

Fourth ventricular ependymoma with a distant intraventricular metastasis: Report of a rare case

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ABSTRACT

Ependymoma is one of the uncommon tumors of the central nervous system (CNS) in the adult age group. These tumors have a distinct propensity for metastasis, both within and outside the CNS. However, dissemination at the time of first presentation and retrograde dissemination of the tumor is rare. We report the case of a patient with fourth ventricular anaplastic ependymoma who presented with left lateral ventricular metastasis which was anatomically different from the primary tumor. We describe the clinic-pathological detail of the patient and discuss the probable pathophysiological basis for this rare presentation and its significance in management of the patient.

Key words: Anaplasia, cerebrospinal fluid, ependymoma, metastasis

Introduction

Ependymomas constitute 2-9% of all intracranial neoplasms. Of these, about 50% present within the first two decades. Intracranial ependymomas account for one-fourth of the cases in adults. Cerebrospinal fluid (CSF) spread is seen in about 8-33% of patients with ependymoma at presentation,^[1,2] and is more common in patients with infratentorial tumors (9.7%) than in those with supratentorial tumors (1.6%) and in patients with high grade tumors (8.4%-20%) than in those with low grade tumors (2-4.5%).^[3] Lumbosacral region is the most common site for “drop” metastases. We report a patient with fourth ventricular ependymoma with a distant upstream left lateral ventricular metastatic lesion, a rare phenomenon not described in literature so far, in spite of the tumor being and closely related to the ventricular system.

Case Report

A 23-year-old man presented with progressive swaying to

either side while walking for five months and progressive headache associated with vomiting for four months prior to presentation. There was no history of seizures, diplopia or similar illness in family members. Examination revealed bilateral papilloedema and bilateral cerebellar signs. The patient was initially evaluated by a general practitioner at local hospital with computed tomography (CT) of the head. It revealed a midline posterior fossa mass lesion, isodense on non-contrast CT and enhancing heterogeneously on contrast injection with obstructive hydrocephalus. He was subsequently referred to our hospital. The patient was first seen at our hospital two months after the initial CT scan. Magnetic Resonance Imaging (MRI) of the brain done about 2 months after initial CT showed increase in the size of the tumor which was isointense on T1WI and T2WI and enhancing heterogeneously on gadolinium contrast injection. The lesion was completely intra-fourth ventricular [Figure 1]. Another lesion was noted in the septum pellucidum extending to the frontal horn of the left lateral ventricle causing obstruction of the foramen of Monro on the left side [Figure 2]. It had the same signal characteristics as that of the tumor. This lesion was not present in the initial CT scan [Figure 3], which was done two months prior to the MRI. There were no other lesions seen on craniospinal MRI.

In view of severe symptoms of raised intracranial pressure, he initially underwent ventriculo-peritoneal shunt placement followed by midline sub-occipital craniectomy and near total excision of the tumor except

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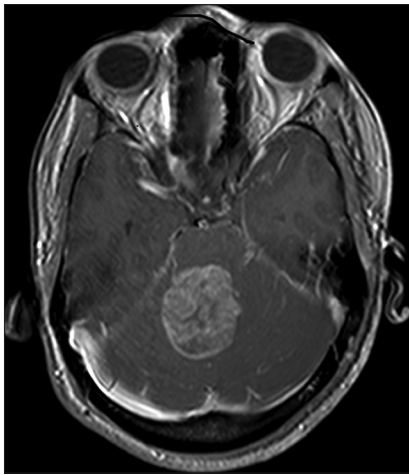


Figure 1: Shows a fourth ventricular mass lesion which was heterogeneous and enhancing on gadolinium contrast

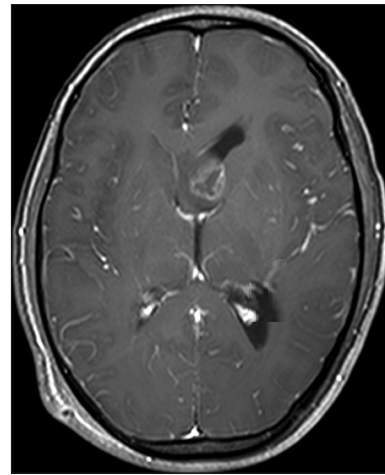


Figure 2: Another lesion was noted in the septum pellucidum extending to the frontal horn of the left lateral ventricle causing obstruction of the foramen of Monro on the left side



Figure 3: Contrast enhanced computed tomographic scan showing no lesion in the septum pellucidum and the lateral ventricle

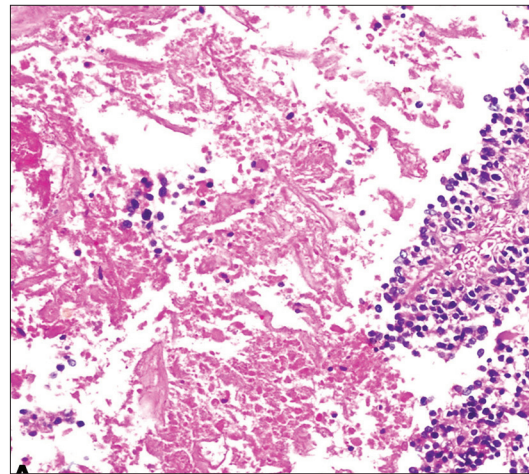


Figure 4: Anaplastic ependymoma showing areas of necrosis (original magnification $\times 160$)

for the part adherent to the brainstem. Post-operatively, he recovered well.

