Carcinoma of the choroid plexus

Case report

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Carcinoma of the choroid plexus is an extremely rare disease with a particularly virulent course. A case is reported in the left lateral ventricle of a young woman who is well 1 year after total excision of the tumor. The four previously reported patients with this disease who did well (two males and two females) were all children. Three of the four were treated with surgery followed by radiotherapy, and one with surgery alone. Although it appears possible that gross total removal may be curative, radiation therapy is suggested because of the distinct possibility that even the least aggressive-appearing lesions may degenerate and become rapidly fatal. Chemotherapy, although not used in any of the cases reported, is suggested as a possible adjunct in the treatment of this disease.

KEY WORDS • choroid plexus carcinoma • choroid plexus papilloma • gross tumor removal • radiotherapy • chemotherapy

CHOROID plexus papilloma is a rare epithelial neoplasm. The reported incidence was 0.5% to 0.6% of all intracranial tumors, according to Zülch,26 and 0.4% to 0.6% in the series of Bohm and Strang.2 In a brain-tumor series of 408 patients under the age of 12 years, Matson and Crofton11 reported the incidence of choroid plexus papilloma to be 3.9%. Carcinoma of the choroid plexus is an even rarer lesion. Dohrmann and Collias6 reviewed the literature and were able to verify only 22 cases as truly being primary carcinoma of the choroid plexus. Valladares, et al.,19 have since reported one additional case. The prognosis for this disease is grim, and the most appropriate management not clear.

We present the case of a young woman with a noninvasive choroid plexus carcinoma arising in the left lateral ventricle. Gross total excision was possible, and she is doing well 1 year after surgery.

Case Report

This 29-year-old physician was well until 1½ years before admission to the Neurological Institute of New York, when she developed a pulsatile noise in the left ear. She noted that the noise could be relieved by left carotid compression, either directly or by turning her head to the right. She had no headaches, nausea, vomiting, visual disturbances, changes in mentation, weakness, seizures, or bowel or bladder dysfunction.

Examination. The patient, an East Indian woman, was in no distress, and her general physical examination was unremarkable. There were no bruits and no stigmata of von Recklinghausen's disease. Funduscopic examination revealed full veins and nasal blurring of the disc margins. Neurological examination was entirely within normal limits. Computerized tomography demonstrated an enhancing mass in the region of the atrium of the left lateral ventricle (Fig. 1). Angiography demonstrated a prominent anterior choroidal artery with a stain in the region of the left atrium (Fig. 2). The posterior parietal branch of the middle cerebral artery was considered to be enlarged. Early draining veins were seen in the region of the stain, and the left internal cerebral vein seemed depressed by a mass. There was a mild degree of hydrocephalus. Preoperative complete blood count, sequential multiple analysis for chemistry (SMAC), urinalysis, clotting profiles, and chest x-ray films were within normal limits.
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FIG. 1. Computerized tomography scans showing an intraventricular tumor that proved to be a carcinoma of the choroid plexus. A: Scan without contrast enhancement. B and C: Scans after infusion of contrast material. Note large vein (C).

FIG. 2. Angiogram of the lesion. Left: Arterial phase demonstrating prominent anterior choroidal artery (single arrow) and enlarged posterior parietal branch of the middle cerebral artery (double arrow). Right: Venous phase showing tumor blush (arrow), early draining veins, and depressed internal cerebral vein.

Operation. A left parietal craniotomy was carried out. The parietal cortex overlying the tumor was markedly atrophic. Following a cortical incision, gross total removal of a very vascular, partially calcified intraventricular neoplasm was achieved.

Postoperative Course. The patient was slow to wake up; she was disoriented and confused, and had a stiff neck due to subarachnoid leakage of blood during surgery. This resolved within a week. A Klebsiella urinary tract infection was treated with gentamicin. Cerebrospinal fluid (CSF) obtained by lumbar puncture was shown to contain no malignant cells on cytological examination by a Millipore filter method. She is well 1 year after surgery.

Pathological Examination. The neoplasm consisted of sheets of polygonal neoplastic cells with generally...
Fig. 3. Photomicrographs of the choroid plexus carcinoma. Left: The neoplastic cells vary greatly in size and show considerable nuclear pleomorphism. H & E, × 400. Right: The cells in this part of the neoplasm have uniform cytological and nuclear features resembling choroid plexus papilloma. A few calcium-containing bodies (arrow) are included in the field. H & E, × 160.

well defined cell borders (Fig. 3A). The cells varied considerably in size and contained eosinophilic granular cytoplasm. The nuclei showed marked variation in size, shape, and staining intensity. The chromatin was coarsely granular, and there was sometimes a distinct acidophilic nucleolus. Occasional cells had large bizarrely shaped nuclei or more than one nucleus. No mitotic figures were encountered. The neoplasm was traversed by many small thin-walled blood vessels. In a few areas, the lesion had features of a choroid plexus papilloma; the neoplastic cells had a uniform columnar shape and a papillary arrangement (Fig. 3B).

