Choroid plexus tumors: problems in diagnosis and management

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Choroid plexus tumors are uncommon neoplasms of the central nervous system. A series of 11 cases from the Vancouver General and British Columbia Children’s Hospitals, treated during the last 12 years, are reviewed. Some of the management problems commonly encountered with these tumors are discussed. Many of these tumors are associated with severe hydrocephalus at the time of diagnosis, and the perioperative management of this hydrocephalus remains a matter of some debate. The timing of and the necessity for shunting are major considerations. Large subdural fluid collections are often discovered in the postoperative period, and these occasionally cause symptoms of increased intracranial pressure. Reasons for this problem are suggested and possible steps for its prevention are proposed.

The similarity between papillary ependymomas and choroid plexus papillomas has sometimes caused difficulty in pathological diagnosis. Choroid plexus carcinomas, of which there were two in this series, also present a diagnostic challenge. Differential diagnosis affects the further treatment and prognosis for the patient.

Key Words • brain neoplasm • choroid plexus tumor • hydrocephalus

Choroid plexus tumors are uncommon neoplasms of the central nervous system, accounting for 0.4% to 1.0% of all intracranial tumors. The evolution of diagnostic and management techniques, well documented in several reports and reviews of over 400 cases, shows a progressive understanding of the pathophysiology of the problems associated with these tumors. This has led to significant improvement in long-term outcome since the first attempt at surgical removal reported by Bielschowsky in 1902. However, there still remain some unsolved problems.

We have reviewed the records of 11 patients who demonstrated the typical spectrum of difficulties encountered in the management of these tumors. Of particular interest are strategies for control of the severe hydrocephalus and of the large subdural fluid collections that often developed postoperatively. In addition, problems with pathological diagnosis and management of choroid plexus carcinoma are discussed.

Summary of Cases

Eleven cases of choroid plexus tumors have been managed at the Vancouver General Hospital and British Columbia Children’s Hospital during the last 12 years (Table 1). Eight of the patients were children, aged from 8 to 18 months (mean 12 months), and three were adults, aged 21, 50, and 58 years. Six were males and five females. All patients presented with symptoms and signs of raised intracranial pressure (ICP), including vomiting, drowsiness or lethargy, and headache or irritability. In addition, patients with posterior fossa lesions also exhibited signs of brain-stem and cerebellar involvement, including cranial nerve abnormalities, pyramidal tract signs, and ataxia.

Four of the tumors were found in a lateral ventricle, three in the fourth ventricle, three in the third ventricle, and one at the cerebellopontine angle. Two of the lesions were malignant choroid plexus carcinomas: one in the fourth ventricle and two in the left lateral ventricle. On radiological investigation, all patients had some degree of hydrocephalus at the time of diagnosis; however, only six of the 11 required a ventricular shunting procedure. Three of these underwent shunt placement before surgery and three after. Two patients (Cases 4 and 6) developed large postoperative subdural fluid collections which required subdural-peritoneal shunting.

Two patients (Cases 1 and 5), both children, had nonresectable choroid plexus carcinomas; one died 2 months after biopsy and the other died 2 days after partial removal of the lesion. The remainder had choroid plexus papillomas, five of which were totally re-
### Diagnosis and management of choroid plexus tumors

