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CASE REPORT

Leptomeningeal and subependymal seeding of diffuse intrinsic pontine glioma: a case report

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Abstract

DIPG (diffuse intrinsic pontine glioma) is a deadly cancerous tumor of the brainstem that spreads across the pons. The tumor's infiltrative nature, as well as the tumor's critical pathway and nuclei compression, contributes to the tumor's extremely poor prognosis and limited existing therapeutic options. A previous study revealed that in 40 patients with brainstem glioma, 13 (33%) patients had leptomeningeal spreading. In this paper, we reported a 7-year-old female patient who presented with a history of decreased consciousness and weakness of the right limb. Her magnetic resonance imaging (MRI) revealed a pontine mass. She was given 35 fractions of 54 Gy whole-brain radiotherapy. The post-radiotherapy MRI evaluation showed multiple nodules in periventricular region, and was suggestive of leptomeningeal and subependymal seeding of the pontine glioma in the lateral ventricles. This case report elucidated the leptomeningeal seeding in a pediatric patient with diffuse intrinsic pontine glioma.

Keywords Diffuse intrinsic pontine glioma · DIPG · Leptomeningeal seeding

Introduction

Diffuse intrinsic pontine glioma (DIPG) is a lethal malignant pediatric brainstem tumor that grows diffusely in the pons [1]. This devastating disease arises in midline structures, comprises 80% of all brainstem tumors in children, and has a median age at diagnosis of 6–7 years [2, 3]. Motor weakness, cranial neuropathies, and cerebellar sign are the most common clinical manifestations on its initial presentation [2]. Over the last 20 years, the survival rate of patients with DIPG has remained static, with a median survival of about 10 months and a 2-year survival rate of less than 10% [2, 4]. Critical pathway and nuclei compression with its infiltrative nature contribute to extremely poor prognosis caused by this tumor, in addition to limited current treatment options [3]. We presented an unusual case of DIPG with leptomeningeal dissemination and subependymal spread in a pediatric patient.

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Case description

A 7-year-old girl presented with a history of decreased consciousness during the last 2 weeks following an episode of seizure, which occurred 3 times in the last 2 weeks. The patient had also suffered from weakness of the right limb for the past 7 months, which had been getting worse with dysphagia, anorexia, and vomiting since 1 month ago. Initial head CT scan with contrast revealed a hypodense lesion in the left cerebral peduncle, but initial MRI showed a large mass in the pontine area that was suggestive of DIPG. At the initial MRI, no leptomeningeal dissemination nor subependymal spread was found (Fig. 1). She was treated with 35 fractions of 54 Gy whole-brain radiotherapy on the clinical target. An evaluative brain MRI after 6 months of radiation therapy showed a relatively irregular heterogeneous enhancing nodule with central calcification in the left pontine area with mild adjacent edema and intratumoral hemorrhage in SWI sequence, which are consistent with high-grade pontine glioma. The brain MRI also revealed a focal nodule in the left frontal cortex with perifocal edema, a nodule in the left temporal cortex with rim enhancement, a nodule in the dorsal side of the right posterior corpus callosum, multiple nodules in the anterior and posterior horn of bilateral periventricular region, and intraventricular nodule in the anterior

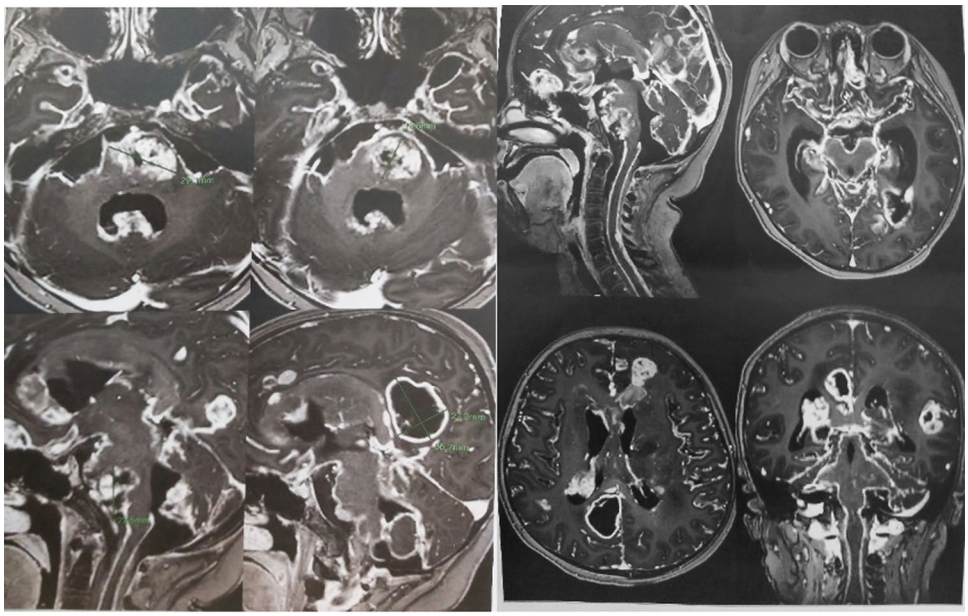

Fig. 1 Brain MRI at 6-month follow-up revealed multiple leptomeningeal and subependymal dissemination

horn of lateral ventricles, which are suggestive of leptomeningeal and subependymal seeding of the pontine glioma. The patient underwent supraorbital keyhole craniotomy for frontal nodule biopsy with a right eyebrow incision. The patient died due to cerebral edema and central herniation 9 days after the surgery. Histopathological examination revealed a cell-rich tumor with pleomorphic, hyperchromatic, and moderately cytoplasmic tumor cells consistent with anaplastic astrocytoma-not other specified.

