HOROID plexus carcinoma is an exceedingly rare neoplasm whose existence was debated as late as the 1950s. It represents less than 0.5% of all intracranial neoplasms and occurs most often in infants and children between the ages of 15 and 36 months, although older children and adults may also be affected. These neoplasms are most frequently found in contiguity with the ventricular ChPE. Choroid plexus papillomas and ChPCs have been infrequently described in the cerebellopontine angle, but most of these lesions were thought to arise from tufts of ChPE protruding through the foramina of Luschka. Two cases of choroid epithelial cyst and five of ChPP have been described in locations where an attachment to the normal ChPE could not be identified. To the best of our knowledge, this is the first report of a ChPC in a location completely unassociated with the ventricular system and normal choroid plexus.

Case Report

History. This 6-year-old right-handed girl presented with a 6-week history of headaches and decreased use of her right side. On admission, a CT scan revealed a large cystic mass in the left frontal lobe region of the brain. There was no history of fever, chills, or a known tick bite. The patient had been treated at the same hospital 3 years previously for vomiting and headaches that occurred after an unwitnessed fall in her home. A CT scan obtained at that time was significant for a nondisplaced left linear temporoparietal skull fracture and was otherwise negative; her history was otherwise noncontributory. There was no family history of congenital neoplasm.

Examination. On physical examination, the patient was alert and oriented. She was holding her right arm in a flexed and pronated position close to her body. She was afebrile and had normal vital signs. The second through 12th cranial nerves were intact bilaterally. The patient had profound weakness of her right upper extremity and mild weakness of her right lower extremity. Her speech was clear and fluent. No focal sensory or cerebellar abnormalities were detected, and results of the remainder of the physical examination were unremarkable. Findings of routine laboratory studies, including a complete blood count with differential and a limited chemistry panel, were within normal limits.

Imaging Studies. Head CT scans performed with and without contrast agents revealed a large left frontal complex mass within a cystic cavity. The mass measured 5 × 5 cm and consisted of a central, lobulated, and markedly contrast-enhancing pedunculated soft tissue component. The reported that the patient had been more difficult to rouse over the 3 days prior to admission. Associated symptoms included numbness and tingling in her right arm, nausea, and vomiting. There was no history of fever, chills, or a known tick bite. The patient had been treated at the same hospital 3 years previously for vomiting and headaches that occurred after an unwitnessed fall in her home. A CT scan obtained at that time was significant for a nondisplaced left linear temporoparietal skull fracture and was otherwise negative; her history was otherwise noncontributory. There was no family history of congenital neoplasm.

KEY WORDS • brain tumor • choroid plexus tumor • children

Abbreviations used in this paper: ChPC = choroid plexus carcinoma; ChPE = ChP epithelium; ChPP = ChP papilloma; CK = cytokeratin; CT = computerized tomography; MR = magnetic resonance.
cystic cavity measured 5.8 × 4.6 cm and had a minimally enhancing rim (Fig. 1). The mass was not associated with the adjacent left lateral ventricle. Considerable mass effect was present, and subfalcine herniation was identified, although the ventricles were not enlarged. The patient was started on intravenous dexamethasone and fosphenytoin, and she underwent tumor resection later that same day.

Operation. A left frontal craniotomy was performed; on opening the dura, a cyst was encountered immediately. The cyst was opened and led directly to the tumor mass. The wall of the cyst cavity was transparent, and there was no evidence of tumor in the cyst wall. The tumor itself was firm and white. Feeding vessels were found deep near the area of the ventricular ependyma, but the ependyma of the ventricle was not breached during the operation. A gross-total excision of the tumor was performed. The patient tolerated the procedure well, and there were no intraoperative complications.

Pathological Examination. Gross examination of the fresh tumor specimen was significant for multiple fragments of tan-pink, soft and friable tissue collectively weighing 41.7 g and measuring 8 × 5 × 3 cm. Tissue samples weighing 13.2 g were sent to the Pediatric Oncology Group study. The remainder of the tissue was fixed in 10% formalin and processed for paraffin embedding. The paraffin blocks were sectioned at 4-μm intervals, and these sections were stained with hematoxylin and eosin for microscopic examination. Histologically, the tissue was composed of papillae lined by layers of malignant cells; these cells formed solid sheets in many areas. The cells had malignant histological features, including an increased nuclear-to-cytoplasmic ratio, high mitotic index, and marked cytological atypia (Figs. 2 and 3). The differential diagnosis included ChPC, papillary anaplastic ependymoma, and metastatic carcinoma.

