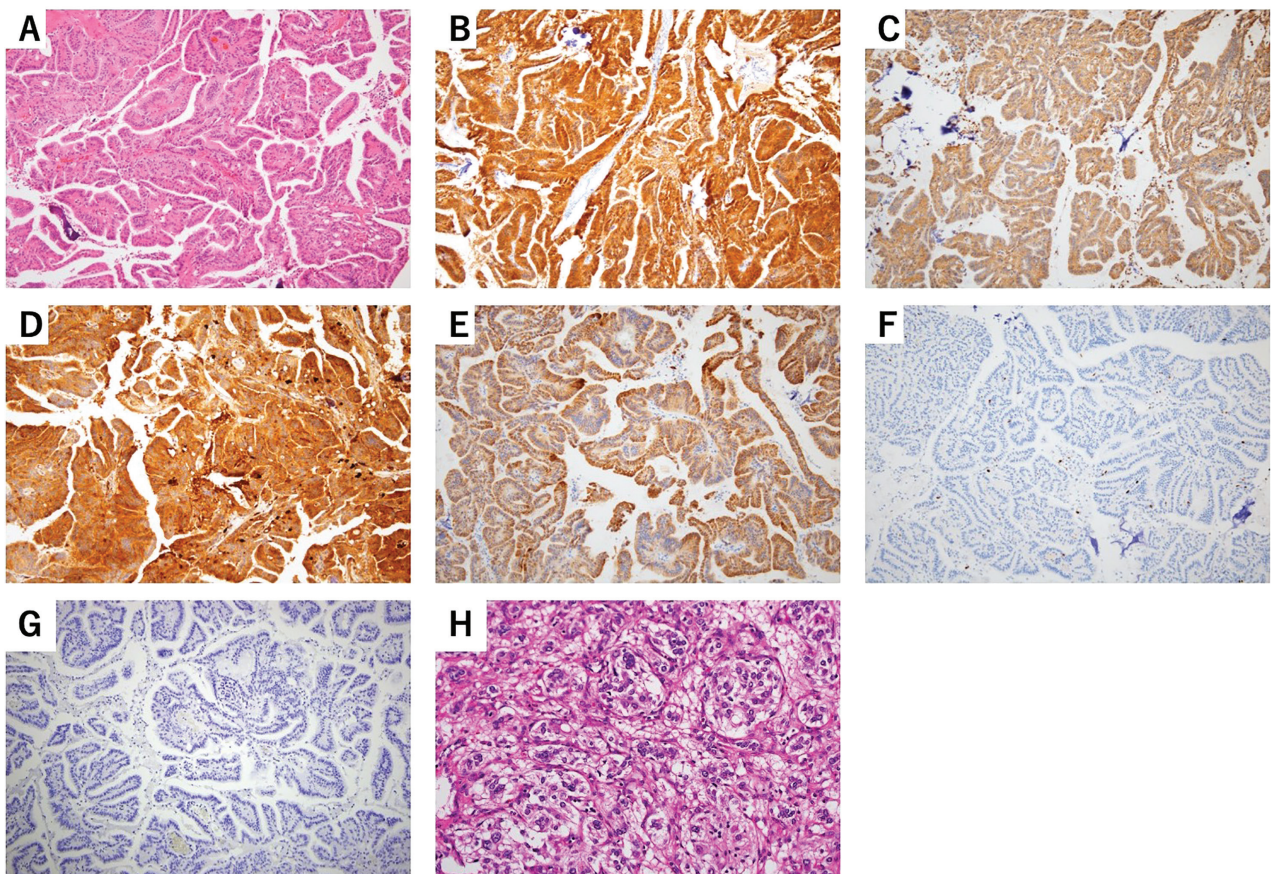


Fig. 3 Pathological images of the CPP (A–G). (A) H&E staining shows cuboidal to cylindrical epithelium proliferating in a papillary structure with an axis of vascular connective tissue. Immunostaining showed (B) S-100 positive, (C) vimentin positive, (D) prealbumin positive, (E) AE1/AE2 positive, and (F) p53 negative staining. (G) Ki-67 labeling index was 1.4%. (H) Pathological image of the pheochromocytoma shows large multilineage cells proliferate in a spore-like arrangement. H&E: hematoxylin and eosin.

diagnosed as pheochromocytoma (Fig. 3H). Although he had no specific family history, we suspected the possibility of von-Hippel–Lindau (VHL) disease due

to the presence of pheochromocytoma. However, genetic testing by sequencing analysis did not identify any *VHL* gene alterations.

Discussion

We reported a case of CPP in the fourth ventricle associated with pheochromocytoma, including the treatment process. CPP usually occurs alone in the ventricles of the brain, grows slowly and progressively, and develops as a symptom of increased intracranial pressure due to hydrocephalus. In image findings, CPP is usually depicted on MRI as a substantial lesion with strong contrast enhancement and well-defined borders. CPP also shows occasional calcification within the tumor on plain CT, with a reported rate of about 24%.³⁾ Differential diagnosis of other tumors based on the image findings may include ependymoma and meningioma. In our case, hemangioblastoma was considered due to the presence of pheochromocytoma, but this was ruled out by the results of cerebral angiography. In retrospect, the image findings in our case were typical of CPPs.

