Choroid Plexus Carcinoma:  
A Report of Two Cases and Review of the Literature

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Abstract

Choroid plexus carcinoma is a rare intracranial neoplasms, affecting mainly very young children. The most common site of origin is within one of the lateral ventricles.

The diagnosis of choroid plexus carcinoma is based on histological examination. Frequently subarachnoid seeding occurs and investigation at diagnosis should include examination of the cerebrospinal fluid and magnetic resonance imaging of the spinal cord. Extranodal metastases are rare.

Prognosis for long-term survival ameliorates. Total surgical resection of the tumor should be attempted. Both radiotherapy and chemotherapy are used as adjuvant therapies for primary tumors. No clear difference in effectiveness of these therapies could be found. However craniospinal irradiation seems to be more effective when leptomeningeal seeding is present.

Key words

Choroid plexus – Carcinoma – Metastases – Review

Case reports

Case 1

A previously healthy 5.5-year-old girl was admitted to the hospital in June 1992. Since one month prior to admission she complained of headache and abdominal pain and sometimes she vomited. General and neurological examination revealed a somnolent girl with a dilated fixed right pupil and a decreased pulse; on pain, decerebrate posture occurred. A computed tomography of the brain showed a large, parietooccipital, contrast-enhancing lesion with extensive perifocal edema and a shift of the midline to the left. Surgery was performed and a vascular tumor extending from the choroid plexus of the right lateral ventricle was macroscopically completely resected. Microscopic examination revealed a proliferation of epithelial cells, arranged in a trabecular, acinar, or cribriform pattern, or lying in patternless sheets. A papillary pattern was absent. Part of the tumor showed severe cytoplasmic atypia and brisk mitotic activity. Dispersed foci of necrosis were found. Immunohistochemically, the tumor cells were strongly positive for the epithelial marker CAM 5.2 (Becton & Dickinson, Leiden, The Netherlands) (Fig. 1), but negative for keratin (Biogenex, Duiven, The Netherlands), S100 (ITK, Uithoorn, The Netherlands) and Glial Fibrillary Acidic Protein (GFAP; gift of Dr. Van Muijen, Nijmegen, The Netherlands). Ultrastructurally, the tumor cells showed interdigitating cell membranes with dispersed desmosomes and...
plump microvilli. Part of the tumor cells rested on basal lamina. No cilia were found. On the basis of these findings the diagnosis of choroid plexus carcinoma was made. On magnetic resonance imaging of the spinal cord and analysis of the cerebrospinal fluid no evidence for subarachnoid seeding was found. After recovery from cranial spinal irradiation of 35 Gy and a local tumor boost of 55 Gy, chemotherapy was given consisting of monthly courses of “eight drugs in one day” (7). After two courses chemotherapy had to be stopped because of seizures, psychosis with confusion and aggression. Until now, 3 years after the diagnosis, there is no evidence for a local tumor recurrence or metastasis. A left homonymous hemianopsia and a mild left hemiparesis were caused by severe tissue loss in the right parietooccipital area after surgery. A significant mental loss occurred as well.

Case 2

A 2.5-year-old girl was admitted to the hospital in November 1993. She always had been in excellent health. During the last two months she complained of abdominal pain and sometimes she vomited. She became progressively lethargic and one week prior to admission she developed headache, pain in the neck and a squint. General and neurological examination revealed bilateral papilledema, a left sixth cranial nerve palsy and a mild left hemiparesis. A CT scan showed an intensively enhancing lobulated mass in the occipital horn with extension to the right parietal lobe, with perifocal edema and a midline-shift to the left (Fig. 2). A smaller lesion was seen at the left parietal cortex (Fig. 2). At surgery, a friable and highly vascu-

Fig. 2 Cerebral CT of Case 2 (November 1993): showing an intensively enhancing lobulated mass in the occipital horn with extension in the right parietal lobe and a smaller lesion at the left parietal cortex.

larized tumor was thought to be macroscopically removed. Microscopic examination revealed a papillary tumor (Fig. 3). The fibrovascular cores of the papillae were covered by multiple layers of highly atypical epithelial cells. The tumor showed brisk mitotic activity and focal necrosis. Immunohistochemical staining for GFAP S100, keratin and Cam 5.2 was negative, while part of the tumor cells showed a membranous staining for Epithelial Membrane Antigen (EMA, LEK). The tumor was diagnosed as a (papillary) choroid plexus carcinoma.

Chemotherapy was chosen as adjuvant therapy because of the young age of the patient. First a combined chemotherapy of vincristine, etoposide, carboplatin and cyclo-

Fig. 3 Papillary choroid plexus carcinoma of Case 2: Hematoxylin & Eosin, original magnification x 100.

