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# **Original Article**

# Case series of choroid plexus papilloma in children at uncommon locations and review of the literature

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Received: 20 March 15 Accepted: 31 July 15 Published: 28 September 15

# Abstract

**Background:** Choroid plexus papillomas (CPPs) comprise around 1% of intracranial neoplasms. The most common location is atrium of the lateral ventricle in children and fourth ventricle in adults. Other rare locations include third ventricle, cerebellopontine (CP) angle and cerebral parenchyma, with only a few cases reported. Authors report three cases of CPP at uncommon locations in pediatric patients. The rarity of these locations, diagnostic dilemma and management aspects are discussed along with an extensive review of the literature.

**Methods:** Retrospective institutional data analysis of histopathologically confirmed pediatric CPPs from 2010 to 2014.

**Results:** Authors noted three cases of CPP in children in uncommon locations-one each in the posterior third ventricle, fourth ventricle, and CP angle. All were males in the first decade. Two cases presented with features of obstructive hydrocephalus while the latter presented with compressive effects. Complete excision was achieved in two cases while subtotal removal was performed in one case (fourth ventricular) because of excess blood loss. Mean follow-up duration was 24.6 months (range 20–30 months). One case (of subtotal removal) had fair recovery while other two had excellent outcomes.

**Conclusions:** Posterior third ventricle, fourth ventricle, and CP angle are uncommon locations for these tumors in children. Complete surgical removal is the treatment of choice and approach needs to be tailored according to the site and size of the lesion. Blood loss is a major concern in young children as they are highly vascular tumors. Complete removal leads to excellent long-term survival rates. Adjuvant treatment is not required.

**Key Words:** Cerebellopontine angle, choroid plexus papilloma, fourth ventricle, pediatric, posterior third ventricle



# **INTRODUCTION**

Choroid plexus papillomas (CPPs) are uncommon tumors of the central nervous system arising from the choroid plexus. They constitute around 0.5-1% in adults and 3-4% in children.<sup>[2,15,30]</sup> The atrium of the lateral ventricle and fourth ventricle forms the commonest locations in children and adults, respectively.<sup>[3,12,33,40]</sup> Raised intracranial pressure (ICP) is the presenting feature in

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How to cite this article: Prasad GL, Mahapatra AK. Case series of choroid plexus papilloma in children at uncommon locations and review of the literature. Surg Neurol Int 2015;6:151.

http://surgicalneurologyint.com/Case-series-of-choroid-plexus-papilloma-inchildren-at-uncommon-locations-and-review-of-the-literature/

children in the majority of cases.<sup>[32]</sup> Other clinical features depend upon the site of the lesion. Rare locations include third ventricle, cerebellopontine (CP) angle, cerebral parenchyma, cerebellum, and others.<sup>[10,17,21,25,38]</sup> Surgical removal is the treatment of choice, and surgical approaches need to be tailored according to the location, size, and extent of the lesion.<sup>[12,34,41]</sup> Authors report three cases of CPP in pediatric age group located in uncommon locations such as the posterior third ventricle, fourth ventricle, and CP angle. The diagnostic dilemma and management issues are discussed along with a review of the literature.

# **METHODS**

Authors conducted a retrospective data analysis of histologically confirmed CPPs in patients aged  $\leq 16$  years operated at our institute from 2010 to 2014 after obtaining Institutional Ethics Committee approval. Three cases were found to be present in rare locations one each in the posterior third ventricle, fourth ventricle, and CP angle. The clinico-radiological features, surgical details, and outcome were analyzed in detail. Furthermore, a review of literature is included.

