Choroid plexus papillomas: long-term follow-up results in a surgically treated series

STEPHEN J. McGirr, M.D., MICHAEL J. Ebersold, M.D., BERND W. Scheithauer, M.D., LYNN M. Quast, R.N., AND EDWARD G. Shaw, M.D.

Department of Neurologic Surgery, Section of Surgical Pathology, and Division of Radiation Oncology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

The medical records and histological specimens from 26 patients with choroid plexus papillomas operated on at one institution were reviewed retrospectively. Four patients died perioperatively, and 21 of the remaining 22 patients were followed through March, 1986; the patient lost to follow-up review was last seen 14 years postoperatively. Of the 14 patients who underwent gross total removal of their tumor, one had a recurrence at 11 years postoperatively and two died in the perioperative period. Of the 12 patients who underwent subtotal removal of their tumor, two died in the perioperative period. The two patients who did not have radiation therapy postoperatively are free of apparent disease at 6 and 8 years after their operation. Eight patients underwent radiation therapy after subtotal removal of their tumor; four of these remain alive and well, and four have died of progressive disease.

The role of irradiation in the treatment of subtotally resected lesion remains controversial, but this therapy is thought to be indicated for recurrent disease after a surgical excision that is as complete as possible. Histopathologically, the presence of occasional mitotic figures, microscopic infiltration, ependymal differentiation, or mild to moderate atypia was not correlated with likelihood of complete resectability or tendency to recurrence.

KEY WORDS • choroid plexus • papilloma • radiation therapy • brain neoplasm

Choroid plexus papillomas are rare slow-growing neoplasms of the choroid plexus that arise within the ventricles or cerebellopontine angles in children and adults.7 Their presence is often heralded by hydrocephalus due to ventricular obstruction or cerebrospinal fluid (CSF) overproduction.11,21,22,31,35 In rare instances of spontaneous hemorrhage, associated hydrocephalus may be due to malabsorption of CSF.1,12,30,35 By virtue of their benign nature and intraventricular location, choroid plexus papillomas are amenable to surgical extirpation with the expectation that total excision will be curative and that recurrences should be infrequent.15,18

Because of the rarity of the lesion, there are few large operative series,4,6,22,32 and virtually none of them document long-term follow-up results. Therefore, controversy exists as to the appropriate management of subtotally resected tumors, of lesions that show microscopic infiltration of brain parenchyma, or of lesions that have atypical histological features. The role of irradiation in the management of these tumors similarly has been difficult to assess.5 In an attempt to resolve these uncertainties, the medical records and histological specimens from 26 patients with choroid plexus papilloma operated on at our institution between 1944 and 1985 were reviewed retrospectively. The clinicopathological features of these cases and their follow-up findings are the basis of this report.

Summary of Cases

Clinical Material

The study group included 15 males and 11 females with a mean age of 29.7 years (range 5 months to 61 years). The distribution of ages at operation was: one patient (4%) under 1 year; four (15%) between 1 and 10 years; two (8%) between 10 and 16 years; and 19 (73%) adults.

The tumors in the children and adolescents occurred exclusively in the lateral ventricles: two in the left and five in the right. Among the 19 adults, four tumors were found in the cerebellopontine angle and the remainder arose in the fourth ventricle.
Clinical Examination

At presentation, two children had an increased fronto-occipital circumference, two had hemiparesis, and seven had homonymous visual field defects. Headache, nausea and vomiting, diplopia, seizures, apnea and bradycardia, and syncope were reported in one child each.

In adults, headache was the most common presenting symptom, occurring in 18 patients. Cranial nerve deficits were noted in six, involving one or more of the sixth through 10th cranial nerves. Five patients complained of syncope, nystagmus, or vertigo. Four each had nausea and vomiting, gait changes, or blurred vision. Two presented with hemiparesis, and one patient had seizures.

Surgical Treatment

Of the 14 patients who underwent gross total removal of their tumors, two received postoperative radiation therapy. Twelve patients underwent subtotal resection, eight of whom were irradiated postoperatively. One of the patients who had subtotal removal underwent only biopsy and shunting, followed by postoperative radiation therapy.

Radiation Therapy

In all, 10 patients received radiation therapy: seven to the brain only and three to the craniospinal axis. The treatment was given with orthovoltage equipment in the early years of the study (three patients) and with megavoltage equipment in later years (seven patients). The tumor dose ranged from 2940 to 5580 cGy; the median dose was 4091 cGy (all doses were calculated at midplane). The median dose per fraction was 165 cGy. Eight patients were treated with localized brain fields (one of these also received spinal axis irradiation); two patients underwent whole-brain irradiation as part of a craniospinal treatment. In the three patients who underwent spinal irradiation, the doses were 2840 to 4000 cGy.