**TABLE 1**

*Clinical summary of 11 patients with tumors of the choroid plexus*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, Sex</th>
<th>Symptoms</th>
<th>Location</th>
<th>Shunt Placed</th>
<th>CSF Analysis</th>
<th>Surgery</th>
<th>Pathology</th>
<th>Postop Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18 mos, F</td>
<td>irritable, vomiting, stiff neck, left 3rd &amp; 6th nerve paresis for 1 mo</td>
<td>4th ventricle</td>
<td>postop</td>
<td>cancer cells, protein 59 mg%, clear</td>
<td>biopsy</td>
<td>CPCa</td>
<td>chemotherapy; died 2 mos after onset of symptoms</td>
</tr>
<tr>
<td>2</td>
<td>3 mos, F</td>
<td>sunset eyes, vomiting for 1 mo</td>
<td>3rd ventricle</td>
<td>preop</td>
<td>protein 103 mg%, clear</td>
<td>attempted stereotaxic biopsy, then total removal</td>
<td>CPP</td>
<td>pupils slow, seizures</td>
</tr>
<tr>
<td>3</td>
<td>18 mos, F</td>
<td>vomiting, irritable, hypertonia, depressed gag reflex, other reflexes increased; husky voice since birth</td>
<td>4th ventricle</td>
<td>no</td>
<td>protein 79 mg%, clear</td>
<td>subtotal removal</td>
<td>CPP</td>
<td>improved gag reflex, voice, swallow</td>
</tr>
<tr>
<td>4</td>
<td>6 mos, M</td>
<td>enlarged head, sunset eyes, bilat 6th nerve paresis, irritable &amp; lethargic for 3 months</td>
<td>3rd ventricle</td>
<td>no</td>
<td>not done</td>
<td>total removal</td>
<td>CPP</td>
<td>seizure, bilat SDFC's requiring subdural-peritoneal shunt</td>
</tr>
<tr>
<td>5</td>
<td>5 mos, M</td>
<td>vomiting, lethargy, sunset eyes, enlarged head</td>
<td>lt lateral ventricle</td>
<td>no</td>
<td>protein 600 mg%, xanthochromic</td>
<td>partial removal (50%)</td>
<td>CPP</td>
<td>died 2 days postop</td>
</tr>
<tr>
<td>6</td>
<td>12 mos, M</td>
<td>irritable, lt 6th nerve paresis</td>
<td>lt lateral ventricle</td>
<td>preop</td>
<td>protein 196 mg%, clear</td>
<td>total removal</td>
<td>CPP</td>
<td>rt hemiparesis, bilat 6th nerve paresis, bilat SDFC's requiring subdural-peritoneal shunt reop 1 yr postop: total removal, no deficit</td>
</tr>
<tr>
<td>7</td>
<td>17 mos, M</td>
<td>irritable, drowsy, vomiting, enlarged head for 1 mo</td>
<td>lt lateral ventricle</td>
<td>preop</td>
<td>protein 94 mg%, clear</td>
<td>subtotal removal (95%)</td>
<td>CPP</td>
<td>poor adduction of both eyes</td>
</tr>
<tr>
<td>8</td>
<td>18 mos, F</td>
<td>irritable, poor walking, bilat 6th nerve paresis, papilledema</td>
<td>rt lateral ventricle</td>
<td>no</td>
<td>not done</td>
<td>total removal</td>
<td>CPP</td>
<td>hemorrhage, infected shunt 6 yrs postop</td>
</tr>
<tr>
<td>9</td>
<td>21 yrs, M</td>
<td>vomiting, leg weakness for 18 mos, papilledema</td>
<td>3rd ventricle</td>
<td>postop</td>
<td>not done</td>
<td>total removal</td>
<td>CPP</td>
<td>dysphagia, ataxia, rt 7th nerve paresis; reop 3 yrs later, died 6 mos postop of respiratory arrest</td>
</tr>
<tr>
<td>10</td>
<td>50 yrs, F</td>
<td>ataxia, headache, dizzy, rt 7th nerve paresis, papilledema</td>
<td>rt cerebello-pontine angle</td>
<td>postop</td>
<td>not done</td>
<td>partial removal (50%)</td>
<td>CPP</td>
<td>irradiation, improved postop, died of pneumonia 5 yrs later</td>
</tr>
<tr>
<td>11</td>
<td>58 yrs, M</td>
<td>ataxia, vomiting, lt hand clumsy, nystagmus, depressed lt gag reflex &amp; facial sensation</td>
<td>4th ventricle</td>
<td>no</td>
<td>not done</td>
<td>biopsy</td>
<td>CPP</td>
<td></td>
</tr>
</tbody>
</table>

* CSF = cerebrospinal fluid; CPCa = choroid plexus carcinoma; CPP = choroid plexus papilloma; SDFC = subdural fluid collection.