# **CASE DESCRIPTIONS**

#### Case 1

A 5-year-old boy presented with complaints of headache and vomiting of 3 months duration. Neurological examination revealed papilledema and mild upgaze paresis. Noncontrast computed tomography (CT) showed an isodense frond-like lesion in the posterior third ventricle with hydrocephalus [Figure 1a]. Magnetic resonance imaging (MRI) showed a lobulated, intensely enhancing lesion in the region of the posterior third ventricle with obstructive hydrocephalus. The lesion was isointense on T1 and slightly hypointense on T2 sequences having a frond-like appearance and measuring 4.1 cm  $\times$  1.9 cm  $\times$  2.3 cm [Figure 1b-e]. A ventriculoperitoneal (VP) shunt was performed, followed by definitive surgery. A supracerebellar infratentorial approach was performed in sitting position. The tumor was soft to firm, friable, reddish, vascular, and attached with a single pedicle to the choroidal vessels. The arterial feeder was secured early, and an en bloc complete removal was achieved. Postoperative imaging showed no residual tumor and child had excellent outcome after surgery [Figure 1f].

Histopathology showed a papillary tumor lined by columnar epithelium with centrally placed nuclei. There was no mitosis or necrosis [Figure 2a]. Tumor stained positive for pancytokeratin and synaptophysin [Figure 2b and c] while epithelial membrane antigen (EMA) staining was negative [Figure 2d]. Overall findings were suggestive of CPP.

#### Case 2

A 5-year-old boy presented with gait ataxia of 7 months duration and 2 months of headache and nasal regurgitation. Child was drowsy, but following commands; had a visual acuity of finger counting close to face, papilledema, and impaired gag reflex bilaterally. A noncontrast CT head showed a hyperdense midline posterior fossa mass lesion involving the fourth ventricle extending into the left foramen of Lushka with obstructive hydrocephalus. On MRI, the lesion was isointense on T1 and heterogeneously hyperintense on T2 sequences, showed intense enhancement and measured 4.8 cm  $\times$  3.5 cm  $\times$  5.2 cm [Figure 3a-d]. A VP shunt was inserted in view of his alteration in sensorium. With a presumptive diagnosis of an ependymoma, the patient underwent midline suboccipital approach in the prone position. Intra-operatively, the tumor was friable, very vascular, and reddish-pink in appearance. Only, a subtotal excision could be achieved because of excessive blood loss. Imaging (noncontrast CT) done in the postoperative period showed operative site hematoma which had to be evacuated on an emergency basis. Child showed gradual improvement and was doing well at the last follow-up of 20 months after surgery, with no regrowth of the residual lesion. Histopathological features were compatible with a diagnosis of CPP.

# Case 3

An 8-year-old boy presented with 5 months duration of headache, vomiting, facial asymmetry, gait imbalance, and left-sided hearing loss. Neurological examination revealed bilateral papilledema, left sided abducent nerve paresis, Grade 3 LMN facial palsy, sensorineural hearing loss, and cerebellar signs. On MRI, a well-defined lobulated extra-axial left CP angle lesion was noted, appearing isointense, and heterogeneously hyperintense on T1 and T2 sequences respectively with moderate hydrocephalus and showing intense homogenous enhancement [Figure 4a-c]. A left sided retrosigmoid approach and gross total excision was performed. Child had excellent outcome after surgery and at the last follow-up of 42 months, child was doing well with no residual tumor on imaging. Histopathology was suggestive of CPP.

# **DISCUSSION**

CPPs are benign, uncommon neoplasms of the central nervous system. Derived from the neuroectoderm and arising from the choroid plexus lining the ventricles, overproduction of cerebrospinal fluid (CSF) is the hallmark of these tumors.<sup>[15,25,32]</sup> Hydrocephalus is noted in the majority of cases. The reasons for this include overproduction of CSF or obstruction of CSF pathways directly by the tumor or repeated microhemorrhages leading to arachnoid adhesions or elevated CSF protein concentrations.<sup>[12,15,25,39]</sup> They are most commonly located in the atrium of lateral ventricles in children and fourth