Laidlaw reticulum staining demonstrated that reticulum within the neoplasm was confined to the walls of blood vessels. No glial processes were identified with phosphtungstic acid-hematoxylin among the neoplastic cells or in the papillary fronds. Mucicarmine staining was negative. There were a few scattered round hyaline bodies within the tumor that stained positive with periodic acid-Schiff (PAS), and were resistant to diastase. The bodies varied in size from a few micrometers to about 20 µm in diameter. The largest bodies seemed to be extracellular, but some of the small PAS-positive bodies were clearly cytoplasmic. Other features of the neoplasm included occasional small aggregates of foamy macrophages, hemosiderin, large collections of cholesterol clefts, and a few psammoma bodies and other calcium-containing bodies. Occasionally, small papillae were covered with cuboidal epithelium, resembling choroid plexus. The neoplasm did not invade or infiltrate neural tissue included in the specimen.

Discussion

Choroid plexus papillomas arise from the choroidal epithelium and can be differentiated histologically from choroid plexus meningiomas, which arise from the stroma. Choroid plexus papillomas are known to occur more frequently in the fourth ventricle than in the lateral ventricles, and more frequently in the lateral ventricles than in the third ventricle. They tend to be found in the left lateral ventricle more often than in the right lateral ventricle. In the adult, the fourth ventricle seems to be the preferred location, and for children occurrence in the lateral ventricles is more common.

A review of the literature revealed that this pattern is not entirely comparable in patients with choroid plexus carcinoma (Table 1). None of the children with this disease had fourth ventricular tumors. Among the
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**TABLE 1**