The follow-up period ranged from 5 months to 9 years (mean 5.5 years). During that time, two of the adults died: one 3 years after diagnosis as a result of complications associated with an attempt to remove a recurrent tumor (Case 10) and one due to an unrelated event (Case 11). The remaining patients with choroid plexus papillomas have exhibited some improvement postoperatively. Only one child and one adult have become symptom-free. Two cases are presented in more detail since they highlight some of the problems of management.

#### Case Reports

**Case 4**

This 6-month-old boy presented with a 3-month history of irritability, lethargy, and increasing head size. Examination showed an enlarged head with bulging fontanels and splayed sutures. He had poor upward gaze and a bilateral sixth nerve paresis. A cranial ultrasound study and subsequent computerized tomography (CT) scan showed massive obstructive hydrocephalus secondary to a large third ventricle tumor (Fig. 1 left). At surgery through a left frontal parietal craniotomy and transcortical incision, a choroid plexus papilloma was totally removed from the third ventricle.

Postoperatively, the patient was left with a mild right hemiparesis and subsequently suffered a focal seizure involving the right side. This required treatment with antiepileptic drugs. A follow-up CT scan showed large bilateral subdural fluid collections; the ventricle was greatly reduced in size but was still abnormally large (Fig. 1 right). A subdural-peritoneal shunt was inserted, and follow-up CT scans revealed gradual disappearance of the subdural fluid collections. The mild right hemiparesis resolved and the child has since been seizure-free.
lesions, is well documented. The age distribution is also
proportional cerebellar and brain-stem signs for posterior fossa
hemorrhage. At autopsy, the tumor was found to be diffusely infiltrat-
ing mass in the cerebellar vermis. Cerebrospinal fluid
(CSF) analysis showed protein and glucose levels of
59 mg% and 27 mg%, respectively. A substantial num-
ber of malignant cells were also revealed. At surgery
through a suboccipital craniectomy, a gray gelatinous
tumor was found infiltrating the cerebellar vermis.
Meningeal spread was evident, and only partial removal
was possible. The pathological diagnosis was choroid
plexus carcinoma.
Postoperatively, the child had persistent hydroceph-
alus and required insertion of a ventriculoperitoneal
(VP) shunt. She was started on a course of chemo-
therapy but rapidly deteriorated. A CT scan showed
progression of the tumor. She developed further brain-
stem involvement and subsequently died of respira-
tory arrest 3 months after the onset of symptoms. At
autopsy, the tumor was found to be diffusely infiltrat-
ing the cerebellar parenchyma and was widely spread
throughout the subarachnoid space, surrounding sev-
eral cranial nerves. The diagnosis of choroid plexus
carcinoma was confirmed.