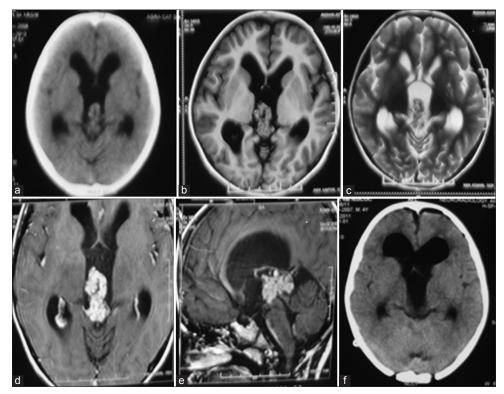


Figure 1: Case 1. Noncontrast computed tomography showing an isodense lobulated lesion in the posterior third ventricle with obstructive hydrocephalus (a). Plain magnetic resonance imaging axial sections showing the lobulated tumor appearing isointense on T1 and slightly hypointense on T2 sequences (b and c). Axial and sagittal postcontrast magnetic resonance images showing intense, homogeneous enhancement of the lesion, and located caudal to the deep venous system (d and e). Postoperative computed tomography showing no residual tumor with pneumoventricle seen in bilateral frontal horns (f)

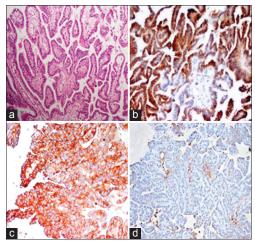


Figure 2: Histopathological images showing a papillary tumor with smooth papillae lined by single layer of columnar cells with no mitosis (a). Immunohistochemical images staining for pancytokeratin and synaptophysin were positive (b and c) while being negative for epithelial membrane antigen (d). Features were compatible with choroid plexus papilloma

ventricles in adults.<sup>[3,12,20,33,40]</sup> In children, a few cases of fourth ventricular CPPs have been reported with an incidence of 10–20%;<sup>[1,7,9,23,24,29,37,44]</sup> however, they are rare in locations such as posterior third ventricle and CP angle [Tables 1 and 2].<sup>[11,21,25,28,36,39,43]</sup>

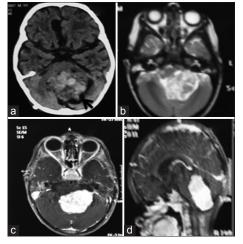


Figure 3: Case 2. Noncontrast computed tomography showing a heterogeneously hyperdense lesion in the midline posterior fossa with small peripheral cysts (black arrow) (a). A mild extension to the left cerebellopontine angle can be noted. Axial T2-weighted magnetic resonance images showing the lesion to be heterogeneously hyperintense (b). Axial and sagittal postcontrast magnetic resonance images showing intense, homogeneous enhancement of the lesion (c and d)

#### **Clinical features**

Guerard, in 1832 described the first case of CPP.<sup>[5]</sup> CPP constitute around 0.5–1% of brain tumors in adults and

3-4% in children.<sup>[2,3,30]</sup> They have a predilection for young children and more than half to two-third are seen in a first decade, especially under 5 years of age.<sup>[2,15,25]</sup> Although, a few studies have shown a higher incidence in females, the majority have shown no such predilection.<sup>[2,34,37]</sup> However, in our series, all were males in the first decade. These neoplasms present with features of raised ICP (because of hydrocephalus) or compressive effects on adjacent tissues. Neurological deficits are usually progressive, and clinical features depend on patient's age and the site of the lesion. Infants usually present with enlarging head size, drowsiness, and vomiting. Older children present with headache, vomiting, and visual disturbances.<sup>[20]</sup> These tumors being intraventricular, usually grow to a significant size before the patient becomes seeks attention. However, in cases of a posterior third ventricle lesion, the patient might have symptoms even with a small tumor because of early obstruction of the aqueduct of sylvius.<sup>[21,22]</sup> Headache, vomiting, upgaze paresis are the manifestations of posterior third ventricle lesions.<sup>[16]</sup> Cerebellar signs and features of raised ICP are seen in fourth ventricular tumors.<sup>[24,29]</sup> Cranial nerve palsies (VI-XII) and cerebellar signs are the features seen in CP angle lesions.[11,39,41]