*Summary of the clinical course in 25 cases of choroid plexus carcinoma*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Authors &amp; Year</th>
<th>Age, Sex</th>
<th>Location</th>
<th>Type &amp; Duration of Symptoms</th>
<th>Pathology</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Esser, 1926</td>
<td>22 yrs, M</td>
<td>4th vent</td>
<td>ICP, 2 wks</td>
<td>infiltration, mitoses, no met</td>
<td>craniotomy</td>
<td>died 2 wks postop</td>
</tr>
<tr>
<td>2</td>
<td>Graves &amp; Fliess, 1934</td>
<td>9 mos, M</td>
<td>LLV</td>
<td>ICP, 2 wks</td>
<td>moderate anaplasia</td>
<td>vent drainage</td>
<td>died</td>
</tr>
<tr>
<td>3</td>
<td>Vraa-Jensen, 1950</td>
<td>17 yrs, F</td>
<td>RLV</td>
<td>ICP, 2-3 mos</td>
<td>cran: no mitoses; 2nd cran: atypical</td>
<td>RT</td>
<td>died, autopsy: local invasion, pulmonary met</td>
</tr>
<tr>
<td>4</td>
<td>Cardauns, 1957</td>
<td>23 yrs, M</td>
<td>4th vent</td>
<td>ICP, fatigue, visual disturb</td>
<td>no mitoses</td>
<td>craniotomy</td>
<td>died 4 days postop</td>
</tr>
<tr>
<td>5</td>
<td>van Hoytema, 1957</td>
<td>10 mos, M</td>
<td>LLV</td>
<td>ICP</td>
<td>frequent mitoses</td>
<td>biopsy</td>
<td>died less than 1 mo after</td>
</tr>
<tr>
<td>6</td>
<td>Matson &amp; Crofton, 1960</td>
<td>2 yrs, F</td>
<td>RLV</td>
<td>ICP, 2 mos</td>
<td>local invasion</td>
<td>2 craniotomies</td>
<td>died 5 mos after 2nd op</td>
</tr>
<tr>
<td>7</td>
<td>4 mos, F</td>
<td>LLV</td>
<td>ICP, 5 wks, occ seizures</td>
<td>meningeal seeding</td>
<td>inoperable</td>
<td>died 5 wks postop</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>9 mos, M</td>
<td>LLV</td>
<td>ICP, 1 mo, fever, seizures</td>
<td>local invasion</td>
<td>craniotomy, RT</td>
<td>well 3 yrs later</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Bohn &amp; Strang, 1961</td>
<td>3 yrs, F</td>
<td>RLV</td>
<td>ICP, 3 mos</td>
<td>—</td>
<td>craniotomy</td>
<td>died 3 mos postop</td>
</tr>
<tr>
<td>10</td>
<td>33 yrs, M</td>
<td>RLL</td>
<td>ICP, 6 mos</td>
<td>—</td>
<td>craniotomy</td>
<td>died 6 mos postop</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>32 yrs, M</td>
<td>LLV</td>
<td>ICP, 72 mos</td>
<td>—</td>
<td>craniotomy</td>
<td>died 6 mos postop</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>7 mos, F</td>
<td>LLV</td>
<td>ICP, 7 mos</td>
<td>—</td>
<td>craniotomy, RT</td>
<td>well at 11 yrs</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>12 yrs, F</td>
<td>LLV</td>
<td>ICP, 4 mos</td>
<td>—</td>
<td>craniotomy, RT</td>
<td>well at 1 yr</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>2 yrs, F</td>
<td>LLV</td>
<td>ICP, 4 mos</td>
<td>—</td>
<td>craniotomy</td>
<td>died 4 mos postop</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>33 yrs, F</td>
<td>3rd vent</td>
<td>ICP, 5 mos</td>
<td>—</td>
<td>craniotomy</td>
<td>died 6 mos postop</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Vinken &amp; Sloof, 1965</td>
<td>17 mos, M</td>
<td>LLV</td>
<td>ICP, 4 wks</td>
<td>invasion, mitoses, met to chiasm</td>
<td>—</td>
<td>died 2 wks later, autopsy: adrenal neuroblastoma seizures, died 6 wks postop</td>
</tr>
<tr>
<td>17</td>
<td>Lewis, 1967</td>
<td>4 yrs, M</td>
<td>RLV</td>
<td>ICP, 3 mos</td>
<td>—</td>
<td>craniotomy</td>
<td>—</td>
</tr>
<tr>
<td>18</td>
<td>20 mos, F</td>
<td>LLV CPA's</td>
<td>lapse of consciousness, ICP</td>
<td>numerous mitoses, invasion of brain stem, lt temp lobe, both CPA’s</td>
<td>craniotomy, RT</td>
<td>died 6 mos later</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Tham, et al., 1969</td>
<td>66 yrs, F</td>
<td>lt CPA</td>
<td>lt facial weakness, dizzy 3 mos</td>
<td>mitoses, invasion of pons, petrous bone, met to LLV</td>
<td>biopsy</td>
<td>died 2 days later</td>
</tr>
<tr>
<td>20</td>
<td>Banna, 1971</td>
<td>11 mos, M</td>
<td>RLV</td>
<td>ICP, 2 mos</td>
<td>no seeding</td>
<td>craniotomy</td>
<td>well 2 yrs later</td>
</tr>
<tr>
<td>21</td>
<td>Shuangshoti, et al., 1971</td>
<td>47 yrs, M</td>
<td>RLV</td>
<td>ICP, 3 mos</td>
<td>mitoses, invasion, necrosis in LLV, pineal body, meninges</td>
<td>died</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Brochu &amp; Lefebvre, 1971</td>
<td>53 yrs, M</td>
<td>RLV</td>
<td>ICP</td>
<td>disseminated met, mitoses</td>
<td>biopsy</td>
<td>died 1 mo later</td>
</tr>
<tr>
<td>23</td>
<td>Dohrmann &amp; Collias, 1975</td>
<td>55 yrs, F</td>
<td>4th vent</td>
<td>ICP, 3 mos</td>
<td>atypical cells, low-grade anaplasia</td>
<td>craniotomy, RT</td>
<td>well 4 mos later</td>
</tr>
<tr>
<td>24</td>
<td>Valladares, et al., 1980</td>
<td>11 mos, M</td>
<td>LLV</td>
<td>ICP, 3 mos</td>
<td>positive cytology, supraclav. node 4 yrs postop no mitoses</td>
<td>craniotomy, RT</td>
<td>no recurrence on CT 6 mos after node excision well 1 yr postop</td>
</tr>
<tr>
<td>25</td>
<td>Carpenter, et al., 1982</td>
<td>29 yrs, F</td>
<td>LLV</td>
<td>intracranial noise</td>
<td>—</td>
<td>craniotomy</td>
<td>—</td>
</tr>
</tbody>
</table>

*ICP = increased intracranial pressure; vent = ventricle; LLV = left lateral ventricle; RLV = right lateral ventricle; met = metastases; cran = craniotomy; RT = radiotherapy; CPA = cerebellopontine angle; occ = occasional.*

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adult cases, four had tumors that were thought to arise in the fourth ventricle. Six had tumors in the lateral ventricles, four in the right and two in the left. In one case the tumor arose in the third ventricle.