Fig. 4 MRI cerebrum of Case 2 (October 1994, T1-weighted image): demonstrating several intraventricular, intracerebral and leptomeningeal metastases.
### Table 1

<table>
<thead>
<tr>
<th>Symptoms at Admission</th>
<th>%</th>
<th>Number of Patients</th>
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<tbody>
<tr>
<td>Visual problems (22%)</td>
<td>15</td>
<td>94</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>19</td>
<td>117</td>
</tr>
<tr>
<td>Headache/dizziness</td>
<td>13</td>
<td>78</td>
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<tr>
<td>Nausea/vomiting</td>
<td>16</td>
<td>99</td>
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<tr>
<td>Hemiparesis/paresis</td>
<td>12</td>
<td>73</td>
</tr>
<tr>
<td>Cerebral ataxia/paresis</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>Papilledema</td>
<td>6</td>
<td>36</td>
</tr>
<tr>
<td>Enlarged head</td>
<td>12</td>
<td>73</td>
</tr>
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</table>

### Table 2

<table>
<thead>
<tr>
<th>Number of Symptoms</th>
<th>%</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>59</td>
</tr>
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### Discussion

Two years after the first complications, important neurological sequelae were observed. A new anterior communicating artery aneurysm was detected, with severe neurological deficits. The aneurysm was successfully treated with a surgical clipping procedure. The patient made a complete recovery and returned to his previous occupation.

However, in June, a large intraorbital mass was diagnosed. A laparoscopic excision of the mass was performed, with complete excision of the mass and no recurrence. The patient is currently asymptomatic and returning to his previous activities.

In conclusion, this case highlights the importance of prompt diagnosis and intervention in cases of aneurysmal disease, as well as the potential sequelae that may arise from such conditions.

References:

Table 1: Localization of choroidal plexus carcinoma in children and adults

<table>
<thead>
<tr>
<th>Side</th>
<th>Right</th>
<th>Left</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult</td>
<td></td>
<td></td>
<td></td>
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</tbody>
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*Note: Data is presented as number of cases per group.*
of hemisymphromes (11%). Neurological examination revealed in about 33% of the patients symptoms of hemisymphromes, cranial nerve palsy (25%), ataxia and gait disturbances (17%). Papilledema was the most common clinical finding (35%).

Choroid plexus carcinomas have no specific radiological characteristics. On computed tomography, relation to ventricles is a radiological clue. Choroid plexus carcinomas usually have irregular margins surrounded by hypodensities due to edema because of infiltration in adjacent neural tissue. A marked contrast enhancement is noted (16, 37, 49). Hydrocephalus, usually of the obstructive type, is generally less severe than found in the case of benign choroid plexus papillomas, where hypersecretion of cerebrospinal fluid occurs (10, 16, 37, 42). Tumor calcification is uncommon (13, 14, 16, 22, 37, 47, 61). Magnetic resonance imaging does not provide more information about the nature of the tumor than computed tomography, but facilitates three-dimensional visualization before surgical treatment, postoperative evaluation of residual and recurrent tumor, and detection of leptomeningeal metastases (16, 37, 61).

We found 46 cases in the literature with investigation for dissemination at the moment of diagnosis, recurrence of the tumor or autopsy (Cases 1 and 2 and ref. 1, 4, 10, 14, 15, 17, 18, 22, 24, 28–30, 33, 34, 36, 38–39, 41, 43, 45, 46, 52, 54, 55, 59–63). Investigation was done with analysis of the cerebrospinal fluid for malignant cells and/or lumbar myeloxylography and, more recently, with magnetic resonance imaging. Twenty-two patients (48%) did not show cerebrospinal dissemination. Subarachnoid seeding was found in 20 patients (43%). Occasionally metastases outside the central nervous system are described: pleura and lung (63), ascitic fluid (46), peritoneum (46) and bone (17, 33). We report one case with several metastatic tumors in the omentum, bladder, uterus and rectum. We agree with Griffith that the real incidence of cerebrospinal dissemination is not known (30). Staging studies evaluating the entire neuraxis are particularly important after local tumor recurrence is proven, but a negative result does not exclude the development of subsequent metastases (38).

The diagnosis of choroid plexus carcinoma is based on histological examination; in typical cases, the tumor shows architectural disarray with poorly formed papillae, high cellularity, severe cytonuclear atypia and a high mitotic index (12). These carcinomas usually show immunohistochemical staining with epithelial markers (keratin, Cam 5.2, EMA), but compared to plexus papillomas staining with markers for glial differentiation (S100, GFAP) is diminished or absent (2, 19, 21, 25, 51, 58). Like in plexus papillomas, in plexus carcinomas ultrastructural features of normal choroid plexus epithelium (basal lamina, interdigitations of cell membranes, apical microvilli, desmosomes, scattered cilia) may be present (25, 47). The distinction between plexus carcinomas and plexus papillomas is sometimes difficult, atypical plexus papillomas may show significant cytonuclear atypia and scattered mitotic figures (12). In our two cases the severe cytonuclear atypia and high mitotic index qualified these tumors as plexus carcinomas. Histopathologically, other malignant tumors like malignant ependymoma and metastatic carcinoma may resemble a choroid plexus carcinoma. In contrast to plexus carcinomas, malignant ependymomas generally show clear-cut glial differentiation and GFAP-staining (12, 48).