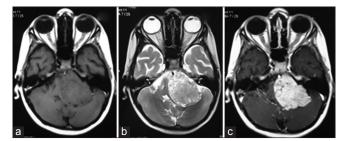


Figure 4: Case 3.Axial plain magnetic resonance imaging showing a left sided extra-axial cerebellopontine angle lesion which appears isointense and heterogeneously hyperintense on TI and T2 sequences, respectively, with compression and deformation of the brainstem (a and b).Axial postcontrast magnetic resonance images showing homogeneous enhancement of the lesion (c)

Other reported unusual manifestations of these tumors include psychosis, bobble-head-doll syndrome, endocrine disorders, and temporal lobe epilepsy.<sup>[15,20,25]</sup> In our study, one child presented with features of raised ICP while the other two presented with features of progressive mass effect over adjacent structures due to an expanding lesion.

#### Imaging

On CT, most lesions appear as isodense/hyperdense well-defined lobulated mass with intense homogeneous enhancement.<sup>[4,26]</sup> Microhemorrhages and calcifications are believed to be the etiology for the hyperdensity. These tumors may contain calcification of varying degrees in around 4-20% of cases.<sup>[4,15,26]</sup> The investigation of choice is MRI, and the classical appearance is that of a well-demarcated, extra-axial mass lesion possessing frond-like projections, and showing intense enhancement with no parenchymal invasion.<sup>[2,15]</sup> Very rarely, it can manifest as a poorly enhancing or nonenhancing lesion.<sup>[29,36,44]</sup> Signal intensities can vary from hypo to isointense on T1 and variable hyperintensity on T2 sequences respectively.<sup>[26,37,41]</sup> Hydrocephalus and flow voids are common.<sup>[2,15,20,37,41]</sup> Engulfment rather than the invasion of the choroid plexus has been described in trigonal lesions. Although not performed in recent times, enlargement of a choroidal feeder artery was the usual finding noted on angiography.[15,37,41] The presence of a tumor blush and early filling of veins draining the tumor are other indirect markers of these lesions.<sup>[26,38]</sup> In spite of all the available diagnostic modalities, an accurate preoperative diagnosis, is often not possible when situated in such unusual locations.<sup>[17]</sup> Hence, these tumors need to be always considered in the list of differential diagnosis in any child with intracranial tumor and supportive imaging findings. In children, the common differential diagnoses can be listed based on the location: Posterior third ventricle-ependymomas, pineocytomas, pinealoblastomas, germ cell tumors, and

Table 1: Literature review of	pediatric choroid pl	lexus papillomas of i	posterior third ventricle region*
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Age/sex	Clinical features	Surgical approach	Resection	Follow-up
4 months/female	Bulging fontanelle	Occipital transtentorial	Complete	3 years
8 months/female	Drowsiness, enlarged head size, papilledema	VP shunt followed by transcallosal	Complete	8 years
2 years/male	Enlarged head size, delayed milestones	VP shunt followed by supracerebellar infratentorial	Subtotal	4 months
9 years/female	Visual disturbance, nausea, vomiting	Occipital interhemispheric	Complete	3 years
6 years/male	Holocranial headache, vomiting, papilledema	ETV followed by supracerebellar infratentorial	Complete	NA
	4 months/female 8 months/female 2 years/male 9 years/female	4 months/female Bulging fontanelle   8 months/female Drowsiness, enlarged head size, papilledema   2 years/male Enlarged head size, delayed milestones   9 years/female Visual disturbance, nausea, vomiting	4 months/femaleBulging fontanelleOccipital transtentorial8 months/femaleDrowsiness, enlarged head size, papilledemaVP shunt followed by transcallosal2 years/maleEnlarged head size, delayed milestonesVP shunt followed by supracerebellar infratentorial9 years/femaleVisual disturbance, nausea, vomitingOccipital interhemispheric	4 months/femaleBulging fontanelleOccipital transtentorialComplete8 months/femaleDrowsiness, enlarged head size, papilledemaVP shunt followed by transcallosalComplete2 years/maleEnlarged head size, delayed milestonesVP shunt followed by supracerebellar infratentorialSubtotal9 years/femaleVisual disturbance, nausea, vomitingOccipital interhemisphericComplete

