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Case Report

A Rare Case of Non-Metastatic, Intraventricular, High-Grade Glioma in a Pediatric Patient

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Abstract

High-Grade Gliomas (HGGs) are a relatively rare malignancy among children and adolescents in the United States. Moreover, the overwhelming majority of HGGs occur in the intraparenchymal tissue of the cerebral lobes, cerebellum, and the brainstem with ventricular neoplasms accounting for less than 5% of all cases of malignant, high-grade gliomas. Furthermore, given that intraventricular, high-grade tumors have ready access to the ventricular system for seeding malignancy to other parts of the body, lack of metastasis constitutes a unique finding. Both aforementioned rarities are exemplified in the case presentation here of a 11-year-old male who presented with sudden worsening headache and vomiting with head imaging and pathology ultimately showing an intraventricular IDH-wildtype high-grade glioma centered in the left lateral ventricle with invasion into the corpus callosum and cingulate gyrus without metastasis representing a unique treatment challenge to medical providers.

Keywords: Pediatric; High-grade; HGG; Intraventricular; Glioma

Introduction

Gliomas are tumors of glial cells (also called neuroglia) including astrocytes, oligodendrocytes, microglia, and ependymal cells when located in the central nervous system (CNS). In pediatric patients, gliomas are the most common CNS tumor at 35% of all cases in patients aged 19 years or younger [1,2]. The World Health Organization (WHO) classifies gliomas into four histological categories with grades 1-2 being low-grade and grades 3-4 being high-grade. High-grade gliomas (HGGs) include anaplastic astrocytoma, anaplastic oligodendroglioma, anaplastic ependymoma, and glioblastoma. Altogether, HGGs account for approximately one-third of all pediatric gliomas and 8% - 12% of all pediatric primary CNS tumors [3-5]. The overwhelming majority of pediatric HGGs is anatomically located in the cerebral hemispheres, thalamus, hypothalamus, and the basal ganglia with only a paucity located in the ventricular space [6].

Case Report

An 11-year-old male with no past medical history presented to the emergency department (ED) for headache and vomiting. His symptoms began four days prior to arrival with headache and neck pain first that gradually worsened with subsequent development of non-bloody, non-bilious emesis one day prior to arrival to the ED. He localized his headache to the frontal midline and reported accompanying photophobia. He denied recent illness, foreign travel, fever, chills, weakness, dizziness, or changes in hearing, vision, strength, or sensation. Physical examination was only remarkable for tenderness to palpation at the posterior neck. Laboratory blood counts and metabolic panels were unremarkable for acute pathology. However, a head computer tomography (CT) scan without contrast showed an irregular hyperattenuating mass at the midline spanning the bilateral lateral ventricles measuring 2.8 x 2.7 x 2.1 cm with 4 mm left-to-right mass effect on corpus collosum. Brain and spinal magnetic resonance imaging (MRI) with and without contrast demonstrated a heterogeneous, lobulated, and predominantly intraventricular enhancing mass centered in the left atrium abutting the choroid plexus crossing the midline to the contralateral lateral ventricle and extending superiorly with invasion into the posterior body of the corpus callosum and cingulate gyrus bilaterally without metastases. No hydrocephalus or significant transependymal flow were noted. The patient was admitted to the Pediatric Intensive Care Unit (PICU) with resolution of headache and pain with intravenous dexamethasone among other supportive medications and management. On hospital day #6, the patient underwent a left parietal neuroendoscopic approach with stereotactic navigation for intraventricular brain tumor biopsy and debulking. On hospital day #8, the patient was discharged on a dexamethasone taper with pathology report pending and outpatient follow-up with neurosurgery.

The patient returned to the ED on two subsequent occasions.