Table 3 Treatment and outcome: disease-free survival period ≤ follow-up.

<table>
<thead>
<tr>
<th>Surgery Adjuvant therapy</th>
<th>Complete resection n t ( )</th>
<th>Partial resection n t ( )</th>
</tr>
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<tbody>
<tr>
<td>None</td>
<td>10 60 [5–118]</td>
<td>43 32 [12–48]</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>10 64 [4–240]</td>
<td>30 34 [5–72]</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>5 54 [8–156]</td>
<td>43 34 [5–72]</td>
</tr>
<tr>
<td>Radio- + chemotherapy</td>
<td>1 12</td>
<td>18 28</td>
</tr>
<tr>
<td>Total</td>
<td>26 58</td>
<td>10 33</td>
</tr>
</tbody>
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n: number of patients; t: range of disease-free survival period (in months); t: median disease-free survival period.

Reviewing the literature it is not possible to establish the optimal therapy for choroid plexus carcinomas. Therapy was described for 121 of the 231 patients. Four children just underwent inspection of the brain; follow-up data were not available for 2 patients. A group of 25 (21%) patients died preoperatively or within two months after surgery; they are considered as perioperative deaths and are excluded from Table 3. The treatment varied from surgical resection alone to more aggressive therapy with surgery followed by radiotherapy and/or chemotherapy. The follow-up period ranged from 3 months to 20 years. Most authors described gross total, subtotal or partial resection of the tumor. However, in many cases postsurgical evaluation of the tumor is not available. Information about the exact field and dosage of radiotherapy is often lacking and the chemotherapeutic scheme varies widely. A group of 28 patients who died within the period of follow-up, had a median survival of 13 months after diagnosis. Surgery without adjuvant therapy can be curative as shown in Table 3 (Case 1 and ref. 1, 4–6, 10, 11, 14, 17, 18, 20, 22–25, 28, 32, 39, 50–52, 56, 60, 64). Table 3 indicates that, whenever possible, complete resection of the choroid plexus carcinoma has to be pursued. We did not find a difference between surgery alone and surgery followed by radiotherapy when complete resection was performed. This was also noted by Packer et al and Pierga et al (52, 56). The shorter median relapse-free period for patients who underwent complete resection followed by chemotherapy may be due to the more recent use of chemotherapeutic treatment as adjuvant therapy. Adjuvant therapy following surgery of choroid plexus carcinoma is useful when only partial resection of the tumor was obtained. There is no difference in disease-free interval between the groups receiving either chemotherapy or radiotherapy after partial resection: median period of 34 and 32 months respectively (Table 3).

No difference could be found between children and adults concerning the outcome of adjuvant therapy as there were only a few adults amongst the 16 reported cases with a detailed follow-up history after diagnosis. Knowing the possible long-term sequelae of irradiation with intellectual deterioration, leukoencephalopathy, endocrinopathy, especially in the very young children, delay of radiotherapy is sought until the age of at least four years is reached. This delay of radiotherapy is important because 44% of the patients with choroid plexus carcinoma are younger than 2 years. Several schemes of drugs have been used but the value of each of them cannot be evaluated due to the small number of patients in each scheme. Because of her age, our youngest patient received chemotherapy after gross total resection of the tumor. Interestingly, the metastasis which was present at the moment of diagnosis disappeared under chemotherapy whereas ten months after
surgery several intracerebral, spinal and cranial leptomeningeal metastases had occurred. Reviewing the literature, leptomeningeal seeding of the tumor can disappear after craniospinal radiotherapy (54, 56, 59), whereas chemotherapy is less favorable (1, 10, 24, 52).

Conclusion

Reviewing the literature, initial staging studies evaluating the entire neuraxis should be performed at the moment of diagnosis of a choroid plexus carcinoma, as subarachnoid seeding occurs in almost half of the patients. Even under chemotherapy or radiotherapy, a significant number may occur by ventriculo-peritoneal shunting. Evaluation of the entire neuraxis should be performed at the time of diagnosis. Despite several chemotherapeutic schemes having been used and therefore more cases or protocols are needed to decide for the best therapy.

But this review suggests that whenever possible complete resection of the tumor has to be pursued, and no further therapy is necessary.

References


