Case Report

Journal Of Clinical & Medical Images Case Reports

Open Access, Volume - 2

Fatal outcome from the rapid progression of metastatic CNS ATRT

Cristian Cirjan[1]; Philippe Mercier[2]; Pournima Navalkele[3,4*]

[1]*Saint Louis University, Saint Louis, MO.*

[2]*Department of Neurosurgery, Saint Louis University, Saint Louis, MO.*

[3]*Department of Pediatrics, Saint Louis University, Saint Louis, MO.*

[4]*Department of Pediatrics, Cardinal Glennon Children's Hospital, St. Louis Uni-versity, 1465 South Grand Blvd., St. Louis, MO 63104.*

Received Date : April 05, 2022
Accepted Date : Apr 22, 2022
Published Date : May 09, 2022
Archived : www.jcmimagescasereports.org

***Corresponding Author:** Pournima Navalkele, Department of Pediatrics, Cardinal Glennon Children's Hospital, St. Louis University, 1465 South Grand Blvd., St. Louis, MO 63104
Email: Pournima.navalkele@gmail.com

Abstract

Young pediatric patients with Central Nervous System (CNS) Atypical Teratoid Rhabdoid Tumor (ATRT) often present with metastasis and have a very poor prognosis. This case report elucidates the fatal outcome from the rapid progression of metastatic CNS ATRT soon after starting chemotherapy and raises concern about CNS tumor lysis syndrome.

Keywords: CNS ATRT; Pediatric; tumor lysis; chemotherapy; cerebral edema; case report.

Abbreviations

CNS: Central Nervous System; ATRT: Atypical Teratoid Rhabdoid Tumor; MUV: Medical University of Vienna

Introduction

Central Nervous System (CNS) Atypical Teratoid Rhabdoid Tumor (ATRT) is a rare but highly aggressive form of embryonal brain tumor of infancy and early childhood and often presents with metastasis at diagnosis. Historically, therapies have led to a 2-year event free survival of mere 11% [1]. Use of newer chemotherapy protocol has modestly salvaged this poor outcome. This case report elucidates the fatal outcome from the rapid progression of metastatic CNS ATRT soon after starting chemotherapy and raises concern about potential CNS tumor lysis.

Case presentation

A toddler was admitted to our hospital with sub-acute onset of fevers, ataxia, vomiting, anorexia, weight loss, headaches, motor and speech regression and developed acute onset seizures. MRI brain showed a mildly enhancing, diffusion restricting mass centered in the pineal region, resulting in aqueduct stenosis and lateral ventriculomegaly. Contrast-enhancing lesions within the bilateral occipital lobes and cerebellum indicated CNS metastasis. Immediately, she underwent urgent third ventriculostomy, tumor biopsy and external ventricular drain placement. Pathology showed Atypical Teratoid Rhabdoid Tumor (ATRT), WHO grade IV, with SMARCB1/ INI1 loss. CSF cytology showed malignant tumor cells. Germline rhabdoid predisposition syndrome was ruled out on peripheral blood testing. On hospital day 13, safe maximal primary tumor resection was performed by neurosurgeon with immediate postoperative MRI brain confirming near total resection of primary tumor and MRI spine showing metastatic tumor progressing to the spine.

On hospital day 24, she began chemotherapy based on Medical University of Vienna (MUV) protocol. The choice of MUV chemotherapy was based on the published 5-year event-free survival of 89% in patients with CNS ATRT, including those with metastatic disease [2]. The protocol consists of three 9-week courses of a dose-dense regimen including doxorubicin, cyclophosphamide, vincristine, ifosfamide, cisplatin, etoposide and high dose methotrexate, augmented by intrathecal therapy followed by high-dose chemotherapy (HDCT) with autologous hematopoietic stem cell reinfusion followed by focal radiation therapy. The authors reported no serious adverse events in relation to this protocol, including cerebral edema or cardiac toxicities. As a reference, the Children's Oncology Group clinical trial ACNS0333 showed a 2-year event-free survival of 39% [3]. The Dana-Farber Cancer Institute protocol for ATRT showed a 2-year event-free survival of 53% [4]. Approximately 36 hours into doxorubicin infusion, she developed acute respiratory distress with chest x-ray showing pulmonary infiltrates prompt-

Citation: Pournima Navalkele. Fatal outcome from the rapid progression of metastatic CNS ATRT. J Clin Med Img Case Rep. 2022; 2(3): 1138.