Well-formed periodic acid-Schiff–positive basement membranes were present. Immunohistochemical staining was performed on paraffin-embedded sections. The malignant cells stained diffusely positive for a pancytokeratin cocktail (AE1:3), epithelial membrane antigen, and vimentin. The tumor had focal areas of positivity for glial fibrillary acidic protein and also S100 protein, which is a marker of neural differentiation. Immunohistochemical stains for polyclonal carcinoembryonic antigen, placental alkaline phosphatase, and an epithelial non-CK were nonreactive. A diagnosis of ChPC was made.

Postoperative Course. The patient’s postoperative course was uncomplicated. Her headaches ceased, and she was able to raise her right arm without difficulty. A CT scan performed 3 weeks after resection demonstrated a cavity without identifiable tumor and partial resolution of the cerebral edema (Fig. 4). The patient was discharged on postoperative Day 4 with resolution of her neurological deficits. Serial MR studies of the head with gadolinium contrast administration were performed periodically in the outpatient setting. Three months after resection, the wall of the resection cavity appeared slightly thickened and irregular. The patient had no signs or symptoms of tumor recurrence, but MR imaging performed 6 weeks later demon-
strated that the cavity thickening was increasing in size and level of contrast enhancement. Moreover, the contrast-enhancing lesion was present in the same location as the previously resected neoplasm (Fig. 5). The patient was diagnosed as having a recurrent ChPC. She was then treated with chemotherapy for the first time with one course of vincristine, cyclophosphamide, and mesna. This was followed 6 weeks later by a second course of chemotherapy consisting of cisplatin and VP-16, in addition to radiation therapy. The patient then entered an experimental chemotherapy trial consisting of carmustine and irinotecan hydrochloride at another institution. She had no signs or symptoms of intracranial disease until 2.5 years after the initial resection. At the time this paper was written, the patient had recently presented with renewed right upper-extremity weakness. A head CT scan was significant for a large cystic recurrent tumor in the same location as her previous lesion, except for a new satellite focus located superiorly in the posterior left frontal lobe.

Discussion

Choroid plexus tumors typically arise from ChPE. Hence, most of these tumors are based in the ventricular system in locations where choroid plexus is normally present. For the purposes of discussion, only those cases of choroid plexus lesions arising in a site separate from the normal choroid plexus will be considered.

Three cases of choroid plexus cysts and six cases of ChPP have been reported to have arisen in a location unassociated with the normal choroid plexus; these are outlined in Table 1. There are several theories on how these lesions might originate in such unusual locations. Azzam and Timperley and Greene proposed that choroid plexus cysts might arise from primitive ectopic secretory ChPE that is present within the brain substance but outside of the ventricular system (primary ectopia) or from ependymal tissue that became segregated during the developmental stage of the brain (secondary ectopia). Because many of these ectopic choroid plexus lesions are in proximity to ChPE, it is also possible that these lesions arise within the normal nearby choroid plexus and become separated from it later as the tumor evolves.

Unlike all previously reported cases, this patient har-
bored a ChPC. In addition, she had a history of significant head trauma sustained 3 years before the discovery of her tumor. A head CT scan obtained to investigate the earlier trauma was negative for parenchymal mass lesions or cysts. This finding argues against the presence of a congenital ChPP or choroid plexus cyst that later transformed into a carcinoma. Therefore, this patient’s head trauma is important because it led to a baseline head CT scan prior to the development of her brain tumor.

