

A Medical Mystery Tour: Choroid Plexus Carcinoma

Introduction

Choroid plexus carcinoma (CPC) is a rare malignant intracranial tumor of the neuroepithelial tissue that lines the ventricles and supplies cerebrospinal fluid (CSF). We present the case of an adult with CPC to illustrate the importance of an accurate history and demonstrate the mysteries medicine has yet to unfold.

Case Presentation

A 39-year-old female presents to the Family Medicine Residents' Clinic with complaints of "blurred vision." Upon questioning, the patient denies the initial complaint and says she sees "shadows or images of people that I cannot get away from." She states she was seen one month previously for an otitis media and placed on oral amoxicillin. After starting the amoxicillin she began to have the visual disturbances. She states that the images do not talk to her and that they come and go throughout the day. She denies ever having symptoms like this previously.

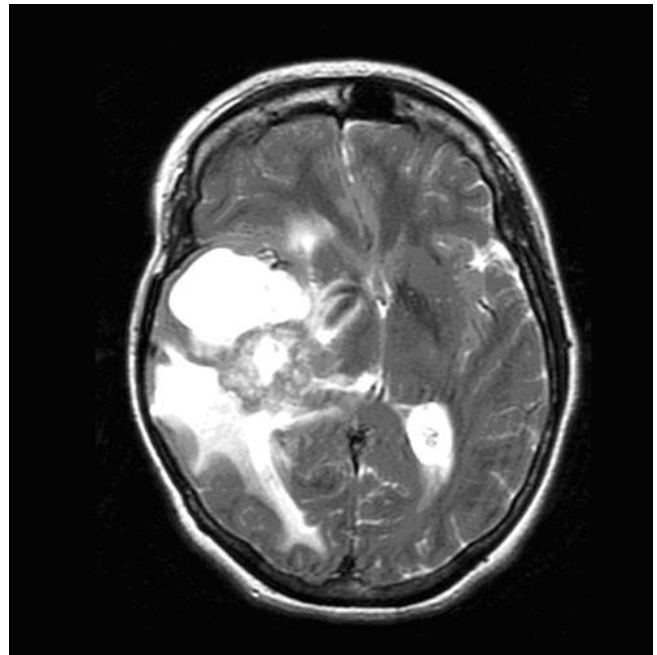
Her history is significant for being diagnosed with a brain tumor in 1987. At the age of 21, she was found to have a choroid plexus papilloma (CPP) and treated with surgical resection followed by 28 radiation treatments. The patient had been completely asymptomatic since.

At the time of current presentation, she denied any headaches or any other neurological symptoms. She had no previous history of psychiatric illness and was not taking any chronic pharmacotherapy. She was without any other complaints. Examination confirmed a large craniotomy scar over the right cranium but demonstrated no other anomalies.

Initial blood work including complete metabolic panel and complete blood counts were normal. An MRI was ordered, which showed a large complex cystic mass in the right temporal lobe. This mass extended from the frontal and parietal areas into the basal ganglia and predominantly the thalamus. The edema around the mass and its effect on the

surrounding tissue produced an uncal herniation with resultant pressure upon the brainstem.

Figure 1. MRI T2 weighted image: Coronal view.



The initial findings were thought to be consistent with glioblastoma multiforme. The patient was admitted and started on IV Decadron. Her symptoms improved and she was discharged with neurosurgical follow-up.

At the neurosurgical appointment, it was felt that surgical debulking of the mass was necessary to avoid catastrophic neurological disintegration. With the provisional diagnosis of a high grade astrocytoma, the patient was taken to the OR. She had approximately 85% of the lesion removed. It was felt the remainder was too close to the thalamus to be effectively removed without causing severe impairment.

Tissue samples were sent to two major diagnostic centers. The pathologists at one center, who received four samples of tissue, felt that the diagnosis best

reflected a choroid plexus carcinoma. The pathologists at the other center, who received two samples of tissue, felt that the first sample was likely a choroid plexus papilloma and the second sample was choroid plexus carcinoma.