Discussion
Our analysis of the present group of patients largely
conforms to the findings of other series reported in the
literature. The clinical presentation of nonspecific signs
of increased ICP for all lesions, associated with addi-
tional cerebellar and brain-stem signs for posterior fossa
lesions, is well documented. The age distribution is also
similar, with 70% of patients being less than 2 years
old. However, the distribution of tumors is somewhat
irregular: slightly more third ventricle and posterior
tumors than usual and also the two malignant
tumors were found in children. Most series report a
preponderance of lateral ventricle tumors in children,
with very few malignancies.14,17,19
Although choroid plexus tumors are for the most
part benign lesions, there may be a significant risk of
morbidity and mortality associated with their surgical
treatment.3 The long-term outcome in this group (and
others) reflects the difficulties encountered in the man-
agement of these patients. The use of modern diag-
nostic techniques, microsurgery, and safe neurosurgical
anesthesia has greatly reduced the number of deaths
resulting from management; however, the incidence of
morbidity may still be significant.11
Prior to the availability of CT scanning, ventriculog-
raphy was a common method of radiological diagnosis
of these tumors. However, several cases of rapid dete-
rioration and death associated with this procedure were
reported, leading many authors to abandon this tech-
nique when angiography became widely available.19 The
cause of death is not fully understood, but most likely
it was due to acute brain shifts associated with rapid
ventricular drainage. Other proposed causes include
bleeding from the tumor, an acute rise in ICP due to
injected air or contrast medium, or a rapid increase in
CSF production as a result of an acute alteration in
CSF dynamics.14 With the advent of CT, ventriculog-
raphy is no longer necessary; however, the problem of
ventricular drainage must still be considered in cases of
hydrocephalus.
Many reasons have been suggested for the develop-
ment of hydrocephalus in patients with choroid plexus
tumors. Obstruction of the CSF pathway by the tumor
itself is most commonly proposed, especially with tu-
mors originating in the third or fourth ventricle. How-
ever, it is unlikely that a tumor arising in the lateral
ventricle will obstruct the CSF pathway causing hydro-
cephalus unless it is very large. In this latter situation
it has been hypothesized that hydrocephalus may be
caused by hypersecretion of CSF by the tumor, by
pulsation of the large tumor mass, or by blockage of
CSF absorption by high protein concentrations and
blood breakdown products from multiple small hem-
orrhages within the tumor.15
In the seven patients in our series with third or fourth
ventricle tumors, hydrocephalus was clearly due to ob-
struction of the CSF pathway. The four patients with
lateral ventricle tumors had such large masses that on
CT scans the aqueduct appeared to be compressed,
causing obstructive hydrocephalus. The CSF protein
level was recorded in six patients and was elevated in
every one. In addition, Case 6 had likely suffered a
hemorrhage from the tumor, as the CSF was also xan-
thochromic. No conclusion can be made as to the role
of the elevated CSF protein content played in the de-
velopment of hydrocephalus in these patients, as three had
a shunting procedure preoperatively, one had a shunt
inserted postoperatively, and two did not have a shunt
placed.

M. C. Boyd and P. Steinbok
Diagnosis and management of choroid plexus tumors

The management of the hydrocephalus is controversial, the timing or necessity for shunting being the major issues. Pascual-Castroviejo, et al., reported three patients who received VP shunts after diagnosis. Two of these died shortly after shunting; however, both had undergone ventriculography prior to the shunting procedure. The third patient, who was diagnosed by CT, survived; thus, the ventriculography rather than the shunting may have been the cause of death.

Raimondi and Gutierrez, in an extensive review of choroid plexus tumors in 1975, recommended that patients with third and fourth ventricle tumors causing hydrocephalus have shunts placed as soon as the diagnosis was made, followed by a delay of 7 to 14 days before definitive surgery. They removed the shunt 4 to 5 days postoperatively to prevent the development of intracranial hypotension and cyst formation. Although they did not routinely replace shunts in patients with hydrocephalus associated with lateral ventricle tumors, they did caution that total removal of the tumor does not guarantee control of the hydrocephalus. Another approach to the problem was described by Joona and Grant, who used preoperative external ventricular drainage in one of their two patients. Neither of their patients required a postoperative VP shunt. None of the 16 patients reported by Matson and Crofton required ventricular shunting. They believed that successful removal of the papilloma in 11 patients with resulting resolution of the hydrocephalus weighed heavily in favor of the CSF overproduction theory of hydrocephalus etiology.

Currently, the recommended treatment for choroid plexus papillomas is total excision if possible. Laurence, in agreement with Matson and Crofton, suggested that this be done prior to any consideration for shunting, as removal of the tumor may resolve the hydrocephalus. He did, however, state that a shunt may be required should hydrocephalus persist postoperatively. This may occur if the surgical procedure has failed to relieve the obstruction or if a secondary basal block causing communicating hydrocephalus is present. More recently, this “wait and see” approach has been applied to other obstructing lesions, particularly those in the fourth ventricle.

