Journal of Neuro-Oncology 3: 259–262 (1985).

Response of a recurrent choroid plexus tumor to combination chemotherapy

Bernard L. Maria[1], Michael L. Graham[2], Lewis C. Strauss[2] & Moody D. Wharam[3]
From the Departments of [1]Neurology, [2]Oncology and [3]Radiation Oncology, The Johns Hopkins School of Medicine, Baltimore, MD

Key words: choroid plexus papilloma, carcinoma, radiotherapy, chemotherapy

Summary

Choroid Plexus tumors are rare. Surgery and biopsy is diagnostic, and radiotherapy has been used as the treatment of choice for choroid plexus carcinoma (CPC) and recurrent choroid plexus papilloma (CPP). We report the first case of CPP responding to combination chemotherapy consisting of cisplatin, bleomycin and vinblastine (CBV). This chemotherapy regimen should be considered for future trials in patients with choroid plexus tumors and recurrence after surgery and/or radiotherapy.

Introduction

Choroid plexus tumors account for less than 1 percent of all primary intracranial tumors in children (11). Although most of these are benign papillomas (CPP) with histology mimicking the architecture of normal choroid plexus, malignant variants (carcinoma or CPC) may occur, making complete removal and cure difficult (2). Previously reported children with CPC have had a relatively brief survival from onset of symptoms (3). The case presented here is the first reported primary choroid plexus tumor with a response to combination chemotherapy.

Case report

A.W. is an 8 year old caucasian female who was in good health until February of 1982 when, at the age of 6, she developed recurrent vomiting and severe headaches of two months duration. She was referred to The Johns Hopkins Pediatric Neurology Service. Neurological examination showed an alert child with bilateral papilloedema and hypereflexia on the right. Cranial computed tomography (CT scan of the head) showed a large irregular enhancing mass close to the trigone of the left lateral ventricle. She underwent biopsy and subtotal removal of a choroid plexus papilloma (Fig. 1). Because this was thought to be a benign choroid plexus tumor, she received no radiotherapy. A CT scan done four months postoperatively showed increase in tumor size with apparent intraparenchymal extension, and another craniotomy was performed in July 1982 for debulking before treatment with a total dose of 5,040 Rad's (4 500 Rad's to the brain and 540 Rad's to a tumor cone down).

Pathologic diagnosis was unchanged from the first operation and spinal tap was negative for cytologic abnormalities. The patient tolerated radiotherapy well and her neurologic deficit at the end of treatment consisted of a persistent superior quadranopsia which had been previously noted. CT scans until 1984 showed no evidence of tumor recurrence. In March 1984, two years from diagnosis, the patient developed vomiting with severe headaches and gait ataxia. Physical examination showed

Address for offprints: Bernard L. Maria, M.D., Division of Pediatric Neurology, Department of Neurology and Pediatrics, The Johns Hopkins Hospital, Baltimore, Maryland.

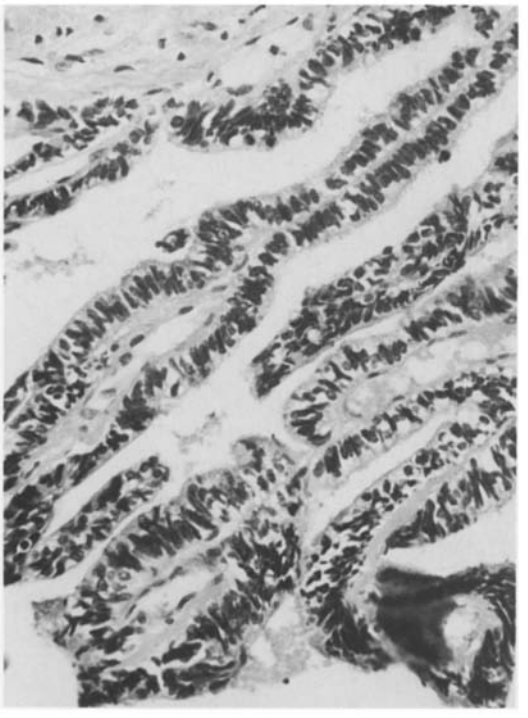

Fig. 1. Photograph of a neoplasm with numerous papillary fronds and fibrovascular cores. The superficial epithelium is columnar with nuclei in the basal portion of the cells (216 × magnification).