Pathology

On gross examination intraoperatively, the majority of tumors were pink to purple, showed frond-like surface irregularities, and had a cauliflower appearance. Although most were soft, vascular, and friable, a small proportion (20%) showed such extensive calcification as to compromise the frozen-section procedure.

For the purpose of clinicopathological comparison, the tumors were divided into typical (42%) and atypical (58%) papillomas. Microscopically, the typical tumors were composed of arborizing papillae with collagen in their stroma, lined by single-layered or pseudostratified cuboidal to columnar epithelium with oval, basally

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Fig. 1. Photomicrographs of a typical choroid plexus papilloma. Left: Specimen with a characteristic arborizing growth pattern and fibrous stroma of the papillae. H & E, x 100. Right: Cuboidal to columnar epithelial cells are uniformly disposed in a single layer or pseudostratified pattern. Note the regularity of the nuclei. H & E, x 250.
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situated nuclei (Fig. 1). Nuclear configuration, size, and chromatin density varied little, and mitotic figures were absent or rare (less than one per 40 high-power fields). In no instance was mucin production noted. Lamellar microcalcifications, typically present within the stroma of papillomas, were occasionally so conspicuous as to obscure the underlying epithelial nature of the tumor; in extent they were mild in 50% of specimens, moderate in 8%, and marked in 12%.

Ependymal differentiation was noted focally in 27% of these tumors (Fig. 2 left). This feature was apparent in 36% of the typical tumors and 20% of the atypical tumors. Such cells contained parallel, longitudinally arranged phosphotungstic acid-hematoxylin-positive fibrils within their processes which were immunoreactive for glial fibrillary acidic protein. Apparent infiltration of otherwise benign-appearing choroid plexus papillomas into the underlying brain parenchyma was microscopically evident in two (8%) of the 26 cases (Fig. 2 right). The interface could be described as irregular in four additional instances (15%).

Atypical papillomas showed one or more of the following histological abnormalities: multifocal cytological atypia, very rare mitotic figures, and architectural complexity. In no case was atypia considered to be severe. Mitotic indices varied from one to 10 mitotic figures per 40 high-power fields; all mitotic figures were morphologically normal (Fig. 3 left). Cytological atypia was characterized by nuclear enlargement, irregularity, and hyperchromasia. These features were mild to moderate in degree (Fig. 3 right). Although atypical papillomas retained a basically papillary pattern of growth, structural abnormalities were noted in nearly all instances.

Follow-Up Results

There were four perioperative deaths, all in patients undergoing operation prior to 1950. The 22 remaining patients were followed through March, 1986, except for one neurologically improved patient who was lost to follow-up review at 14 years after operation. The postoperative follow-up period ranged from 6 months to 40 years (mean 10.8 years): less than 2 years in two; 2 to 5 years in seven; five to 10 years in five; 10 to 20 years in three; and more than 20 years in five.

Fourteen patients underwent gross total removal of their tumors. Two of these patients died in the perioperative period; both had undergone surgery prior to 1950. Eleven of the remaining 12 patients have had no evidence of recurrent disease. Two patients underwent radiation therapy despite having had gross total resection of their tumor. Neurologically, seven patients with gross total tumor removal were normal at follow-up review, three were improved, and one was unchanged compared with their preoperative status. Histological evaluation disclosed a typical choroid plexus papilloma in three of these patients and atypical papilloma in eight. One patient who was treated with gross total

FIG. 2. Photomicrographs of choroid plexus papillomas. Left: Ependymal differentiation is manifested by tumor cells with elongated fibrillated cytoplasmic processes resembling those of an ependymoma (upper field). H & E, x 160. Right: In some cases the interface between tumor and stoma was irregular, resulting in a pattern of "pseudoinvasion." This example showed no significant histological atypia. H & E, x 25.

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resection alone had recurrence of the tumor 11 years postoperatively. This patient was free of disease for the 3 years following a second gross total resection. Both the primary and recurrent tumors in this patient were histologically benign.

Twelve patients had subtotal removal of their tumors. Two who underwent surgery prior to 1950 died in the perioperative period. Of the remaining 10, eight were given radiation therapy; four of these had progression of disease and died, and the other four were alive without evidence of disease at follow-up review. Three of the four patients with failed radiation therapy had a tumor recurrence within the radiation ports. In the fourth patient, the site of failure was unknown. The neurological status of the four surviving patients was improved in two and worse in two. In these four patients, histopathological evaluation showed ordinary choroid plexus papilloma in three and an atypical papilloma in one. Histopathological evaluation of the tumors from the patients who died showed two ordinary choroid plexus papillomas and two atypical papillomas.