The diagnosis in this case was difficult because of the atypical location of the neoplasm. The differential diagnosis of this neoplasm has been extensively reviewed in a previous publication on ChPC. The histomorphological features of this particular neoplasm are also seen in malignant papillary ependymomas, germ cell tumors, and metastatic papillary carcinomas. Papillary ependymomas (myxopapillary ependymomas) do not express well-formed periodic acid-Schiff–positive basement membranes and are diffusely positive for glial fibrillary acidic protein. They usually occur in the filum terminale. Germ cell tumors are usually positive for placental alkaline phosphatase. Metastatic carcinomas are unusual in children with no history of a cancer syndrome. Metastatic carcinomas are characteristically positive when stained with an epithelial non-CK stain and polyclonal antibody against carcinoembryonic antigen, and this neoplasm was negative for both of these markers.

Recently, in a study published by Gyure and Morrison the authors described the application of antibodies for CK7 and CK20 to 35 ChPPs. The majority of these neoplasms stained positively for CK7 and negatively for CK20; however, six of the tumors were negative for both antibodies, as was the neoplasm in our case. To our knowledge, the reactivity of ChPCs to immunohistochemical stains for CK7 and CK20 has not yet been reported. Further investigation into this area is warranted to determine the typical pattern in ChPCs.

Papillary renal cell carcinoma can have strikingly similar morphological characteristics to ChPC, but these neoplasms are very rare in children and typically present as an abdominal mass. This patient has manifested no signs or symptoms of another neoplasm despite follow-up examinations at regular intervals. At the time this paper was written, 30 months had elapsed since the resection of her brain tumor.

Transthyretin (prealbumin) positivity is suggestive of but not specific for choroid plexus differentiation. Unfortunately, this antibody was unavailable in our laboratory, and the test was not performed on our patient’s neoplasm. Nevertheless, this case has the typical immunohistochemical profile of a ChPC.

**Conclusions**

To the best of our knowledge, this is the first reported case of a ChPC arising in a location unassociated with the normal choroid plexus and ventricular system. The oncogenesis of this lesion is unknown. An unusual feature of this case is the availability of a negative CT study 3 years before presentation. Gross-total resection is the only proven treatment modality in young children, and this was achieved in our patient. Unfortunately, her tumor recurred in the same location 3 months postoperatively.

Such an atypical location could prove confounding to the neurosurgeon, radiologist, and surgical pathologist alike. We report this case to document it as a diagnosis to consider in the evaluation of intraparenchymal brain neoplasms in children.

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**TABLE 1**

**Literature review of choroid plexus lesions that were unconnected to the normal choroid plexus**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age, Sex</th>
<th>Type of Lesion</th>
<th>Location of Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greene, 1951</td>
<td>60 yrs, M</td>
<td>ChPP</td>
<td>rt cerebellar hemisphere</td>
</tr>
<tr>
<td>Robinson, 1955</td>
<td>67 yrs, M</td>
<td>ChPP</td>
<td>rt cerebellar hemisphere</td>
</tr>
<tr>
<td>Handa &amp; Bucy, 1956</td>
<td>34 yrs, F</td>
<td>choroid plexus cyst</td>
<td>rt temporal lobe</td>
</tr>
<tr>
<td>Azam &amp; Timperley, 1981</td>
<td>32 yrs, F</td>
<td>choroid plexus cyst</td>
<td>lt cerebral hemisphere</td>
</tr>
<tr>
<td>Inoue, et al., 1987</td>
<td>4 mos, F</td>
<td>choroid plexus cyst</td>
<td>suprasellar region</td>
</tr>
<tr>
<td>Kimura, et al., 1992</td>
<td>34 yrs, F</td>
<td>ChPP</td>
<td>rt cerebellopontine angle</td>
</tr>
<tr>
<td>Li &amp; Savolaine, 1996</td>
<td>34 yrs, M</td>
<td>ChPP</td>
<td>posterior 3rd ventricle*</td>
</tr>
<tr>
<td>Nakano, et al., 1997</td>
<td>42 yrs, F</td>
<td>ChPP</td>
<td>posterior 3rd ventricle*</td>
</tr>
</tbody>
</table>

* This ChPP was actually located within the third ventricle but was unassociated with the nearby choroid plexus.

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**FIG. 5.** Coronal MR image obtained 8 months postresection revealing a contrast-enhancing lesion within the tumor cavity in the same location as the previously resected tumor. The lateral ventricle is uninvolved by the recurrent neoplasm.
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References

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