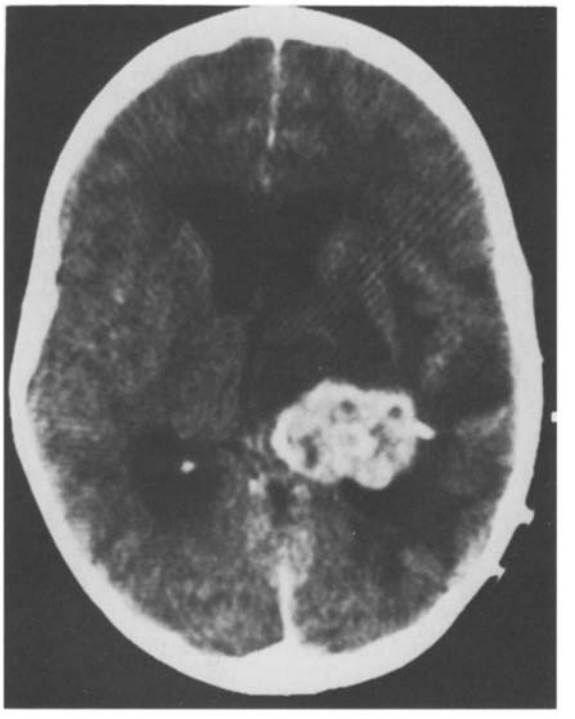

Fig. 2. CT Scan. A large enhancing tumor occupying the atrium of the left lateral ventricle with mass effect and edema. Shunt tip is also visualized lateral to the mass.

right lower facial weakness, right homonymous hemianopsia, bilateral ankle clonus and a wide-based ataxic gait. CT Scan of the head showed a large left hemispheral cyst at the tumor site with mass effect and shift from left to right. A cysto-atrial shunt was placed and she improved markedly. Post-operatively, her right homonymous hemianopsia was significantly decreased but CT scan showed an enhancing mass at the atrium of the left lateral ventricle. Serial CT scans showed that the enhancing mass was enlarging rapidly, with surrounding edema and mass effect (Fig. 2). Examination in May 1984 showed a more marked hemiparesis and she was readmitted for evaluation and treatment. She received a chemotherapy program of cisplatin, vinblastine and bleomycin (CBV) (4).

Vinblastine (0.15 mg/kg) and cisplatin (60 mg/m^2) were given on days 1 and 2 and bleomycin (15 mg dose) was given on days 2, 9, and 16 of a 21-day cycle which was repeated for four cycles. Minimal high-frequency hearing loss was detected by audiometry at the conclusion of therapy; renal function was not detectably impaired. The right hemiparesis and hemianopsia resolved leaving the previous (presumed surgical) superior quadrantanopsia. CT scan showed a marked reduction in the enhancing tumor. No increase in tumor has been noted on follow-up CT scan twelve months after starting chemotherapy and tapering of the steroids (Fig. 3).

Discussion

Primary carcinoma of the choroid plexus is rare and is mostly found in children between the ages of two and four (5). The clinical manifestations of this tumor are few, and nonspecific signs of increased intracranial pressure are most common (6). A number of uncommon mass lesions arise within the cerebral ventricular system and diagnosis is usually made at the time of exploratory surgery. Histological distinction between benign and malignant choroid plexus tumors can be difficult. Subarachnoid

