Journal of Pediatric Neurology & Medicine

Baute, J Pediatr Neurol Med 2017, 2:2
DOI: 10.4172/2472-100X.1000122

Case Report Open Access

A Case Report of Atypical Teratoid/Rhabdoid Tumor with Diffuse Leptomeningeal Carcinomatosis and Review of Current Literature

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Received date: May 23, 2017; **Accepted date:** June 14, 2017; **Published date:** June 21, 2017

Abstract

We present a rare case of craniospinal atypical teratoid/rhabdoid tumor (ATRT) with leptomeningeal carcinomatosis in young adult. A previously healthy 25 year old man presented to the hospital after a one week history of intermittent confusion, intractable headache and a single new onset seizure. Two lumbar punctures were completed and both revealed elevated RBC, elevated protein and predominantly lymphocytic pleocytosis. Both lumbar punctures were unrevealing with normal cytology and flow cytometry. Contrasted magnetic resonance imaging (MRI) of the brain revealed extensive intracranial leptomeningeal and cranial nerve enhancement. Contrasted MRI of the spinal cord revealed extensive leptomeningeal and dural enhancement with multifocal areas of nodular mass-like enhancement along the entire spinal cord. Spinal biopsies were performed and a pathological diagnosis of ATRT was made. Aggressive radiotherapy and chemotherapy treatment were started. Unfortunately, the patient expired within 12 months of the initial diagnosis.

Keywords: Atypical teratoid rhabdoid tumor; ATRT; Nervous system tumor; hSNF5/INI-1

Introduction

In this case report, we present a rare case of brain and spinal atypical teratoid rhabdoid tumor with leptomeningeal carcinomatosis in an adult. ATRT is a rare primary central nervous system (CNS) tumor that is predominantly seen in childhood with peak incidence from birth to third year of life. It is rarely seen in adulthood. There are less than 50 adult cases of ATRT reported in the literature to date [1]. The true incidence in adults is not yet known. In contrast to pediatric cases, AT/RT in adults is typically supratentorial-infratentorial and spinal cord involvement is relatively uncommon [2]. Due to lack of specific clinical and neuroimaging features, ATRTs are typically misdiagnosed. This was a diagnostically challenging case that required correlation with histopathology to determine the correct diagnosis. To the best of our knowledge, this is the first case report of primary ATRT in a young adult involving the craniospinal axis with diffused leptomeningeal involvement.

Case Presentation

A previously healthy 25 years old Caucasian man presented to the hospital after a one week history of intermittent confusion, intractable headache and a single new onset seizure. Earlier in the week prior to presentation, he presented to a local urgent care with intractable headache, nausea and vomiting. He was diagnosed with food poisoning and was discharged home with anti-emetics. A few days later, he re-presented to the local ED with increased confusion and falls. He was combative and did not recognize his family. While in the ED, he was noted to have a generalized tonic clonic seizure lasting for 1-2 min. He was transferred to our facility for further work-up and management.

The patient had no known past medical history, specifically no prior history of seizures. He was not taking any medications. He denied any tobacco or illicit drug use. He had no family history of seizures.

Investigations

In the ED, the patient was combative and not following any commands. He was given multiple doses of lorazepam for sedation. He had an initial lumbar puncture that revealed markedly elevated RBC (100,444), elevated protein (657), predominantly lymphocytic pleocytosis (755) and normal glucose (60). Opening pressure was inaccurately measured with the patient in the prone position with a recording of >50 cm of H_2O. He was empirically started on acyclovir and broad spectrum antibiotics due to concerns for viral/bacterial meningitis or encephalitis. He later had a routine electroencephalogram that did not show any epileptiform discharges. He was subsequently transferred to our facility for further work-up.