Regarding the process of treatment, it was decided that the removal of the intracranial tumor should be prioritized over the adrenal tumor, which was suspected to be pheochromocytoma, because the patient suffered from symptoms of increased intracranial pressure associated with hydrocephalus. As a result, careful blood pressure control allowed us to complete the surgery without significant hemodynamic changes in the perioperative period. Even asymptomatic pheochromocytoma can cause perioperative hemodynamic instability, as can symptomatic pheochromocytoma.⁴⁾ If hypertensive crisis occurs, it may be fatal. In the case of symptomatic intracranial tumors associated with pheochromocytoma, the severity of the syndrome should be appropriately determined. Depending on the severity of symptoms caused by intracranial tumors, treatment of pheochromocytoma may be considered a priority, even in the case of asymptomatic pheochromocytoma.

Several genetic abnormalities have been identified in relation to the development of CPP. For example, Aicardi syndrome is an X-chromosome-related dominantly inherited disorder characterized by callosal agenesis, retinal choroidal abnormalities, and epilepsy, which is often associated with CPP.⁵⁾ Li-Fraumeni syndrome is a cancer predisposition syndrome caused by germline mutations in the TP53 tumor suppressor gene. This disease may be associated with choroid plexus carcinoma, and in rare cases, it has been reported to be associated with CPP.⁶⁾ Other diseases, such as hypomelanosis of Ito, and the constitutional 9p duplication, have been reported to be associated with CPP.⁷⁾ However, a majority of these CPP cases found with underlying germline abnormalities are pediatric, as opposed to a healthy adult in this case.

Pheochromocytoma is a catecholamine-producing tumor composed of chromaffin cells, typically localized to the adrenal gland. Pheochromocytoma is associated with several familial tumor syndromes and is currently known to be associated with multiple endocrine neoplasia type 2, VHL syndrome, neurofibromatosis type 1 (NF1), and paraganglioma syndromes.²⁾ It can be complicated by intracranial tumors, such as cerebellar hemangioblastoma and endolymphatic sac tumor in VHL, and glioma in NF1.

Investigating the relationship between hereditary tumors associated with pheochromocytoma and CPP, there is only one reported case of CPP associated with VHL,⁸⁾ but no pheochromocytoma was found in this case. Therefore, this is the first case report of CPP associated with pheochromocytoma.

In this case, no *VHL* alteration was detected. However, the diagnosis rate of *VHL* by sequencing method is 89%,⁹⁾ so *VHL* has not been completely ruled out. We were unable to perform a more detailed genetic search for both tumors. There were no pathological malignant findings in either CPP or pheochromocytoma in this case. Malignant progression has been reported in each of these two tumors, and some of the genetic abnormalities, such as those associated with *SDHB* and *TP53*, involved have been identified.^{10–12)} In the future, genetic analysis of cases similar to the present one may reveal a common genetic background between pheochromocytoma and CPP, which may lead to a better understanding of the malignant progression of both tumors.

Informed Consent

Informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflicts of Interest Disclosure

The authors have no conflicts of interest.

References

- 1) Bahar M, Hashem H, Tekautz T, et al.: Choroid plexus tumors in adult and pediatric populations: the Cleveland Clinic and University Hospitals experience. *J Neurooncol* 132: 427–432, 2017
- 2) Lenders JWM, Eisenhofer G, Mannelli M, Pacak K: Pheochromocytoma. *Lancet* 366: 665–675, 2005
- 3) Kendall B, Reider-Grosswasser I, Valentine A: Diagnosis of masses presenting within the ventricles on computed tomography. *Neuroradiology* 25: 11–22, 1983
- 4) Lafont M, Fagour C, Haissaguerre M, et al.: Perioperative hemodynamic instability in normotensive

- patients with incidentally discovered pheochromocytomas. *J Clin Endocrinol Metab* 100: 417–421, 2015
- 5) Frye RE, Polling JS, Ma LC: Choroid plexus papilloma expansion over 7 years in Aicardi syndrome. *J Child Neurol* 22: 484–487, 2007
 - 6) Cruz O, Caloretti V, Salvador H, et al.: Synchronous choroid plexus papilloma and Wilms tumor in a girl, disclosing a Li-Fraumeni syndrome. *Hered Cancer Clin Pract* 19: 1, 2021
 - 7) Kamaly-Asl ID, Shams N, Taylor MD: Genetics of choroid plexus tumors. *Neurosurg Focus* 20: E10, 2006
 - 8) Blamires TL, Maher ER: Choroid plexus papilloma. A new presentation of von Hippel-Lindau (VHL) disease. *Eye (Lond)* 6 (Pt 1): 90–92, 1992
 - 9) Nordstrom-O'Brien M, van der Luijt RB, van Rooijen E, et al.: Genetic analysis of von Hippel-Lindau disease. *Hum Mutat* 31: 521–537, 2010
 - 10) Jeibmann A, Wrede B, Peters O, et al.: Malignant progression in choroid plexus papillomas. *J Neurosurg* 107: 199–202, 2007
 - 11) Yankelevich M, Finlay JL, Gorski H, et al.: Molecular insights into malignant progression of atypical choroid plexus papilloma. *Cold Spring Harb Mol Case Stud* 7: a005272, 2021
 - 12) Gimenez-Roqueplo AP, Favier J, Rustin P, et al.: Mutations in the SDHB gene are associated with extra-adrenal and/or malignant pheochromocytomas. *Cancer Res* 63: 5615–5621, 2003

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