Meanwhile the patient postoperatively had resultant left-sided weakness. While her rehabilitation was prolonged, she did regain most of her function with only mild deficits. She was finally discharged from the hospital three weeks after her surgery. Afterwards, the patient went to live with her family out of state.

The story resumes six months later when the patient returns to the area for an oncology consultation. It is unknown what exactly was done while the patient was out of state, although it appears she did receive some chemotherapy; however, the patient had no studies to confirm or deny the success of treatment. An MRI confirmed little interval change in the rest of the lesion and the patient remained asymptomatic.

Chemotherapy was resumed and she underwent treatment for five months. Follow-up MRI confirmed that the lesion continued to grow despite the chemo. The patient requested a second opinion concerning other forms of treatment. She was referred to a major medical center and was the topic of a tumor board held by videoconferencing. It was felt that the only option left was further surgery and radiation therapy.

The patient refused to have any further surgery done given the risk of permanent damage to the basal ganglia. She felt that radiation would be acceptable if there was an option of alternative primary treatment. She did not want to consider any further chemotherapy. At that point, the patient asked about surgery with cyberknife stereotactic radiotherapy at another hospital located close to Champaign-Urbana. She was given a referral to that center.

It is unknown whether the patient underwent the procedure at the other hospital but there is note of further biopsy specimens collected in a scanned record obtained from the other hospital. It is suspected the patient had another traditional craniotomy performed.

The patient has not been in contact with this facility for the last nine months and her current condition is unknown.

Literature Review

The choroid plexus is a specialized neuroepithelium that lines the walls of the ventricles. This tissue is responsible for producing CSF that is an ultrafiltrate of blood with specialized proteins. There are two main classes of tumors derived from the choroid plexus. The first is a benign tumor called a choroid plexus papilloma. The

second is a malignant tumor known as choroid plexus carcinoma.¹

In general tumors of the choroid plexus are rare accounting for only 0.4–0.6% of all intracranial neoplasms. Choroid plexus tumors usually arise in children within the first decade of life. In the overall population papillomas outnumber carcinomas at a rate of 5 to 1. The development of choroid plexus tumors in adults is rare and appears to be only studied as singular cases or small case-controlled studies.²⁻⁴

The usual presentation of choroid plexus tumors in adults is with headache due to increased intracranial pressure. Often there is significant hydrocephalus noted on visualization. This patient's presentation with visual disturbances without headache is uncommon.⁵

Choroid plexus papillomas usually are treated with surgical excision. A meta-analysis of choroid plexus tumors treated in Germany revealed that of 495 cases of CPPs, 80.4% were treated with complete surgical excision. However, the same study revealed that a second surgery was not as successful in the incompletely excised subgroup.⁶ The use of adjuvant therapy such as radiation is controversial with both advocates and detractors.^{3,7}

Choroid plexus carcinomas are also usually treated with surgical excision. In that same meta-analysis of 371 cases reviewed, 39.6% had complete resection. Prognosis was improved with the subgroup of incompletely excised patients who had a second surgery. The chances of second surgery were low at 22. Six were highly dependent on the location of the lesion. In the case of our patient, further surgery was not attempted as most of the rest of her lesion was infiltrated into the basal ganglia. The use of chemotherapy and radiation for primary lesions is accepted within the literature.⁶ The prognosis of CPC is poor with a five year survival rate of 26–40%.²

Discussion

This case is unique in two aspects. First, this case is not the diagnosis of a primary CPC. The record states the patient's previous history of CPP 20 years earlier. At that time, she likely had a subtotal resection and then a possibly controversial radiotherapy. Afterwards, she was in complete remission for an unknown period of time. This is unknown as the patient later confirms that she did not get any follow-up imaging. Therefore the question arises, is this malignant transformation of the benign choroid plexus tumor?

