Cerebellopontine Angle Primary Choroid Plexus Carcinoma Present in an Adult: Case Report and Literature Review

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Abstract

Choroid plexus tumors (CPTs) are rare intraventricular neoplasms that primarily occur in children and are rare in adults. Of the CPT subtypes, choroid plexus carcinomas (CPC) are highly aggressive and malignant and of World Health Organization (WHO) Grade III. Dissemination through the cerebrospinal fluid space is the inevitable natural course of the disease.

In this case report, we present a 33-year-old female with a past medical history notable for schizophrenia and bipolar disease who suffered from left-sided acute vision loss and hearing loss. Magnetic resonance imaging (MRI) demonstrated multiple enhancing masses found in the left cerebellopontine angle (CPA), right internal auditory canal, the atrium of the left ventricle, and the left foramen of Monroe. After surgical decompression of the CPA tumor, the permanent final pathology was consistent with CPC.

To our knowledge, this is the first reported case of a primary CPC occurring within the CPA in an adult. The unique presentation and progression of this rare adult-onset CPC provide insight for the diagnosis and treatment of other rare instances of CPTs.

Categories: Pathology, Neurosurgery
Keywords: primary choroid plexus carcinoma, cerebellopontine angle tumor, adult

Introduction

Choroid plexus tumors (CPT) are rare and account for 0.3%-0.6% of all brain tumors [1]. CPTs include choroid plexus papilloma, atypical choroid plexus papilloma, and choroid plexus carcinoma (CPC). Of these subtypes, CPC is the most aggressive and malignant (World Health Organization (WHO) grade-III). CPC is primarily a pediatric disease but presents in about 20% of adults and accounts for 15%-20% of all choroid plexus tumors [2]. CPC is derived from modified ependymal cells and commonly presents with hydrocephalus related to ventricular obstruction. Metastatic lesions disseminate through the cerebrospinal fluid (CSF). In children, they frequently arise from the lateral ventricles and the fourth ventricle in adults. Rarely, they occur in the cerebellopontine angle (CPA), suprasellar region, or even in the sacral canal [3]. To the author’s knowledge, we present the first adult case of CPC presenting in the CPA.

Additionally, we conducted a literature review of adult CPC to investigate tumor location, clinical features, symptom duration, surgical outcomes, and adjuvant therapy. A comprehensive search of the literature was performed using Google Scholar and PubMed without date restrictions. During the search, a variety of terms were used in Boolean logic, to include: (1) CPC; (2) adult; (3) CPA; and (4) CPTs. Peer-reviewed studies that focused on CPCs primarily in adult populations were included in the literature review.

Case Presentation

Preoperative course

The patient is a 33-year-old woman who presented to the emergency department with decreased left visual acuity, hearing loss in her left ear, and paresthesia on the left side of her face. Her past medical history was notable for schizophrenia, bipolar disorder, intravenous (IV) drug use, and a 30 pack-year smoking history. On physical exam, she had diminished vision in her left eye, hearing loss in her left ear, and mild aphasia; otherwise, she had a normal neurologic exam. Magnetic resonance imaging (MRI) revealed four lobulated heterogeneous enhancing masses in the left CPA, right internal auditory canal, the atrium of the left ventricle, and the left foramen of Monroe (Figure 1). The largest was in the CPA, measuring 2.1 x 3.5 x 3.1 cm with surrounding vasogenic edema. Computed tomography (CT) of the chest, abdomen, and pelvis and MRI total spine were negative for tumor. She was offered retrosigmoid craniotomy for open biopsy and cranial nerve decompression.
Operative description

The patient was positioned in the lateral position with the left side up. Cranial nerves 7-12 were monitored. An intraoperative lumbar puncture was performed for brain relaxation, and CSF was sent for cytological analysis. A 10 cm curvilinear incision was placed just below an imaginary line between the inion and external auditory canal. A single burr hole was made at the transverse-sigmoid junction, followed by a small retromastoid craniotomy. The craniotomy edges were burred until the edge of the transverse and sigmoid sinuses were visualized. The dura was opened in a C fashion along the transverse sigmoid junction. Using the interoperative microscope, we removed a large section of the tumor and sent it for frozen and permanent pathological specimen. The tumor was debulked utilizing the ultrasonic aspirator while frequently checking the tumor capsule for cranial nerve function using the monopolar Prass probe (Medtronic, Fridley, Minnesota). There was significant tumor adherence to surrounding vessels and cranial nerves. The intraoperative frozen pathology report was consistent with metastatic adenocarcinoma. Given the significant adherence of the tumor to the cerebellum and cranial nerves, we decided to leave the remaining tumor to avoid cranial nerve deficit. The bone flap was replaced at the end of the procedure. Routine postoperative CT was performed (Figure 2).
Postoperative course
The patient’s preoperative left visual acuity and facial paresthesia resolved. Her hearing loss remained after surgery. She was otherwise neurologically intact. The patient left against medical advice prior to postoperative MRI and has not reported for postoperative or oncologic follow-up.