In the two patients who had subtotal resection of tumor and did not undergo irradiation, there was no clinical evidence of disease in the follow-up period (6 and 8 years, respectively). The neurological status of one patient is normal and that of the other is improved from the preoperative status. In one patient the tumor was histopathologically typical and in the other it was atypical.

One patient who underwent subtotal removal alone had a biopsy. In this patient a shunt had been created preoperatively, and radiation therapy was given postoperatively. She was neurologically normal without clinical evidence of disease 18 years later. Histologically, the tumor was typical choroid plexus papilloma. The CSF was examined in eight cases. The protein concentration was increased in four, and xanthochromia or increased erythrocyte count was found in three. Shunt placement was rarely necessary after total or subtotal resection. The procedure was required postoperatively in only one of our 26 patients. Four patients had received shunts preoperatively.

Discussion

Incidence

According to Davis and Cushing,10 choroid plexus papilloma was first described by Guérard in 1883. Estimates of the incidence of this tumor in large series of brain-tumor cases include 0.5% among 200 intracranial tumors,6 0.4% of 3664 intracranial tumors,27 and 0.6% of 9000 intracranial tumors.39 Choroid plexus papillomas are reported to be more common in children than in adults,6,10,22,32,34,37 and in pediatric series a greater proportion of the brain tumors are choroid plexus papillomas: 3.9% of 408 intracranial tumors in patients less than 12 years of age,22 and 4% of 245 cases34 and 3% of 332 tumors32 in patients under 16 years of age.

A review by Herren16 of all cases published prior to 1936 noted that 10% of choroid plexus papillomas

![Fig. 3. Photomicrographs of an atypical choroid plexus papilloma. H & E, × 400. Left: Specimen showing multifocal cytological atypia but no mitotic figures. Right: Specimen of a somewhat more cellular tumor with occasional mitotic figures. Cytological atypia was minimal, and the lesion showed little architectural abnormality.](image-url)
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occurred in patients less than 1 year of age and 30% had developed by age 20 years. Matson and Crofton stated that 48% of all cases reported in the literature up to 1960 had been in children less than 10 years old and that 20% had occurred at under 1 year. Benign choroid plexus papillomas are occasionally bilateral or multiple. Approximately 10% of choroid plexus tumors are reported to be malignant (choroid plexus carcinoma). 32

Location

Bohm and Strang found 32% of choroid plexus papillomas in the lateral ventricles, 60% in the fourth ventricle, and 8% in the third ventricle. Tumor distributions in pediatric-age patients differ from those in adults. A study of 83 childhood papillomas revealed 68% in a lateral ventricle, 7% as bilateral in lateral ventricles, 16% in the fourth ventricle, and 8% in the third ventricle. In another report, the distribution was 43% in the lateral ventricles, 39% in the fourth ventricle, 10% in the third ventricle, and 9% in the cerebellar pontine angle (3.7% were multiple: one patient with tumors in the lateral and third ventricles, and one patient with tumors in the third and fourth ventricles). 34 Choroid plexus papillomas are rarely found in the third ventricle: two cases were reported by Jooma and Grant, one by Fortuna, et al., in a series of 4000 brain tumors, and three by Boyd and Steinbok in a series of 11 patients.

Presentation

Velasco-Siles and Raimondi stated that 70% of children with choroid plexus papillomas presented with increased intracranial pressure or increased fronto-occipital circumference. Matson and Crofton indicated that vomiting was the most common complaint: it was present in 62% of their patients. They called attention to the lack of diagnostic symptoms or signs as well as the relatively rapid evolution of symptoms. Difficulty in walking was noted by two of their patients, headache was present in one patient, and convulsions occurred in another.

Hemiparesis is apparently rare; it was reported in only 9% of patients in the series of Raimondi and Gutierrez. Symptomatic subarachnoid hemorrhage is also uncommon, although xanthochromic CSF is often found, indicating previous subclinical bleeding. Branch and Dyken reported a case of choroid plexus papilloma of the left lateral ventricle presenting with extensor spasms, developmental delay, and an electroencephalographic pattern of hypsarrhythmia.