Choroid plexus carcinomas and papillomas tend to be vascular and very friable. Implantations or seeding of the subarachnoid space occurs with both the benign and the malignant conditions (Table 1). Although choroid plexus papillomas may be calcified, they are rarely seen to be calcified on plain skull films. Angiographically, both papillomas and meningiomas in this region may demonstrate an appropriate “blush,” and clues to malignancy are, as with other malignant entities, large feeding vessels and early draining veins.

Microscopically, the benign tumors resemble normal choroid plexus. Vinken and Slooff quoted Zülch, whose diagnosis of choroid plexus carcinoma in contrast to papilloma included: 1) infiltrative and destructive growth; 2) abundant cellularity; 3) pleomorphic nuclei and cell type; 4) mitoses present; 5) proliferation of vascular structures; 6) necrotic foci; and 7) eradication of boundaries between stroma and parenchyma.

Dohrmann and Collias stated that a diagnosis of primary choroid plexus carcinoma can be difficult to make. Not only may this disease be confused with ependymoma and glioma, but also with metastatic carcinoma. Choroid plexus carcinoma may be differentiated from ependymoma, which is generally less vascular and usually has ciliated cells in which blepharoplasts are present. Choroidal tissue also demonstrates the presence of cholesterol clefts not present in ependymal tissue, glioma, or metastatic tumor. Among the gliomas arising in this region, the subependymal astrocytomas are thought to arise from stromal neuroglia in the ependyma. This, as well as the other entities, may be distinguished from choroid plexus carcinoma, in which areas of normal choroidal tissue are often present. Rubinstein notes that the occurrence of mucin-producing cells should be a clue to the presence of a metastatic process; however, primary mucin-producing choroid plexus papillomas do exist, as with adenomas of other epithelial tissues such as lung, breast, colon, and ovary.

A review of cases of choroid plexus carcinoma shows that almost all patients presented with symptoms of hydrocephalus (Table 1). The only exceptions were our patient and the patient reported by Tham, et al. (Case 19). The hydrocephalus associated with both the benign and malignant conditions may be secondary to obstruction and/or hypersecretion of CSF. These two cases are evidence that a malignant tumor may be present without hypersecretion.

The preoperative history in almost all cases was between 2 and 3 months. The outcome seemed unrelated to the length of the history. Two patients reported with seizures, and one was reported to have “meningeal seeding.” Positive CSF cytology findings were reported in one patient who went on to have systemic metastases but no seizures. It is interesting to note that one patient (Case 16, Table 1), reported by Vinken and Slooff was found at autopsy to have an incidental adrenal neuroblastoma.

Our patient clearly does not fit all the histological criteria of Zülch for the differentiation of choroid plexus carcinoma from papilloma. As such, this lesion seems to be a carcinoma in situ without mitoses or invasion. Definitive surgery, without radiotherapy, seemed to provide a good result for the patient reported by Banna. Radiotherapy did seem to slow the advance of the disease in the two cases of Bohm and Strang, and in those of Matson and Crofton and Dohrmann and Collias, but not in the patient reported by Lewis, whose tumor was seen to be very invasive. The case reported by Vraa-Jensen is of interest in that pathological study at surgery did not demonstrate the presence of mitoses; that patient, who was treated with postoperative radiotherapy, went on to have a recurrence, a second craniotomy, a second course of radiotherapy and, in spite of this, died with systemic metastases. The only patients reported to have traditionally good results were four children: one reported by Matson and Crofton, the patient reported by Banna, and the two reported by Bohm and Strang. All had definitive surgery and three of the four had postoperative radiotherapy. Our patient, an adult, has refused radiotherapy and is doing well; she is back at work now almost 1 year following surgery.

It seems, therefore, that gross total removal may be sufficient to obtain a good result. However, as demonstrated in the case reported by Vraa-Jensen, the lesion may degenerate, even in cases with apparently no mitoses, and we recommend that all patients with this lesion have radiotherapy following surgery.

The use of chemotherapy for the treatment of this disease has not been described. Its use would seem indicated for primary or metastatic disease not responding to surgery and radiotherapy. The choroid plexus is not thought to be protected by the blood-brain barrier, and therefore any of the current protocols for treatment of systemic adenocarcinoma would seem appropriate, with the nitrosoureas probably not being needed. Along these lines, recent studies have shown combined 5-fluorouracil, Adriamycin (doxorubicin), and mitomycin (FAM) to be of some value in palliating advanced adenocarcinoma of the stomach, lung, and pancreas. Woods, et al. have shown Adriamycin and mitomycin (AM) to be useful in the treatment of metastatic adenocarcinoma of an unknown primary source. The value of these agents in the treatment of choroid plexus carcinoma, however, remains to be proven.

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