Six of our patients underwent ventricular shunting procedures, three preoperatively and three postoperatively. Of the three patients with preoperative shunt placement, two had large lateral ventricle tumors and one had a third ventricle tumor. All three lesions appeared to be obstructing the CSF pathway on the CT scan; however, the CSF production rate was not measured to rule out CSF overproduction as a cause of hydrocephalus. The patient with a tumor in the third ventricle had complete resolution of her hydrocephalus prior to definitive surgery. Of the other two, one had occlusion of the lateral ventricle on the side of the tumor, preventing full resolution of the hydrocephalus. The moderate ventricular enlargement persisted in the third patient, possibly due to a thinned noncompliant cortical mantle. The three patients who required postoperative shunts exhibited obstruction to CSF flow: two had progressive tumor enlargement after incomplete resection and one had a postoperative hemorrhage.

Five of the patients did not have ventricular shunting. One died 2 days after partial removal of a malignant lateral ventricle tumor. Although the exact cause of death was not determined, an autopsy showed hydrocephalus. Three patients had resolution of their hydrocephalus, two after total removal of a lateral ventricle tumor and one after 95% removal of a fourth ventricle tumor. In the fifth patient, hydrocephalus resolved after biopsy and radiation therapy of a presumed fourth ventricle ependymoma, which autopsy 5 years later proved to be a choroid plexus papilloma.

The patients who did not have shunts placed preoperatively fared just as well as those who did. The three patients who eventually required postoperative shunts did not suffer any adverse effects from delay of the procedure. The surviving patients who had hydrocephalus preoperatively, but who did not undergo a shunt procedure and have not required a shunt postoperatively, have been spared the potential complications of this procedure.

The problem of postoperative subdural fluid collections is not often discussed in the literature, especially in reports from the pre-CT scan era. One of the patients reported by Matson and Crofton (their Case 10) developed a large subdural fluid collection after a transcortical approach to a lateral ventricle tumor. A subdural-peritoneal shunt was required to control a progressively increasing head size. They suggested filling the ventricle with physiological saline prior to closure of the dura to support the thinned cortex. Laurence also recommended this maneuver, believing that this might prevent tearing of cortical vessels should the thinned cortical mantle collapse. Jooma and Grant reported two patients who developed postoperative subdural fluid collections, one of whom required a subdural-pleural shunt. They attributed this problem to a subdural-transcallosal fistula developing as a result of a transcallosal approach to the third ventricle. They had seen a similar complication in other patients who had been subjected to a transcallosal approach for a lesion in the lateral or third ventricle.

In a recent review discussing problems encountered with the surgical treatment of supratentorial midline tumors in children, Koos, et al., commented on cerebral hemisphere collapse following the decompression of a grossly enlarged ventricular system. They considered that, although the enlarged ventricle may facilitate exposure of the tumor, hydrocephalus should be relieved gradually by shunting prior to direct attack on the tumor. They recommended shunting of the subdural space if a subdural fluid collection became a problem.

Two of our patients developed significant postoperative subdural fluid collections with enlarging head size requiring a subdural-peritoneal shunt. One patient had a VP shunt placed preoperatively and one had not. Both of these patients had undergone a transcortical procedure.
approach to their tumor: one transfrontally for a third ventricle tumor and one transtemporally for a tumor arising at the trigone. Four other patients were also subjected to a transcortical approach to their tumor: three transtemporally for tumors arising in the trigone and one transfrontally for a third ventricle tumor. One patient without a significant subdural fluid collection died 48 hours after surgery. One patient developed hydrocephalus as a result of hemorrhage into a third ventricle tumor bed, but there was no subdural fluid collection. In the two remaining patients, the pia was sutured closed with a 4-0 silk suture over a piece of Gelfoam after the ventricles had been filled with physiological saline, and neither developed subdural fluid collections. One of these patients had undergone shunting preoperatively and one had not.

It appears that a postoperative subdural fluid collection results from persistence of a ventriculosubdural fistula. Preoperative shunting did not seem to prevent this complication in one of our cases but may have helped in another. The patients who developed this problem and also those in whom an attempt was made to close the cortical incision all had severe hydrocephalus and an extremely thin cortical mantle where the cortical incision had been made. The other patients either did not have a cortical splitting incision or had a relatively normal cortical mantle through which the incision was made. This suggests that the thickness of the cortex may play an important role in the development of a postoperative ventriculosubdural fistula and of a subsequent subdural fluid collection. Although it is questionable whether preoperative shunting will aid in prevention of this complication, closure of the cortical incision seems to be useful.