ing initiation of empiric antibiotics and high-flow oxygen. Soon after, she developed asymmetric pupils, severe hyponatremia and apnea leading to intubation and use of hypertonic saline and mannitol. We were unable to perform laboratory investigations for underlying cause of severe hyponatremia while our patient's clinical status was acutely deteriorating. CT head showed increased sulcal and basilar cistern effacement, grey-white matter differentiation was preserved, decreased ventricles and early descending trans tentorial herniation. Chemotherapy infusion was discontinued, and stress dose dexamethasone was started. Subsequent seizures prompted anti-epileptic drug administration. Acute severe bradycardia prompted echocardiogram on which left ventricular shortening fraction dropped from baseline of 36% to 14.5%. Soon after, she became pulseless necessitating cardiopulmonary resuscitation without success. CNS autopsy showed multifocal necrotizing encephalopathy from diffuse tumor metastasis and acute hypoxic encephalopathy.

Discussion

The most important inciting cause leading to our patient's fatal outcome was the rapidly metastasizing tumor. In addition, we speculate if the initiation of chemotherapy contributed to severe acute changes in the CNS compartment, including possible CNS tumor lysis syndrome. In order to validate our speculation, we performed thorough literature review using PubMed database, focusing on CNS neurotoxicity from doxorubicin chemotherapy and more specifically drug induced CNS tumor lysis.

Upon thorough literature review, we confirmed that doxorubicin was not associated with acute-onset SIADH or cerebral edema in cancer patients undergoing active therapy, outside of cases in which it was prescribed as a part of combined chemotherapy with agents associated with SIADH [5, 6]. Animal studies have described acute neurotoxic effect of doxorubicin on rodent despite of its known poor CNS penetration [7]. Very few cases have been reported in the literature describing malignant cerebral edema in conjunction with therapy for CNS tumors. Zhu et al described the case of a 10-year-old girl with glioblastoma, treated with Nivolumab, wherein the malignant cerebral edema took place after each infusion of Nivolumab, with evidence of severe tumor necrosis on CT scans [8]. As in our case, signs of trans tentorial herniation accompanied the edema, in their case requiring dexamethasone initially and ultimately a decompressive craniectomy. Zhu had speculated that augmented T-cell responsiveness due to the immunomodulator effects of nivolumab may have caused an inflammatory response resulting in the cerebral edema. However, subsequent pathology findings did not demonstrate signs of extensive inflammation, but rather evidence of tumor necrosis with localized inflammation. Hodi et al also reported a case with symptomatic cerebral edema around melanoma metastases following ipilimumab therapy [9]. Unlike our patient, both patients responded favorably to dexamethasone therapy and cessation of chemotherapy. Ahmed et al found 6 of 26 patients (23%) with metastatic melanoma with greater than 20% increase in tumor volume due to cerebral edema, hemorrhage, or both following ipilimumab therapy [10].

Most literature on tumor lysis syndrome describes it in peripheral blood compartment, typically in the setting of leukemias and lymphomas. There are rare cases reporting drug induced CNS tumor lysis syndrome involving solid tumors [11]. In their report, Bachegowda et al described the CNS neurotoxicity of seizures within 48 hours of administration of intrathecal methotrexate for management of diffuse large B-cell lymphoma with known CNS metastasis [12]. They associated the development of cerebral edema and disappearance of CNS metastasis (both on MRI and on CSF flow cytometry) as an effect of methotrexate and speculate if CNS tumor lysis could be the pathogenetic mechanism for this effect. We did not find any report elucidating drug induced CNS tumor lysis syndrome involving primary CNS tumors.

This case report highlights the fatality from a highly aggressive CNS ATRT and prompts future research focusing on acute doxorubicin neurotoxicity and understanding the pathophysiology of CNS tumor lysis syndrome.

Funding Disclosure: No funding was received for this manuscript. This manuscript was not generated as part of the employment of authors.

Conflicts of Interest: None of the authors listed has any conflicts of interest. All the authors have contributed significantly to this manuscript and have reviewed the manuscript and agree with the contents.

Acknowledgements: None.

References

1. Von Hoff K, Hinkes B, Dannenmann-Stern E, von Bueren AO, Warmuth-Metz M, Soerensen N, et al. Frequency, risk-factors and survival of children with atypical teratoid rhabdoid tumors (AT/RT) of the CNS diagnosed between 1988 and 2004, and registered to the German HIT database. Pediatr Blood Cancer. 2011; 57(6):978-85. [PMID: 21796761 DOI: 10.1002/pbc.23236] [Epub 2011 Jul 27].