\*All patients had associated hydrocephalus.VP:Ventriculoperitoneal, ETV: Endoscopic third ventriculostomy, NA: Not available

Table 2: Literature re			

Author (year)	Age/sex	Clinical features	Surgical approach	Resection	Follow-up
Hammock et al.[11]	8 years/male	Multiple cranial nerve palsies and cerebellar signs	Retrosigmoid	Complete	NA
Piguet and de Tribolet <sup>[28]</sup>	5 years/male	SAH followed by cerebellar signs and sixth nerve palsy	Lateral suboccipital	Complete	1-year
Spallone et al.[39]	11 years/female	Hearing loss, headache, vomiting	Retrosigmoid	Complete	NA

\*Primary fourth ventricular/posterior fossa tumors with extension to cerebellopontine angle are not tabulated. NA: Not available, SAH: Subarachnoid hemorrhage

astrocytomas; CP angle-ependymomas, schwannomas and meningiomas; fourth ventricle-ependymomas and medulloblastomas.

# Pathology

Grossly, they are capsulated, soft, reddish-pink, and friable tumors with a cauliflower-like appearance. Microscopically, they resemble normal choroid plexus, albeit with minimal/no atypia. These tumors show strong positivity for cytokeratin (CK 7) due to their neuroectodermal origin. All cases express vimentin, S-100 protein, and synaptophysin. There might be focal reactivity for glial fibrillary acid protein (GFAP) and EMA; however, CK 20 and carcino-embryonic antigen are negative.<sup>[20,31,35]</sup> Although, histopathological diagnosis is usually straightforward, some tumors deserve special mention. These include a papillary variant of ependymoma, papillary meningioma, and metastatic papillary carcinoma of the thyroid. Immunohistochemical studies can, however, rule out these possibilities. Metastatic carcinomas show immunoreactivity for EMA and weakly S-100 positive. Ependymomas are strongly positive for GFAP while negative for synaptophysin.<sup>[35]</sup>

#### Treatment

Surgical removal is the treatment of choice, and gross total removal should be attempted in all cases.<sup>[3,7,12,15,25,30,34,42]</sup> As these tumors are highly vascular, exquisite care needs to be taken during surgery, especially in young children in whom these tumors are most commonly seen as few cases of mortality due to perioperative blood loss have been reported.<sup>[7]</sup> Blood loss needs to be contained by securing the main arterial feeder (usually a branch of a choroidal artery) early in the course of surgery followed by tumor coagulation and en bloc or piecemeal removal.<sup>[12,20,21,41]</sup> Advances in catheter technology have made embolization of small caliber feeding vessels possible in the preoperative period and few such successful cases have been reported in literature, however, this mandates radiation and has additional risks such as vessel injury and stroke.<sup>[6,15,42]</sup> Recently, intraoperative usage of tranexamic acid has been reported in infants undergoing surgery for these tumors for reducing blood loss.<sup>[27]</sup> Management of hydrocephalus is an important aspect due to its ubiquitous accompaniment with these lesions seen in the majority of cases. It remains a topic of controversy, and various options include the placement of an external ventricular drain (EVD) (either preoperatively or during surgery), VP shunt or endoscopic third ventriculostomy (ETV). Although a clear consensus is not available regarding which strategy is superior, we feel that the clinical scenario of the patient needs to be taken into consideration in addition to the radiological picture. In a patient presenting with drowsiness with severe hydrocephalus noted on imaging, and facilities for emergency tumor removal are not available, a VP shunt will be the best option. It can be followed by a