Histopathological examination showed a cellular glial neoplasm consisting of proliferating ependymal cells arranged in compact sheets and several intervening perivascular rosettes. The cells exhibited brisk mitotic activity (6 to 7 in 10 high power fields) with areas of necrosis [Figure 4]. These features suggested a diagnosis of anaplastic ependymoma (grade III).

The patient was subsequently referred to radiation oncologist for adjuvant therapy.

Discussion

Ependymoma is a rare tumor of neuroectodermal origin arising from ependymal cells in the obliterated central canal of the spinal cord, the filum terminale,

choroid plexus and white matter adjacent to the ventricles.^[4] Migration of fetal ependymal cell rests from periventricular areas into parenchyma may account for parenchymal location of these tumors in some instances.^[5] Histopathological examination shows moderate cellularity, rare mitoses and monomorphic cellular morphology. Perivascular pseudorosettes and ependymal canals are important histological features. The four variants described are cellular, papillary, clear cell and tancytic ependymoma. Anaplastic ependymoma is characterized by hypercellularity, cellular and nuclear pleomorphism, frequent mitosis, pseudopalisading necrosis and endothelial proliferation.^[6] Metellus *et al.*,^[7] in their study noted three histological factors namely presence of necrosis, microvascular proliferation and mitotic count greater than 5 to be associated with tumor recurrence, metastasis and short progression-free survival in adult patients with intracranial ependymoma. Wolfsberger *et al.*,^[8] in a multivariate analysis, also noted

a high risk of tumor recurrence and worse outcome in patients whose tumors demonstrated a high Ki-67 index than in those with a low index.

Being uncommon in adults, it is difficult to assess the outcome of ependymomas in an adult population. Adults seem to have better prognosis than children with a 5-year survival of 55-90% and 14-60%, respectively. Various factors have been associated with prognosis of patients with ependymoma such as age, sex, location, tumor grade, extent of resection, treatment modalities, local or craniospinal radiation, chemotherapy, gain of 1q and low nucleolin expression by the tumor cells. Of these only the extent of resection has been known as the most important and consistent prognostic factor.^[9]

Metastasis is important in predicting the clinical outcome and the CSF spread of tumor cells is a key factor in staging, prognosis and treatment. Subarachnoid spread of the disease can be detected either by MRI or by CSF cytology. Of these two, MRI has been found to be more sensitive in detecting CSF spread of the tumor,^[10] CSF seeding is more common in anaplastic ependymomas, younger children and infratentorial tumors. In a study of 754 patients with intracranial ependymomas, cytologic evidence of CSF spread was noted in 12% of patients, those symptomatic for metastasis being <5%.^[2]

Appearance of leptomeningeal spread of disease on MRI of the spine are variable and include smooth enhancement along the surface of the spinal cord, enhancing foci in the intradural extramedullary plane, intramedullary plane, nerve root thickening, nodularity, or clumping and thecal sac irregularity. The lumbosacral region, particularly the most caudal aspect of the thecal sac, is the most common location for “drop” metastases. Intracranial imaging manifestations include leptomeningeal nodules, masses or smooth enhancement, and communicating hydrocephalus. These lesions may not demonstrate enhancement as the primary tumor. Our patient had a distinct left lateral ventricular mass lesion, separate from the fourth ventricular tumor. It was thought to be metastatic tumor arising from the retrograde CSF seeding of the primary fourth ventricular tumor, as the lateral ventricular lesion was apparent only on subsequent imaging after the primary evaluation. It is interesting to note the metastatic tumor within the ventricular system in a case of fourth ventricular ependymoma, as it has not been reported in literature so far, in spite of the tumor being within the ventricular system. However, there was no evidence of CSF seeding elsewhere along the central nervous system. CSF seeding is the likely origin of the lateral ventricular tumor, but possibly the tumor characteristics might have

a role in this rare metastatic occurrence. Higher grade of tumor is associated with poor outcome and various tumor characteristics are described in prognosticating the individual tumor. One of the common prognostic markers of outcome and the tumor aggressive behavior is a high MIB-1 labeling index.^[11] Our patient had brisk mitosis and during surgery had intratumoral necrosis suggesting an aggressive nature of the tumor. Aggressive and the metastatic nature of the tumor have been described in literature in association with various adhesion molecules and the factors affecting the intrinsic cellular pathway. Cadherins are calcium dependent cell adhesion molecules implicated in tumor spread. Decreased expression of N-cadherin has been reported in patients with ependymoma with CSF dissemination.^[12,13] The ADAMs (A Disintegrin AND Metalloproteinase) are a family of membrane proteins that have potential to be key modulators of cell-matrix interactions through the activities of their constituent domains. ADAMs 8, 12, 19 are significantly upregulated in ependymoma, particularly in the anaplastic variety and are known to be associated with more invasive behavior.^[5] Decreased expression of antioxidant enzymes in the ependymal tumors are also known to be associated with aggressive nature of the tumor, in particularly with the adult patients.^[14] Though we did not have assay of the intrinsic biological markers, the inherent tumor characteristics might have a role in the more aggressive nature of this tumor which was reflected as necrosis during surgery and brisk mitosis on histopathology. Metastasis to the lateral ventricle possibly represents breakdown of the adhesion molecules in a highly aggressive tumor causing CSF seeding to the third ventricular ependymoma along a path of least resistance in the presence of fourth ventricular obstruction.

Larger studies are required to assess the factors predicting the aggressive behavior of these tumors.

Conclusion

Ependymomas are uncommon tumors in adults. Defining the extent of the disease pre-operatively and gross total excision of the tumor whenever possible, followed by radiotherapy should be the standard of care in the present day. Metastasis is important in predicting the clinical outcome. Distant intra ventricular metastasis represents a rare pathomorphology and possibly aggressive potential of the tumor.

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