Pathological findings
The tumor consisted of pleomorphic epithelial cells, frequently with vacuolated cytoplasm, arranged in a well-defined papillary pattern (Figures 3A–3F). The tumor cells were positive for AE1/AE3, CK7, prealbumin (transthyretin), S100, synaptophysin, and vimentin. They were negative for CEA, CK20, EMA, ER, GATA3, GFAP, Napsin A, p16, PAX8, TTF1, and WT-1. Rare scattered cells were positive for p53. The Ki67 index was visually assessed as 30%–40%. The special stains and immunohistochemical preparations exclude both ependymoma and adenocarcinoma and were consistent with primary choroid plexus carcinoma, WHO grade III.
FIGURE 3: Photomicrographs of immunohistochemically stained choroid plexus carcinoma surgical specimens

(A) H&E, 20x. (B) Increased mitotic activity and necrosis, H&E, 40x. By immunohistochemistry, the tumor cells are positive for (C) CK7, 20x; (D) S100, 20x; (E) transthyretin, 20x; and (F) synaptophysin, 20x.

Discussion

Choroid plexus carcinoma is a highly aggressive, malignant tumor that is more common in pediatrics than in adults. To our knowledge, this is the first case report of CPC presenting in the CPA of an adult patient.

CPC stains positive for cytokeratin and has a variable expression for vimentin, S100, transthyretin, and glial fibrillary acidic protein. CPC is typically negative for epithelial membrane antigen. Our patient was positive for CK7, S100, vimentin, and transthyretin while negative for glial fibrillary acidic protein and epithelial membrane antigen. Gross pathology will usually show a friable papillary or cauliflower-like appearance. Papillary ependymoma is a rare variant of ependymoma and often gives rise to confusion with choroid plexus tumors because of topographic, light microscopic, and ultrastructural similarities. Immunohistochemistry for our patient also revealed scattered p53 positivity. Many cases of choroid plexus carcinoma are associated with Li-Fraumeni syndrome, an autosomal dominant disorder involving a mutation in the germ cell line of p53 tumor suppressor genes [4]. Roughly 50%-60% of patients with CPC were observed to have TP53 gene mutations [5]. Her extended neuro-oncology gene panel reported a positive BCL6 corepressor (BCOR) gene mutation. BCOR gene mutations have rarely occurred in high-grade neoplasms but have never been linked directly with a case of CPC [5-6].

CPCs arise from modified ependymal cells surrounding a core of capillaries and loose connective tissue. CPCs are typically intraventricular, however, extraventricular tumors have been reported [7-9]. Ectopic sites are not commonly reported but include the suprasellar region, foramen magnum, and spinal canal in the absence of other intracranial lesions [10]. Ectopic CPC is thought to arise through CSF dissemination [10]. Our literature search found only two occurrences of cerebellopontine angle CPCs; both had an invasion of CPC from the fourth ventricle through the foramen of Luschka into the CPA [11-12]. The most common site for adults is in the fourth ventricle (63%) while in the pediatric group is the lateral ventricle (72%) [10]. Presentation with multiple CPCs is rare, occurring in only 5% of CPC patients [9]. Metastatic lesions have a higher frequency of being supratentorial [10]. Our patient uniquely presented with a primary CPC in the atrium of the left ventricle and ectopic in the CPA without any invasion from the fourth ventricle. Her
metastatic lesions were supratentorial in the left foramen of Monroe and the right internal auditory canal. CPC is an aggressive type of brain tumor and should remain on differentials where primary tumors present intraventricularly and in ectopic regions on imaging in adults.