definitive surgery after a few days, until stabilization of the general condition. If emergency facilities are available and the general condition appears fair, a temporary EVD will suffice. If, however, the presenting features are only headache and papilledema with a normal sensorium and only a mild-moderate hydrocephalus is noted on imaging, an initial ETV followed by surgical removal or a definitive surgery on a semi-urgent basis are options that can be utilized. Many authors agree that, in most of the cases, a temporary EVD placed during surgery will suffice, taking into consideration the benign nature of these tumors, and the long-term sequelae of shunt procedures; however, a few of them consider placement of VP shunt as a primary step in these tumors with hydrocephalus<sup>[12,25,41]</sup> In our series, two patients (one presenting with altered sensorium and one with severe hydrocephalus and papilledema) underwent preoperative VP shunt while direct tumor removal was done for the third child. Surgical approaches need to be tailored according to the size, location and extent of the lesion. In case of posterior third ventricular lesions, options of infratentorial supracerebellar, occipital transtentorial, transcallosal or a transcortical-transforaminal approaches are available. [16,21,25,36] A midline suboccipital approach using the telovelar corridor will suffice for fourth ventricular lesions.<sup>[12,29]</sup> For CP angle lesions, a midline approach through the cerebellomedullary fissure or the conventional retrosigmoid approach can be utilized, depending on the size, and extent of the tumor.<sup>[11,20,39,41]</sup> In this, a crucial step would be to dissect the caudal pole of tumor from the lower cranial nerves and the most ventral part of the tumor can sometimes be hidden, which may account for the remnants noted on postoperative imaging.[41] Although complete removal is the ideal treatment, it might not be possible in all cases, due to excess blood loss which might not be compensated by infants and young children or due to infiltration into surrounding structures. In situations where there is significant residual/ recurrence of the lesion, redo-surgery might be required at a later stage if the lesion seems operable (for the former cases), or else, adjuvant therapy is given (for the latter situations).<sup>[25,41]</sup> The most common complications noted after surgery include pneumocephalus, pneumoventricle, subdural effusions and persistence of hydrocephalus (in those not previously shunted), and new onset hydrocephalus.<sup>[20,41]</sup> The long-term survival is excellent in completely resected cases of CPP with 10-year survival rates close to 100% being reported in a few series.<sup>[3,19,20,26,34]</sup> As these are WHO Grade 1 lesions, no adjuvant treatment is required in completely resected ones. Although, reports of radiotherapy and radiosurgery in CPP can be found in literature, it might possibly be reserved for inoperable residual tumors or resistant/ aggressive subtypes.<sup>[8,14,41]</sup> Combination chemotherapy has been suggested for recurrent tumors, however, with limited success.<sup>[18]</sup> Recently, successful use of

bevacizumab has been reported in a case of atypical CPP.<sup>[13]</sup> CSF seeding and malignant transformation are uncommon.<sup>[15,41]</sup>

# CONCLUSIONS

CPPs are uncommon, benign, primary intracranial tumors. Posterior third ventricle, fourth ventricle, and CP angle are uncommon locations for these tumors in children. Raised ICP is the most common manifestation. They should always be considered in the differential diagnosis in children in any location, in the presence of supportive imaging findings. Surgical removal is the treatment of choice and approaches need to be tailored according to location, size, and extent of the tumor. These tumors are highly vascular, a feature which must be taken into consideration during surgery, especially in young children. Early securing of the arterial feeder is essential to reduce blood loss. Complete resection is the standard of care, and the long-term survival rate is excellent after complete removal. No adjuvant treatment is required, except in atypical and aggressive cases.

#### Acknowledgment

Authors would like to thank Dr. Kiran Subbarao for supporting with the histopathological images.

# **Financial support and sponsorship** Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

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