The pathological diagnosis of a choroid plexus papilloma may be quite difficult in some cases. Papillary ependymomas often enter into the microscopic differential diagnosis. Choroid plexus papillomas, however, closely mimic normal choroidal plexus and do not contain ciliated cells with blepharoplasts, which are a common feature of ependymomas. A biopsy specimen from one of our patients was thought to show a papillary ependymoma; the patient was given radiation therapy as a result of that diagnosis. Only at autopsy 5 years later was the diagnosis of choroid plexus papilloma made.

Malignant choroid plexus tumors are perhaps more difficult to diagnose than are benign lesions. Although Fortuna, et al., found 21% of all choroid plexus tumors to be malignant, Broad and Allen suggested that this figure may be significantly lower if the strict criteria for malignancy, as listed by Zülch, are adhered to. Metastatic adenocarcinoma, ependymoma, and other gliomas may all be confused histologically with choroid plexus carcinoma. However, as pointed out by Carpenter, et al., choroid plexus carcinoma may be differentiated from these other lesions by the presence of cholesterol clefts and islands of normal choroid plexus within the tumor. Ciliated cells with blepharoepithelia in ependymomas, mucin-producing cells in metastatic adenocarcinoma, and abundant glial fibrillary acidic protein (GFAP) in other gliomas may help separate these tumors from those arising from the choroid plexus. It should be noted, however, that ciliated cells, mucin-producing cells, and GFAP-positive cells have also been found in choroid plexus tumors.

In two of our patients the diagnosis of choroid plexus carcinoma was confirmed at autopsy. One of these, a 5-month-old boy, was thought at biopsy to have a malignant ependymoma, but the diagnosis was revised when more tissue was obtained at the postmortem examination. The survival period for patients with choroid plexus carcinoma is generally poor, particularly in the pediatric age group. Dohrmann and Collias reported a mean survival time of only 9 months for a group of 16 children with a mean age of 2.0 years. The mean survival time for six adults (mean age 39 years) was 3.5 years. A few cases have been reported of long-term survival after total removal of malignant lesions; however, Carpenter, et al., have suggested that surgical excision plus radiation therapy offers the best opportunity for prolonged survival in patients with choroid plexus carcinomas. Both of our patients with malignant lesions were less than 2 years old. Radiation therapy was not considered in either based on recent experience of severe delayed complications in two patients who received cranial radiation at a young age. One patient died in the immediate postoperative period before any treatment could be instituted. The other received chemotherapy but this failed to halt the progression of her disease. She died 3 months after the onset of symptoms.

Although the present group of patients is not large, it does illustrate several problems complicating the management of patients with choroid plexus tumors. The difficulty in preoperative diagnosis experienced by many early clinicians has been significantly reduced with the advent of CT scanning and the widespread availability of cerebral angiography. However, in some cases, particularly in those of malignant tumors, the pathological differentiation may present a challenging problem.

The control of hydrocephalus seems best achieved by direct surgical attack and complete removal of the tumor. Resolution of the hydrocephalus should be closely monitored in the postoperative period, and an appropriate shunting procedure should be performed if the hydrocephalus persists or progresses. The problem of a clinically significant postoperative subdural fluid collection may possibly be prevented by the technical combination of making a small cortical incision, filling the ventricles with physiological saline prior to dural closure, and (perhaps more important) making an attempt to close the cortex with a fine pial suture or with a tissue glue such as Tisseel.*

Although current microsurgical and neuroanesthetic techniques have significantly reduced the operative

* Tisseel manufactured by Immuno AG, Vienna, Austria.
Diagnosis and management of choroid plexus tumors

mortality and morbidity in patients with choroid plexus tumors, few patients completely recover after treatment of their tumor. Perhaps earlier diagnosis combined with better control of hydrocephalus will help to improve the long-term outcome of these patients.

References

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