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Case report

Embryonal brain tumor with unknown primary lesion and massive cerebrospinal fluid dissemination: A case report

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ABSTRACT

The *2007 World Health Organization Classification of Tumors of the Central Nervous System* (CNS) categorized embryonal tumors of the CNS into three classes: medulloblastoma, CNS primitive neuroectodermal tumor, and atypical teratoid/rhabdoid tumor. Due to the lack of specific histological features, it was sometimes difficult to accurately differentiate CNS embryonal tumors pathologically.

Here, we report a case of a young man, who presented with headache. Gadolinium-enhanced magnetic resonance imaging demonstrated massive lesions in the cerebrospinal fluid space, which strongly suggested leptomeningeal dissemination of a brain tumor. The histology showed the tumor comprised densely packed, small cells with scant cytoplasm. Immunoreactivities were positive for synaptophysin and chromogranin A, and negative for glial fibrillary acidic protein, S-100, EMA, and CD20. Because the tumors were located in multiple sites and most of them were within the cerebrospinal fluid space, the primary lesion could not be determined. We diagnosed this case as 'CNS primitive neuroectodermal tumor' by the patient age and predominantly supratentorial distribution of the lesions. After the induction therapy, WHO published its updated classification in 2016. Considering the possibility that the diagnosis is medulloblastoma, we performed additional immunohistochemical analyses, and diagnosed Group 3 medulloblastoma because of the expression of natriuretic peptide receptor 3.

1. Introduction

According to the *2007 WHO Classification of Tumors of the Central Nervous System* (WHO 2007), embryonal tumor of the central nervous system (CNS) comprised medulloblastoma, CNS primitive neuroectodermal tumor (PNET), and atypical teratoid rhabdoid tumor [1]. In 2016, the 4th edition of the *WHO Classification of Tumors of the Central Nervous System* was updated (WHO 2016), representing a major revision from WHO 2007 classification, especially in the group of embryonal tumors [2]. Embryonal tumors of the CNS are now broadly divided into "medulloblastoma" and "other embryonal tumors", and CNS PNET was removed from the diagnostic list.

In this case, the initial treatment finished before the publication of WHO 2016. The histology of this tumor implied embryonal brain tumor or pineoblastoma; however, careful consideration was needed to differentiate medulloblastoma, CNS PNET, and pineoblastoma for the diagnosis because the tumor location was mostly limited to the cerebrospinal fluid (CSF) space and the primary lesion could not be determined.

2. Clinical summary

A 23-year-old man had suffered from headache for 2 months. Gadolinium (Gd)-enhanced T1-weighted MRI of the brain showed multiple lesions in the frontal horn of the bilateral lateral ventricles, third and fourth ventricles, and bilateral cerebellomedullary fissures, suggesting CSF tumor spread (Fig. 1A–D). Gd-enhanced spinal MRI also showed widespread leptomeningeal tumor dissemination at the whole spinal cord (Fig. 1E).

The patient underwent an open biopsy with the use of a tubular retractor, and the tumor tissues were taken (Fig. 1F). The tumor showed pale fluorescence from 5-aminolevulinic acid (Fig. 1G, H). The initial diagnosis of this tumor was CNS PNET due to the predominant supratentorial distribution of the tumors, and the patient received chemoradiotherapy postoperatively. We

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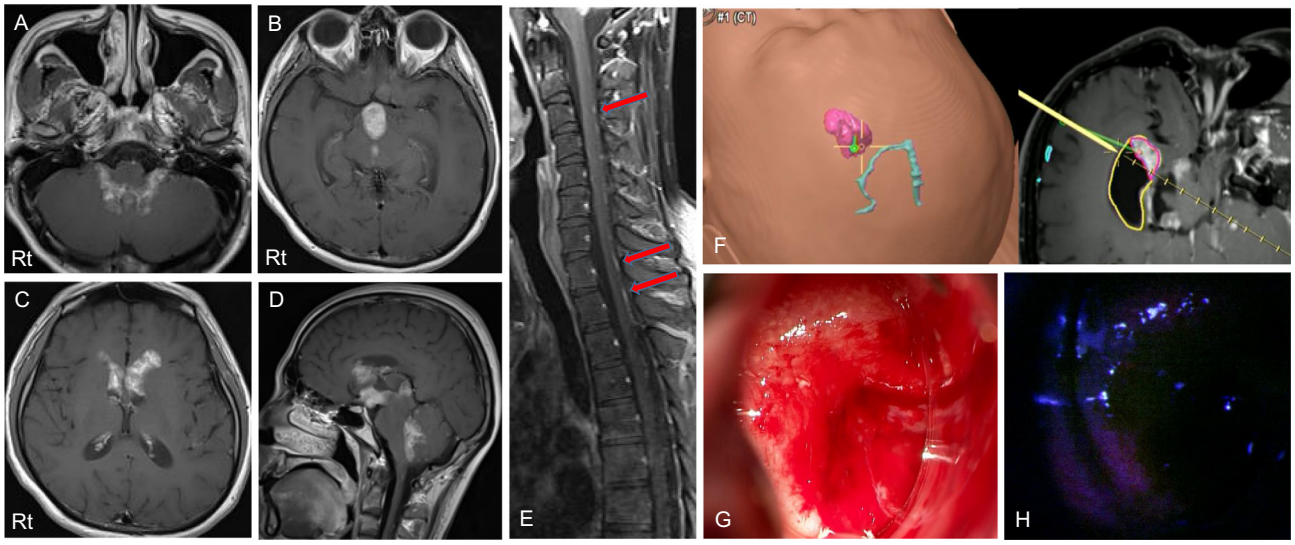

Fig. 1. MRI gadolinium-enhanced T1 weighted images of the brain (A-D) showing massively disseminated tumors. MRI gadolinium-enhanced T1-weighted images of the spine (E). Navigation-based planning to obtain tumor tissues from the frontal horn of the left lateral ventricle (F). Intraoperative findings showing weak 5-aminolevulinic acid-induced fluorescence (G, H).