Radiological Appearance

The angiographic appearance of choroid plexus papillomas has been described. Raimondi and Gutierrez emphasized the presence of hydrocephalus, hypertrophy of the choroidal arteries, either an arteriovenous malformation or a venous aneurysm on the surface of the tumor, and a finely granular tumor stain. Computerized tomography (CT) and magnetic resonance (MR) imaging currently are the investigative procedures of choice in the diagnosis of a choroid plexus papilloma. An alternative diagnostic procedure that may be considered for neonates is ultrasonography, which has the advantages of ease of examination, accuracy, and lower cost. 15

Surgical Considerations

Bielschowsky and Unger attempted the first surgical removal of a choroid plexus papilloma in 1902 but were unsuccessful. Perthes accomplished the first successful removal of such a tumor from the lateral ventricle in 1919. Sachs in 1922 and Davis and Cushing in 1925 resected choroid plexus papillomas from the fourth ventricle. In a series covering the period 1926 through 1958, Bohm and Strang included 25 cases of choroid plexus papillomas treated surgically. In this series, 62% of the patients with lateral ventricle tumors and 27% of those with fourth ventricle tumors died perioperatively. The development of preoperative diagnostic tests (such as MR imaging and CT) and of modern operative intervention (including the operating microscope, bipolar coagulation, lasers, and stereotaxic techniques) has dramatically decreased the surgical morbidity and mortality rates.

The issue of accompanying hydrocephalus and its basis was commented on by Eisenberg, et al., and by Welch, et al. These authors favored the concept that the mechanism of hydrocephalus was tumor-induced overproduction of CSF. Their suggestion that reabsorption was normal was questioned by Raimondi and Gutierrez, who noted that hydrocephalus persisted after surgical removal of the tumor and required shunt placement in 16 of their 23 cases. Close postoperative monitoring was advocated by Boyd and Steinbok, who recommended shunting in patients in whom hydrocephalus persisted or progressed.

Clinically significant distant seeding from an otherwise benign papilloma was noted by Gillis and di-Proio.

Comparison of Present Series With Reported Series

Choroid plexus papillomas are said to be slowly growing benign tumors, and our series does not suggest otherwise. Hydrocephalus is a usual accompaniment and was present in 18 (69%) of our 26 patients.

Our series differs from the literature in our higher proportion of adult patients: only five (20%) were less than 10 years of age and only one (4%) was less than 1 year old. The sex ratio was nearly even (15 males and 11 females). In patients less than 16 years old, all tumors were in the lateral ventricle. The sole location of tumors in adults was the posterior fossa, being in the fourth ventricle in 15 cases and in the cerebellar pontine angle in four. No tumors were found within the third ventricle.

Our series supports the assertion that surgical treatment alone should be adequate to prevent recurrence. Only one of 10 patients had a recurrence after gross...
total excision, and in that case the operation was performed early in this series without an operating microscope.

The role of radiation therapy in the treatment of choroid plexus papilloma remains undefined. Reports discussing radiation therapy have consisted of either single cases or limited series that do not give adequate information regarding treatment details or follow-up results. In our series, two patients who had gross total removal of their tumor received cranial irradiation. Although both patients remained free of recurrence, the low recurrence rate (one of 10) in our group of patients whose tumors were totally resected and who did not receive radiation therapy suggests that the routine use of irradiation in this group is not justified. Eight patients who had subtotal removal of their tumors also underwent cranial irradiation (including spinal axis irradiation in three); tumor recurred in five of these eight patients and the recurrence was directly in the radiation field in at least three. This observation and the finding that two patients who did not receive radiation therapy after subtotal removal of tumor remained free of disease do not support the routine use of postoperative irradiation in this group.

Radiation therapy probably is best reserved for recurrent disease after the most complete surgical resection possible. If given, the radiation should be delivered to localized cranial fields, focusing on the tumor with appropriate margins. There is no basis for either whole-brain or craniopinal irradiation in patients with choroid plexus papilloma. Doses in the range of 5000 to 5500 cGy, similar to those recommended for intracranial ependymomas, seem reasonable.

The presence of occasional mitotic figures, microscopic infiltration, ependymal differentiation, or mild-to-moderate cellular atypia did not correlate with either difficulty of resection or tendency to recurrence. This observation is at odds with the findings by Borcich and Davis who stated that the biological behavior, as determined by patient survival, of choroid plexus papillomas correlated well with the histological features such as complex growth pattern, cytological atypia, and mitotic activity. In their series, the anaplastic carcinomas were found to be aggressive tumors and the patients did poorly despite surgery, irradiation, and chemotherapy. Others have reported that invasion, mitotic figures, nuclear pleomorphism, necrosis, and metastasis are consistent with the diagnosis of malignant choroid plexus papilloma (choroid plexus carcinoma) and imply a uniformly grave prognosis.

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Address reprint requests to: Michael J. Ebersold, M.D., Department of Neurologic Surgery, Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905.