Upon arrival to our facility, the patient was no longer confused. Physical exam revealed only mild horizontal diplopia with lateral gazes and no other focal weakness, numbness or ataxia. A repeat lumbar puncture was obtained. Cerebral spinal fluid (CSF) studies revealed markedly elevated RBC (34,800), elevated protein (1,263), predominantly lymphocytic pleocytosis (789) and normal glucose (66). CSF viral studies including Epstein-Barr virus, cytomegalovirus, herpes simplex virus and varicella zoster were negative. Additionally, IgG and IgM Lyme panel was negative. Bacterial and fungal cultures were negative. CSF cytology and flow cytometry were unremarkable.

Contrasted magnetic resonance imaging (MRI) of the brain revealed extensive intracranial leptomeningeal and cranial nerve enhancement (involving right CN III and CN VI, bilateral CN VIII and CN V) (Figure 1). Contrasted MRI of the spinal axis revealed extensive leptomeningeal and dural enhancement with multifocal areas of nodular mass-like enhancement along the entire spinal cord (Figure

2). Given these results, a CT chest, abdomen and pelvis was performed and it did not show any other primary source of malignancy.

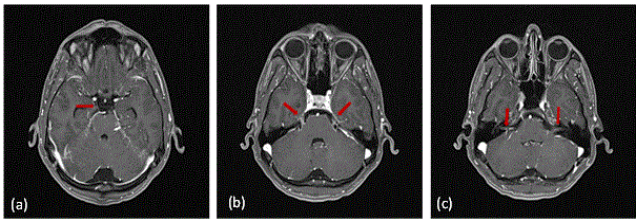

Figure 1: Axial T1 weighted with contrast MR shows enhancement along the right CN III (a), bilateral CN V (b) and VIII (c).

He underwent a T5 laminectomy and subtotal resection of intradural extramedullary mass. Arachnoid and thoracic spinal cord lesion biopsies were sent for surgical pathology. Pathology revealed poorly-differentiated malignant neoplasm that was most consistent with primitive neuroectodermal tumor. Additional FISH cytogenetic studies were sent and came back positive for loss of the hSNF5/INI1 (22q11.23) gene regions, which was diagnostic for atypical teratoid rhabdoid tumor (ATRT).

Differential Diagnosis

The patient's clinical presentation initially suggested an infectious etiology for his encephalopathy. Additionally, the clinical improvement with empiric treatment with acyclovir and broad spectrum antibiotics further supported the suspicion that his encephalopathy was secondary to an infectious etiology. However, when the CSF viral studies came back negative and given the elevated protein (despite correction for the elevated RBCs), we questioned the initial diagnosis. With the nodular mass-like enhancement seen on contrasted MRI of the spine, our differential diagnosis expanded to include granulomatous diseases such as sarcoidosis and malignant process such as CNS lymphoma, leukemia, carcinomatosis meningitis. Spinal biopsies were performed and a pathological diagnosis of ATRT was made.

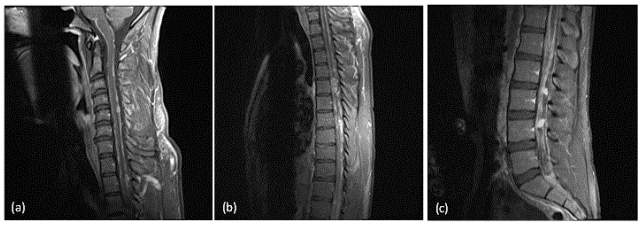

Figure 2: Sagittal T1 weighted contrasted MR demonstrates diffuse leptomeningeal enhancement along the cervical (a), thoracic (b) and lumbar (c) spine. Multifocal mass like enhancements along the spinal cord and nerve roots, representing pathology proven ATRT lesions.

Treatment

Once a diagnosis of ATRT was confirmed, he completed a course of external beam radiation therapy (3600 cGy divided in 24 fractions) to spinal nodules at T2-T5 and L3-L4. He subsequently underwent adjuvant chemotherapy at different institution close to their home. The patient expired within 12 months of the initial diagnosis.

Outcome and follow-up

Despite the aggressive treatment with radiotherapy and adjuvant chemotherapy, the patient expired within 12 months of the initial diagnosis.