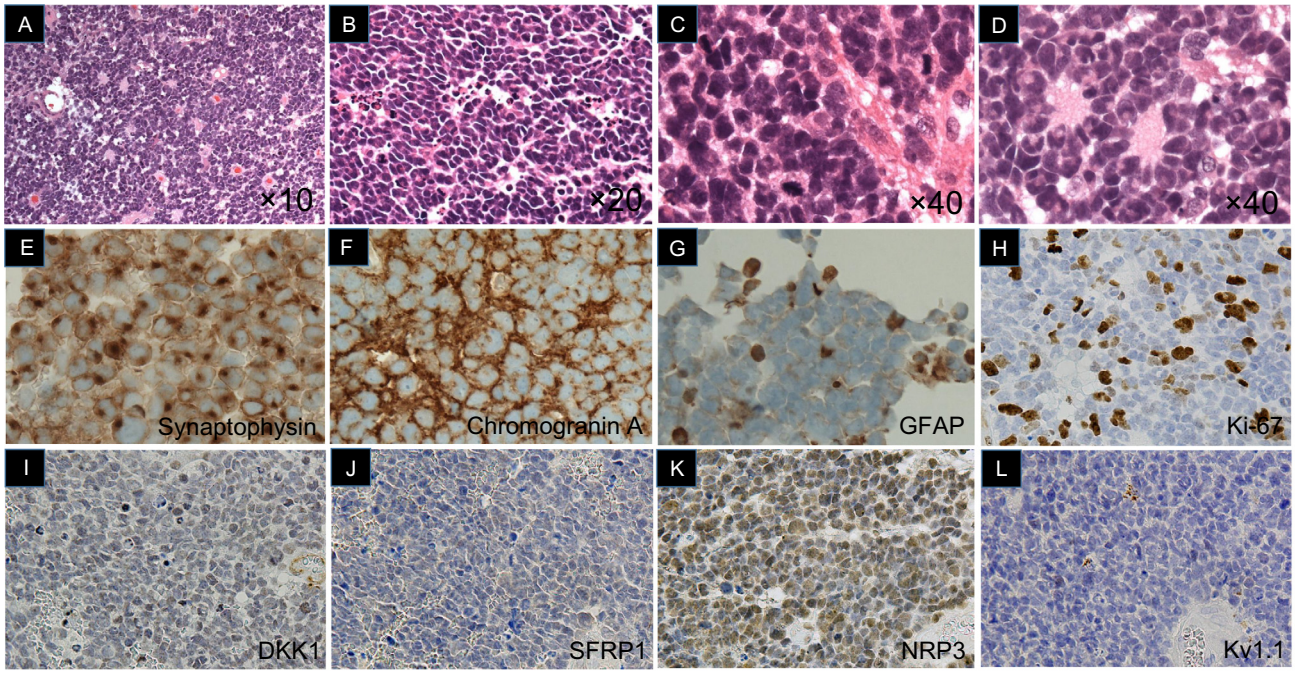

Fig. 2. Hematoxylin and eosin stained section (A, B). Original magnification ×100 (A), ×200 (B). Mitotic figures and Homer-Wright rosettes (C, D). Original magnification ×400. Immunohistochemical stains; synaptophysin (E), chromogranin A (F), glial fibrillary acidic protein (G), Ki-67 (H), DKK1 (I), SFRP1 (J), NRP3 (K), and Kv1 (L). Original magnification ×40.

prescribed ifosfamide, cisplatin, and etoposide (ICE chemotherapy). The first two courses of a total of six courses of ICE chemotherapy were concomitant with radiotherapy for the total dose of 45 Gy and 36 Gy for the whole brain and spine, respectively. During the following 2 years, no recurrence of the tumor has been demonstrated on MR images (Fig. 3).

3. Pathologic findings

Histologic examination revealed that the tumor tissues comprised sheets of densely packed cells with a high nuclear to cytoplasm ratio. Rosette formation and mitotic activity were also observed (Fig. 2A–D). Immunohistochemical study revealed diffuse positivity for synaptophysin and chromogranin A and focal positivity for glial fibrillary acidic protein (Fig. 2E–G). The tumor cells were immunonegative for S-100, EMA, CD3, CD99, and CD20 (data not shown). Ki-67 labeling index was 50% (Fig. 2H). We had diagnosed this case as 'PNET', though there is no histologic distinction between PNET and medulloblastoma.

After WHO 2016 was published, we considered the possibility of 'medulloblastoma' as a diagnosis. Because the immunohistochemistries for Dickkopf1 (DKK1), secreted frizzled-related protein 1 (SFRP1), natriuretic peptide receptor 3 (NRP3), and potassium

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