The symptoms of CPC typically relate to progressive obstructive hydrocephalus due to their intraventricular location. Headache, diplopia, nausea, vomiting, and ataxia are the most common presenting symptoms (Table 1). However, when CPC tumors invade into rare locations, such as the CPA, headache and hearing problems start first, followed by gait disturbance, facial nerve involvement, and visual field deficits. Our patient had hearing loss and facial hypesthesia, which is much more common with CPA-based tumors.

| Study                | Age/Sex | Symptom Duration | Clinical Features                                                                 | Location                                           | Craniotomy Location | Surgical Result | Adjuvant Therapy | Outcome                      |
|----------------------|---------|------------------|----------------------------------------------------------------------------------|----------------------------------------------------|---------------------|-----------------|------------------|-------------------------------|
| Tham et al [12]      | 66/F    | 3 mon            | Left facial hemiparesis, dizziness, headache                                     | FV through the foramen of Luschka into the CPA     | Suboccipital        | Biopsy          | None             | Expired 2 days after the operation |
| Izcil et al [14]     | 54/M    | ~                | Headache, visual, gait disturbances                                             | R LV                                              | Transcallosal       | GTR RT          |                  | Expired 12 mon after surgery  |
| Osada et al [15]     | 53/M    | 5 mon            | Gait disturbance, L hemiparesis                                                  | R LV                                              | Superior Parietal   | SR RT           | No evidence of recurrence 7 mon after the operation |
| Tena-Suck et al [16] | 18/M    | 12 mon           | Headache, nausea, vomiting, visual disturbance, diplopia, ataxic gait, L-sided hemiparesis | FV                                               | Suboccipital        | GTR None        | No evidence of recurrence 2 years after the operation |
| Loster et al [7]     | 68/F    | 8 mon            | Mild expressive aphasia, confusion, difficulty concentrating                    | L anterior temporal (extraventricular)            | Frontotemporal      | GTR CT and RT   | No evidence of recurrence 4 years after the operation |
| Kishore et al [4]    | 24/M    | 2 mon            | Headache, nausea, vomiting                                                      | R LV (temporal horn)                              | Parietal            | GTR RT ~        | ~                             |
| Yip et al [17]       | 21/M    | 1 mon            | Headache                                                                         | L LV (trigone and occipital horn)                 | Posterior interhemispheric precuneus               | GTR CT and RT    | No evidence of recurrence 2 years after the operation |
| Ozdogan et al [18]   | 73/M    | ~                | Headache                                                                         | FV                                                | Transcortical       | GTR None        | ~                             |
| Bohara et al [3]     | 60/M    | ~                | Headache                                                                         | R LV (trigone)                                    | Transcortical, middle temporal gyrus               | SR CT and RT     | Expired 13 mon after the operation |
| Guo et al [8]        | 59/M    | 1 mon            | Speech delay                                                                     | L temporo-parietal (extraventricular)             | Temporo-parietal   | GTR CT and RT   | Recurred 6 mon after resection |
| Pellerino et al [19] | 50/M    | ~                | Dizziness, progressive gait disturbance                                           | FV                                                | ~                  | GTR CT and RT   | Recurred 8 years after resection |
| Zhu et al [20]       | 34/F    | ~                | Headache, double vision, nausea                                                 | L LV                                              | ~                  | GTR RT ~        | ~                             |
| Azhani et al [10]    | 39/M    | 2 weeks          | Headache, L hemiparesis                                                          | R temporo-parietal                                | Trans-sylvian      | SR ~            | Expired 2 weeks after surgery  |
| Kim et al [9]        | 49/F    | 1 week           | Visual disturbance, generalized tonic-clonic seizure                              | Temporo-parietal (extraventricular)               | Transcortical via parieto-occipital junction       | GTR CT           | No evidence of recurrence 10 mon after the operation |
Adjuvant therapy for CPC is controversial. In 2009, Weide published a meta-analysis showing chemotherapy improved the survival of patients with resected CPC. Patients with CPC receiving combined radiation and chemotherapy had the best two-year survival (63%), followed by those with chemotherapy alone (45%), radiotherapy alone (32%), and those without further therapy (15%) [13]. Various agents have been shown to reduce the size of CPCs after resection such as cisplatin, etoposide, cyclophosphamide, procarbazine, carboplatin, methotrexate, doxorubicin, and vincristine [13]. With its rarity, adjuvant chemotherapy after resection remains controversial as the standard of care for patients with CPC [2]. Although the mainstay of treatment of CPC tumors is attempting a gross total resection, post-resection chemotherapy and radiation should be considered as a rational treatment option to improve outcomes.

Conclusions
Choroid plexus carcinoma presenting in the CPA is extremely rare. Gross total surgical resection was limited due to cranial nerve invasion. This is the first reported case of a primary CPC occurring within the CPA in an adult. The unique presentation and progression of this rare adult-onset CPC provide insight for the diagnosis and treatment of other rare instances of CPCs.

Additional Information

Disclosures

Human subjects: Consent was obtained by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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