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His second visit was within one week of being discharged due to recurrence of intractable headaches and vomiting again with head CT in the ED showing a small hemorrhage within the tumor bed with readmission to PICU due to concern for elevated Intracranial Pressure (ICP) with resumption of IV dexamethasone and supportive management and eventual discharge after 7 days with steroid taper. The patient presented again to ED 10 days after his last discharge due to a recurrence of headaches without vomiting again with resumption of IV dexamethasone and supportive management. On hospital day #4, he underwent a transcortical approach left parietal craniotomy with tumor debulking and placement of an External Ventricular Drain (EVD). Due to its high vascularization, only 75% of the tumor could be respected. Patient tolerated the procedure well and EVD was eventually removed due to resolution of headaches and minimal output with repeat head CT showing no intracranial edema or fluid collections. The patient's tumor pathology report finally yielded a diagnosis of a High-Grade Glioma (HGG) composed of cells with angulated, hyperchromatic, and pleomorphic nuclei evidencing mitotic activity and immunohistochemistry negative for IDH1/2 mutations indicating IDH-wildtype genealogy and negative for BRAF, EGFR, or FGFR1/2/3 mutations as well. Unfortunately, further molecular testing could not differentiate a more specific tumor classification due to lack of sufficient tissue from biopsy. Currently, the patient's case is scheduled to be discussed by an interdisciplinary tumor board.

Discussion

The unique combination of a pediatric, IDH-wildtype HGG originating in the ventricular space without metastasis represents an exceedingly rare presentation.

Regarding the patient's IDH-wildtype HGG, a poorer prognosis is conferred as current literature shows that presence of the IDH1/2 mutations to be the most significant factor prognosticating improved survival even when controlling for tumor grade and histology [7]. IDH1/2 mutations are believed to be oncogenic via overproduction of d-(R)-2-hydroxyglutarate (2-HG) resulting in inhibition of histone/DNA demethylases causing histone/DNA hypermethylation and ultimately disrupted cellular differentiation [8]. This gain of function defect in mutant IDH enzymes, however, affords the opportunity for targeted novel drug therapies in the way of IDH enzyme inhibitors in the future; however, to-date no such treatment exists.

The anatomical location of the patient's HGG is also of particular interest both due to its rarity and clinical manifestation. The patient's initial symptoms of headache and nausea/vomiting were typical of mass effect from a tumor. However, the sudden onset of symptoms over four days given the tumor's size is exceptional, likely due to intraventricular growth occurring first before invasion into the corpus callosum resulted in the observed left-to-right mass effect and subsequent headache and nausea/vomiting due to increased ICP. Database querying of the United States' National Program of Cancer Registries (NPCR) and Surveillance, Epidemiology, and End Results (SEER) databases shows that for all cases of malignant, high-grade (WHO stage III-IV) gliomas from 2000-2017 in patients aged 19 years or younger according to the CNS malignancy classifications specified in Forjaz et. al., only 4.8% of all cases had occurred in the ventricular space [9,10]. Although, this represents a rather low overall morbidity burden, the prognosis of ventricular and paraventricular HGGs is exceedingly poor with median survival being 12 months across all ages [11].

Finally, the location and nature of the patient's HGG also introduces challenges to treatment compared to more conventional cases. Treatment options for HGGs in pediatric patients is difficult given their aggressive nature and sensitive locations. Classically, patients are treated with partial, subtotal, or gross total resection for debulking followed by targeted radiation therapy and/or chemotherapy. Although surgical resection confers the greatest survival advantage for pediatric HGGs in aggregate, they are not associated with improved survival in patients with ventricular / paraventricular HGGs [11,12]. As such, the 75% subtotal tumor resection that the patient received may be insufficient to confer significant survival benefit alone. Chemotherapy regimens involving different combinations of lumostine, vincristine, cisplatin, carmustine, cytosine arabinoside, procarbazine, Dimethyl-Triazenoimidazole-Carboxamide (DITC), hydroxyurea, and prednisone have been trialed with varying degrees of success [13]. Given the cytotoxic side effect profile of chemotherapy, many providers elect radiation therapy before chemotherapy in children. However, multidisciplinary collaboration among a plurality of providers would be better able to assess risks and benefits ultimately regarding treatment plan.

Conclusion

In this report, we presented the highly unique case of a 11-year-old male who presented with sudden worsening headache and vomiting with imaging and pathology ultimately showing an intraventricular IDH-wildtype high-grade glioma centered in the left lateral ventricle with invasion into the corpus callosum and cingulate gyrus without metastasis. Against the backdrop of relatively common clinical presentations, this patient's HGG is a notable departure from the norm due to its unique immunohistopathology, anatomical location, high grading, and symptom timeline. These departures from the norm in aggregate represent a significant medical challenge for the patient's multidisciplinary clinician team to address. With future studies investigating how these clinical manifestations inform and alter treatment of pediatric HGGs, clinicians may offer more targeted and better-informed care for patients in the future.

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