Discussion

Prior to advanced neuroimaging modalities, initial autopsy-based studies of brainstem glioma revealed evidence of subarachnoid spread. A study conducted by Halperin et al. (2006) showed subarachnoid involvement when seen only in meninges adjacent to the tumor bed [5]. Leptomeningeal dissemination was previously reported in about 13% cases of DIPG [6]. Moreover, several literatures reported by Lu et al. [1], Gururangan et al. [3], Singh et al. [5], and Tinkle et al. [7] also reported the leptomeningeal spread of DIPG [1, 2, 5, 7]. Interestingly, with the increasing application of the molecular diagnostics and genetic profiling, leptomeningeal spread can be predicted with molecular alterations [7]. Unfortunately, the molecular diagnostic and genetic profiling examinations are still not routinely performed in Indonesia, so it is difficult to find the molecular alteration associated with the leptomeningeal spread of DIPG. Some literature suggested the establishment of surgical tract during biopsy might dispose DIPG to dissemination, but the pathogenesis of this secondary leptomeningeal spread remains poorly understood. However, one study proposed a possible mechanism of this leptomeningeal spread through cerebrospinal fluid seeding and direct migration through the white matter tract [2]. The tumor cells can escape during a surgical biopsy, either from cisternal spaces directly adjacent to the primary lesion or through migration from the cisternal spaces directly adjacent to the tumor bed [1].

A study reported that the patterns of metastasis of DIPG occurred mostly in the leptomeninges of the brain and/or spinal cord or the subependymal regions of the frontal and occipital horns of the lateral ventricles, which is consistent with our study [1, 3]. The molecular mechanisms underlying glioma dissemination throughout the nervous system had been thoroughly described; glioma cells quickly migrate along blood vessels, extracellular matrix (ECM), and myelinated fibers, most notably to reach leptomeningeal and subependymal regions. Cellular transit to distant sites requires the active coordination of ECM adhesion molecules (cadherins, NCAM, ICAM, selectins, and integrins) and proteinases (including matrix metalloproteinases and serine proteinases) [3].

More often than not, leptomeningeal metastases would be expected to cause a communicating hydrocephalus with progressive ventriculomegaly and obliteration of the subarachnoid spaces over the surface of the brain, with the patient eventually dying. Another set of pathological factors must be present in order for an external hydrocephalus to develop. Due to the presence of subependymal tumor spread in the walls of the lateral ventricles, the lack of ventricular enlargement in this case was most likely due to a relative loss of compliance in the ventricular walls. The presence of multiple subependymal metastatic tumor deposits was clearly demonstrated by magnetic resonance imaging (Fig. 1), which was performed late in the clinical course despite the

absence of pathological confirmation for this hypothesis [7, 8].

Leptomeningeal spread was previously documented in 4–33% of patients in pre-MRI investigations, but subsequent studies using brain MRI scans during follow-up showed leptomeningeal spread in 2–67% of patients. Sethi et al. [9] discovered that only four of nine patients had symptomatic leptomeningeal dissemination [9]. In an autopsy investigation of 40 patients with brainstem glioma, 13 (33%) patients had leptomeningeal spreading while 18 (45%) patients had supratentorial dissemination. Additionally, the study discovered that leptomeningeal spread occurred within 1 month of local progression in roughly 30% (5 of 18) of patients, while meningeal spread almost invariably occurred concurrently with local progression [5]. These two studies should increase the awareness regarding the potential leptomeningeal spread in brainstem gliomas, and given the substantial incidence of leptomeningeal dissemination in progression, a total neuraxis MRI surveillance and CSF analysis at presentation are necessary to be performed in DIPG patients [2, 9].

Tissue biopsy from the brain tumor lesion is required for proper diagnosis and appropriate treatment. In our case, a tissue biopsy was performed to obtain the histopathological examination, but due to major complication risk caused by standard craniotomy, a minimally invasive craniotomy approach was considered as the main strategy to obtain the tissue sample for the biopsy. The supraorbital keyhole approach used for frontal nodule biopsy in our case was choosen because this approach gives satisfactory access to anterior and middle skull base lesions, including sellar, suprasellar, and parasellar regions [10]. The primary goal of the keyhole approach is to minimize craniotomy-related trauma and to maximize intracranial exposure without jeopardizing the safety or effectiveness of surgical treatment. Numerous neurosurgeons have reported the following advantages of the supraorbital keyhole approach: (i) A small skin incision on the brow ensures a good cosmetic result; (ii) less brain tissue exposure; (iii) shorter operation time and less use of general anesthetics; (iv) rapid recovery following the operation; (v) preservation of the superficial temporal artery and frontal branch of the facial nerve; (vi) fewer incision complications; (vii) shorter hospital stay and lower hospital costs [11, 12].

Conclusion

Leptomeningeal and subependymal dissemination of DIPG are uncommon and recent studies show it can occur along with local progression. We recommend that all DIPG patients undergo total spine and brain MRI scans at the time of initial presentation and at regular intervals during follow-up to provide a better approach in the treament for patients with DIPG.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00381-022-05482-y.

Declarations

Conflict of interest The authors declare no competing interests.

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