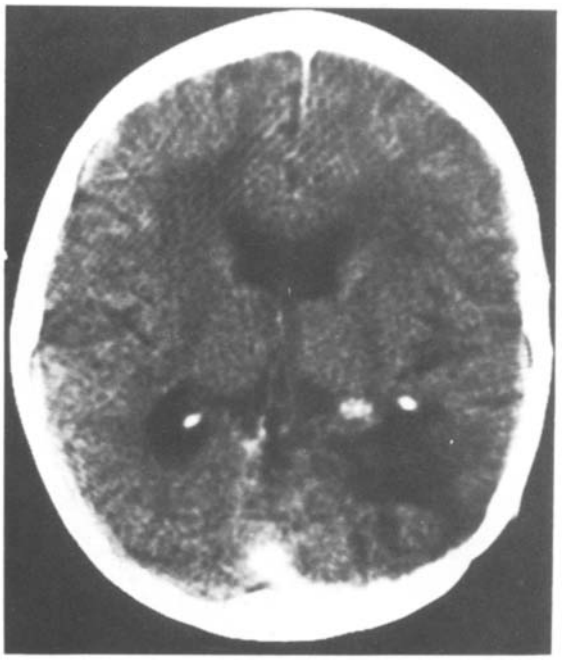

Fig. 3. CT Scan. Marked reduction in the mass and cystic cavity surrounding a small residual area of enhancement.

spread may be noted with either choroid plexus papilloma or carcinoma and was not seen in our patient. As noted in Fig. 1, our patient did not fulfill the strictest criteria of Russell and Rubinstein (7), and Lewis (3) for diagnosis of choroid plexus carcinomas: 1) Invasion of the adjacent neural tissue with infiltrating cells that assume a diffuse growth pattern, 2) Loss of the regular papillary structure of the neoplasm at least where invasion is occurring and obvious malignant alterations in the cells, 3) Transition of normal choroid plexus architecture to an undifferentiated pattern.

Surgical removal has been strongly advocated for the more benign CPP but treatment of more invasive and pleomorphic tumors remains controversial. Prognosis is not well established for either tumor but children with CPC have succumbed 9 months from diagnosis. The initial treatment of malignant supratentorial tumors is usually surgical exploration for resection or biopsy followed by external beam radiotherapy. Radiotherapy has been shown to shrink the capillary bed of a CPP but changes in neoplastic cells have not been significant (8).

There are no available data on median time to tumor progression and survival of patients with CPC receiving radiation therapy. Favorable effect of preoperative radiotherapy in the management of posterior fossa choroid plexus papillomas has been reported and adjuvant radiotherapy may have a role when complete gross resection of CPP is impractical (9). This patient's tumor responded favorably to radiation therapy; clinical and radiological stabilization was achieved for more than 18 months after first recurrence. We cannot exclude the possibility that histology may have changed to a more malignant CPC before instituting chemotherapy since no biopsy was taken at that time. This possibility was of concern because the tumor grew very rapidly, doubling in size in one month (based on CT measurements). Nevertheless, recurrences of choroid plexus tumors have been reported as late as five years after radiation therapy (10).

I^{-125} brachytherapy was considered as an option at second recurrence since location and size of the tumor, and significant operative risks for a major radical procedure were deterrents to surgical re-exploration. Interstitial implantation of radioactive sources was considered because of the reported stabilization of a choroid plexus carcinoma with this form of therapy (11). Nevertheless, cure with radiotherapy for recurrence of malignant supratentorial tumors has not yet been achieved. Potential late central nervous system side effects from additional radiation therapy was also a concern.

The regimen of cisplatin, bleomycin and vinblastine has shown remarkable activity against adult malignancies including melanoma and cancer of the esophagus, bladder, head and neck. Cisplatin alone is active against a variety of pediatric tumors including neuroblastoma, osteosarcoma and brain tumors (12). Information on the efficacy of either bleomycin and vinblastine alone in central nervous system malignancies is sparse, although successful treatment of intracranial germ cell neoplasms with the three-drug regimen has been reported. The three-drug combination has also been effective against extracranial germ-cell neoplasms (13, 14, 15, 16). Although there is conflicting evidence whether or not bleomycin and vinblastine cross the blood-brain barrier (15, 17), it is not known wether presence of a given drug in the cerebrospinal fluid is critical for successful treatment of brain tumors (17).