2. Slavc I, Chocholous M, Leiss U, Haberler C, Peyrl A, Azizi AA, et al. Atypical teratoid rhabdoid tumor: improved long-term survival with an intensive multimodal therapy and delayed radiotherapy. The Medical University of Vienna Experience 1992-2012. Cancer Med. 2014; 3(1):91-100. [PMID: 24402832; PMCID: PMC3930393 DOI: 10.1002/cam4.161] [Epub 2013 Dec 11].

3. Reddy AT, Strother DR, Judkins AR, Burger PC, Pollack IF, Krailo MD, et al. Efficacy of High-Dose Chemotherapy and Three-Dimensional Conformal Radiation for Atypical Teratoid/Rhabdoid Tumor: A Report From the Children's Oncology Group Trial ACNS0333. J Clin Oncol. 2020; 38(11):1175-1185. [PMID: 32105509; PMCID: PMC7145589 DOI: 10.1200/JCO.19.01776] [Epub 2020 Feb 27].

4. Chi SN, Zimmerman MA, Yao X, Cohen KJ, Burger P, Bie-

gel JA, et al. Intensive multimodality treatment for children with newly diagnosed CNS atypical teratoid rhabdoid tumor. J Clin Oncol. 2009; 27(3):385-9. [PMID: 19064966; PMCID: PMC2645855 DOI: 10.1200/JCO.2008.18.7724] [Epub 2008 Dec 8].

5. Hirata Y, Yokote T, Nishiwaki U, Tsuji M, Hanafusa T. Syndrome of inappropriate antidiuretic hormone secretion associated with primary cutaneous anaplastic large cell lymphoma. Br J Haematol. 2012; 157(4):412. [PMID: 22409317 DOI: 10.1111/j.1365-2141.2012.09090.x] [Epub 2012 Mar 13].

6. Kobayashi K, Yokote T, Akioka T, Takubo T, Tsuji M, Hanafusa T. Inappropriate antidiuretic hormone production in diffuse large B-cell lymphoma. Br J Haematol. 2008; 143(1):2. [PMID: 18513282 DOI: 10.1111/j.1365-2141.2008.07255.x] [Epub 2008 May 30].

7. Alhowail AH, Bloemer J, Majrashi M, Pinky PD, Bhattacharya S, Yongli Z, et al. Doxorubicin-induced neurotoxicity is associated with acute alterations in synaptic plasticity, apoptosis, and lipid peroxidation. Toxicol Mech Methods. 2019; 29(6):457-466. [PMID: 31010378 DOI: 10.1080/15376516.2019.1600086] [Epub 2019 Jun 18].

8. Zhu X, McDowell MM, Newman WC, Mason GE, Greene S, Tamber MS. Severe cerebral edema following nivolumab treatment for pediatric glioblastoma: case report. J Neurosurg Pediatr. 2017; 19(2):249-253. [PMID: 27858578 DOI: 10.3171/2016.8.PEDS16326] [Epub 2016 Nov 18].

9. Hodi FS, Oble DA, Drappatz J, Velazquez EF, Ramaiya N, Ramakrishna N, et al. CTLA-4 blockade with ipilimumab induces significant clinical benefit in a female with melanoma metastases to the CNS. Nat Clin Pract Oncol. 2008; 5(9):557-61. [PMID: 18665147 DOI: 10.1038/ncponc1183] [Epub 2008 Jul 29].

10. Ahmed KA, Stallworth DG, Kim Y, Johnstone PA, Harrison LB, Caudell JJ, et al. Clinical outcomes of melanoma brain metastases treated with stereotactic radiation and anti-PD-1 therapy. Ann Oncol. 2016; 27(3):434-41. [PMID: 26712903 DOI: 10.1093/annonc/mdv622] [Epub 2015 Dec 27].

11. Baeksgaard L, Sørensen JB. Acute tumor lysis syndrome in solid tumors--a case report and review of the literature. Cancer Chemother Pharmacol. 2003; 51(3):187-92. [PMID: 12655435 DOI: 10.1007/s00280-002-0556-x] [Epub 2003 Feb 28].

12. Bachegowda LS, Grivas PD, Anand R, Stecker E, Ward K. Intracranial tumor lysis and cerebral edema after administration of intrathecal methotrexate: a case report and discussion. Med Oncol. 2010; 27(4):1079-81. [PMID: 19847678 DOI: 10.1007/s12032-009-9338-1] [Epub 2009 Oct 22].