Discussion

We have presented the first reported case of an adult onset of craniospinal ATRT with diffuse leptomeningeal carcinomatosis. The unique aspect of this case was the acuity of the patient's presentation with intermittent confusion, intractable headache and single episode of seizure. Though his initial symptoms resolved with empiric antiviral and antibiotic therapy, the abnormal CSF results led to more extensive testing which aided in diagnosis. Our case report demonstrates that since the clinical presentation and radiological appearance of ATRT are non-specific, it is essential to correlate with histopathology and cytogenetics to establish the correct diagnosis.

ATRT was first reported in the late 1980's and early 1990's in multiple case reports of patients with isolated CNS ATRTs. Prior to this time, reported case of CNS rhabdoid tumors were often associated with malignant rhabdoid tumors of the kidney. It was in 1995 when the tumor was first characterized as an "atypical teratoid rhabdoid tumor" based on histological evidence [3]. The primary diagnostic component is the presence of rhabdoid cells or in part with a combination of primitive neuroectodermal (PNET), mesenchymal and epithelial cells. 3,4 ATRTs were often categorized with PNETs due to histologic similarities, but they are now separated from other embryonal tumors due to the presence of rhabdoid cells and as well as specific immunohistochemistry. ATRT is the only nervous system tumor for which a pathognomonic alteration of a tumor suppressor gene has been identified. ATRT is characterized by the loss of a tumor suppressor gene that has been identified as the hSNF5/INI-1 gene on chromosome 22 [2].

This gene, however, is only found to be positive in 76% of biopsied tissue and the yield increases as sampling increase [4]. Anatomically, pediatric ATRTs are infratentorial, most commonly in the cerebellum or cerebellopontine angle. In contrast to pediatric tumors, most adult CNS ATRT is supratentorial. In adults, ATRT is most commonly located in the cerebral hemisphere (53%), sella (17%), cerebellum (13%), and spinal cord (7%) [5,6]. On MR imaging, there is typically mixed signal intensity on T1- and T2-weighted images due to necrosis and tumor hemorrhages [7,8]. In children, leptomeningeal enhancement of the tumor at diagnosis can be seen in 20-34% of patients with ATRT on enhanced MR imaging [9]. However, to our knowledge, there have been no reports of leptomeningeal enhancement in adult patients diagnosed with ATRT. At the time of diagnosis, our patient had diffuse leptomeningeal enhancement on enhanced MR imaging. In patients with ATRT, the main cause of death is typically either tumor recurrence or leptomeningeal dissemination [10,11].

It is an aggressive malignancy with a poor prognosis. In comparison to children, there is a longer median survival time with adult onset ATRT (median survival time: 10-17 months in children and 21-26 months in adults) [2,4]. It has been proposed that this may be related to the completeness of surgical resection and tolerance of irradiation [12]. Surgical removal of the ATRT is considered the primary

treatment. Typical adjunct therapy, including chemotherapy, radiotherapy, autologous bone marrow transplantation and stem cell support, appears to yield more long-term survivors [1,11]. Unfortunately, there are no standardized treatment protocols and most of the adult treatment regimens are derived from pediatric experience, which poses a risk of myelosuppression since the recommended doses of chemotherapy in children exceed those tolerated by adults.

Learning points

Atypical teratoid/rhabdoid tumor is a rare and aggressive malignancy that requires histochemical and pathological studies to confirm the diagnosis.

AT/RT is the only nervous system tumor for which a pathognomonic alteration of a tumor suppressor gene has been identified. AT/RT is characterized by the loss of a tumor suppressor gene that has been identified as the hSNF5/INI-1. This is important as it aids in the making the correct diagnosis of AT/RT.

When possible, surgical removal is considered the primary treatment for atypical teratoid/rhabdoid tumor. Adjunctive therapy including chemotherapy, radiotherapy and stem cell transplantation may extend the survival rate. However, despite aggressive therapy, AT/RT has a poor prognosis.

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