To date, options of therapy for choroid plexus

tumors have included surgery alone, surgery plus radiotherapy and surgery followed by radiotherapy at recurrence (8, 18). The effectiveness of radiotherapy is not clear (18). There are no other documented responses of CPP or CPC to chemotherapy, although Rodney *et al.* (19) described a child with CPC who may have responded transiently to vincristine and intrathecal methotrexate. The response observed in this case may have been due to one or two of the agents employed rather than the CBV combination. Cisplatin/bleomycin/vinblastine should be considered as single agents or in combination therapy for future trials with choroid plexus tumors that recurred following surgery and radiotherapy. CBV might also be a therapeutic option at diagnosis in infants in whom radiation therapy might pose a risk of unacceptable long-term toxicity.

References

1. Bohm E, Strang R: Choroid plexus papillomas. J Neurosurg 18:493–500, 1971.
2. Aicardi J, Garcia J, Lepintre J, Chevrie J-J, Thieffry ST: Les Papillomes Des Plexus Choroides Chez L'Enfant. Archs Fr Pediat 25:673–686, 1968.
3. Lewis P: Carcinoma of the choroid plexus. Brain 90:177, 1967.
4. Einhorn LH, Honohue J: Cis-diamine dichloroplatinum, vinblastine, and bleomycin combination chemotherapy in disseminated testicular cancer. Ann Int Med 87:293–298, 1977.
5. Dohrmann GJ, Collias J: Choroid plexus carcinoma. J Neurosurg 43, August 1975.
6. Thompson J, Harwood-Nash D, Fitz C: The neuroradiology of childhood choroid plexus neoplasms. Am J Roentg 118:116–133, May 1973.
7. Russell DS, Rubinstein LJ: Pathology of tumors of the nervous system. Edition 2, London, E Arnold, 1971.
8. Carrea R, Polak M: Preoperative radiotherapy in the management of posterior fossa choroid plexus papillomas. Child's Brain 3:12–24, 1977.
9. Naguib M, Chou S, Mastri A: Radiation therapy of a choroid plexus papilloma of the cerebellopontine angle with bone involvement. J Neurosurg 54:245–247, 1981.
10. Raimondi A, Gutierrez F: Diagnosis and surgical treatment of Choroid Plexus Papillomas. Child's Brain 1:81–115, 1975.
11. Gutin PH: Preliminary experience with I^{125} brachytherapy of pediatric brain tumors. Concepts in Pediatric Neurosurgery II, Karger, Basel, 1984.
12. Khan AB, D'Souza BJ, Wharam MD, Champion LA, Sinks LF, Woo SY, McCullough DC, Leventhal BG: Cis-platinum therapy in recurrent childhood brain tumors. Cancer Treat Rep 66:2013–2020, 1982.
13. De Tibolet N, Barrelet L: Successfully chemotherapy of pinealoma. Lancet 2:1228–1229 (letter), 1977.
14. Neuwelt EA, Frenkel EP, Smith RG: Suprasellar germinomas (ectopic pinealomas): Aspects of immunological characterization and successful chemotherapeutic responses in recurrent disease. Neurosurgery 7:352–358, 1980.
15. Ginsberg S, Krishner J, Reich S, Panasci L, Finkelstein T, Fandrich S, Fitzpatrick A, Schechtman L, Comis R: Systemic chemotherapy for a primary germ cell tumor of the brain: A pharmacokinetic study. Cancer Treat Rep 65:477–483, 1981.
16. Siegal T, Pfeffer MR, Catane R, Sulkes A, Gomori MJ, Fuks Z: Successful chemotherapy of recurent intracranial germinoma with spinal metastases. Neurology (Cleveland) 33:631–633, 1983.
17. Stewart DJ, Leavens M, Maor M, Feun L, Luna M, Bonura J, Caprioli R, Loo TL, Benjamin RS: Human central nervous system distribution of cis-diamine-dichloroplatinum and a radiosensitizer in malignant brain tumors. Cancer Research 42:2474–2479, 1982.
18. Hawkins JC III: Treatment of choroid plexus papillomas in children: A brief analysis of 20 years experience. Neurosurgery 6:380–384, 1980.
19. Rodney D, McComb MD, Burger P: Choroid plexus carcinoma: Report of a case with immunohistochemical and ultrastructural observations. Cancer 51:470–475, 1983.