The literature does describe the possibility of malignant transformation of benign CPP post-treatment. The treatment itself does not seem to be

the underlying cause, as cases with surgery alone seem to result in malignant transformation. The risk of malignant transformation of CPP is reported as 10–30% aggregated over an individual's lifetime with the highest risk within the first 5–10 years. In addition, there are rare atypical versions of choroid plexus tumors, also known as “oncocyctic.” This is usually seen elsewhere in the body in cell lines and neuroendocrine cell lines. First described in 1984, there are very few cases of the oncocyctic version in the literature.^{8,9}

The second unique aspect was the staining of this tumor. One of the outside pathologists commented on the unique nature of the staining. The usual stains for CPC are divided into four types. The first, synaptophysin, differentiates neuronal tissue from non-neuronal tissue (ie, caused by metastatic spread from another organ system). The second, prealbumin does the same, but is specific for choroid plexus as it is one of the few cell lines in the brain that produces it. The third staining is for cytokeratin (CK) that would only be expected usually in epithelial tissue. CK 7 and CK 20 are the usual stains. The fourth staining is for carcinoembryonic antigen (CEA) that is a common tumor marker.

With CPC, usually the stains are synaptophysin positive, prealbumin negative, CK 7 positive and CK 20 negative, and CEA positive to some degree. Histologically, the cells resembled CPC and there was brisk mitosis suggesting a malignancy. However, the synaptophysin was negative, the prealbumin was focally positive, the CKs were as expected, but the CEA was only minimally positive. However, the pathology report from the second outside source queried confirmed the diagnosis of CPC in at least part of the sections sent to them. And as the outside pathologist from the other center confirmed it was a “fascinating and diagnostic difficult problem” that “prompted me to modify my formerly rigid definition of the immuno profile of this rare tumor.”*

Conclusion

From a primary care standpoint, this case has a number of interesting issues and lessons. First of all, it illustrates that medicine often is not given a cogent and complete story. There are starts and stops, and sometimes there are not even starts but just the middle. Imagine the cutoff that must have occurred to those out of state physicians. Look at the ending we received to this case. Medicine continues to provide this sense of incompleteness that either emotionally frustrates or piques your curiosity.

Second, what does primary care bring to the diagnosis of CPC? Initially just the rapid diagnostic workup and it does not seem to deal with much

afterward. However, in this case, primary care helped to bridge the gap when the patient came back to Champaign-Urbana. The resident who had initially ordered the MRI was able to provide stability to the patient's transition back into the system and thus she received timely oncology consultation. It is likely that if the patient does return to the system, her continued interaction will be well guided by a return to her resident PCP.

Third, despite possible detractors, an electronic medical record system helped to keep all the health information together. Within our own medical record system, I was able to find scanned copies of her biopsy reports from all three hospitals. Both medical and radiation oncology reports were complete. The summary of her operation and extended stay within the hospital were also available. On the flip side, as we encourage the use of electronic medical records, our access to the paper record lessens. Within this case are many clinic and hospital consultations that begin with the line “patient seen without the benefit of the clinic record.” It becomes important to emphasize the continued need to be able to access the paper record.

*Interview with Dr. Bernd Scheithauer, Division of Anatomic Pathology, the Mayo Clinic, Rochester, MN. Conducted 11/2006 and 1/15/07.

Bharat Gopal, MD, works in Family Practice at Carle Clinic, Urbana, IL and serves as the Senior Associate Program Director of the Family Medicine Residency Program at the University of Illinois College of Medicine at Urbana-Champaign.

Nazneen Hashmi, MD, is a Fellow in Geriatrics at Carle Foundation Hospital, Urbana, IL.

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CME Questions 7a-d

Please select the correct answer for the following:

- 7a. There are two main classes of tumors derived from the choroid plexus. Both are malignant.
 - a. True
 - b. False
- 7b. Tumors of the choroid plexus are quite common and account for the majority of intracranial neoplasms.
 - a. True
 - b. False
- 7c. The majority of choroid plexus tumors occur in adults.
 - a. True
 - b. False
- 7d. The typical presentation of a choroid plexus tumor in adults includes:
 - a. Headache
 - b. Visual Disturbances
 - c. Hydrocephalus
 - d. All of the above