Neuroradiology

Communicating hydrocephalus and coexisting nonenhancing tumor: An ominous sign for patients with neurofibromatosis type 1?

Ryo Miyahara MD\textsuperscript{a}, Satoshi Tsutsumi MD\textsuperscript{a,}\textsuperscript{*}, Satoshi Adachi MD\textsuperscript{b}, Hisato Ishii MD\textsuperscript{a}, Akihide Kondo MD\textsuperscript{b}, Yukimasa Yasumoto MD\textsuperscript{a}

\textsuperscript{a}Department of Neurological Surgery, Juntendo University Urayasu Hospital, 2-1-1 Tomioka, Urayasu, Chiba, 279-0021, Japan
\textsuperscript{b}Department of Neurological Surgery, Juntendo University School of Medicine, Tokyo, Japan

ARTICLE INFO

Article history:
Received 22 January 2018
Accepted 24 March 2018
Available online

Keywords:
Communicating hydrocephalus
Nonenhancing pontine tumor
Leptomeningeal GBM
Neurofibromatosis type 1

ABSTRACT

A 26-year-old woman with familial neurofibromatosis type 1 sustained headache that worsened for 1 month. Neuroimaging revealed a mild ventriculomegaly and nonenhancing lesion in the pons. In spite of repeated cerebrospinal fluid examinations and magnetic resonance imaging, the etiology was not determined. The affected pons markedly enlarged in the following 2 months, with extensive leptomeningeal dissemination. Biopsy through hemilaminectomy of the T9 was diagnosed as glioblastoma multiforme. Prompt histologic examination should be performed when patients with familial neurofibromatosis type 1 manifest communicating hydrocephalus coexistent with a nonenhancing tumor.

© 2018 the Authors. Published by Elsevier Inc. under copyright license from the University of Washington. This is an open access article under the CC BY -NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Glioblastoma multiforme (GBM) is one of the most challenging malignancies to treat, with a 5-year survival rate of 5% [1,2]. It infrequently presents leptomeningeal dissemination as a secondary manifestation [3–5]. In extremely rare instances, it presents with primary leptomeningeal GBM [6,7]. Patients with neurofibromatosis type 1 (NF1) are documented as predisposing to GBM and leptomeningeal gliomatosis [8,9]. Hydrocephalus in these patients is commonly obstructive around the aqueduct [10]. Here we present a young adult with NF1 who sustained communicating hydrocephalus and nonenhancing pontine tumor and was eventually diagnosed with GBM.

Case presentation

A 26-year-old woman with familial NF1 sustained headache that worsened for 1 month. Central nervous system tumors...
had not been identified in her. At presentation, the patient showed right abducens nerve palsy but did not show other clinical symptoms including meningeal irritation. Cerebral magnetic resonance imaging (MRI) revealed a mild tetraventriculomegaly with patent aqueduct, linear enhancement along the ventral medulla, and a coexisting nonenhancing mass in the pons (Fig. 1A–C). Spinal MRI found a small nodular lesion between the T8 and T9 levels on the dorsal surface of the cord (Fig. 1D–F). At the time, contrast examination was not performed for an unknown reason. Lumbar cerebrospinal fluid (CSF) tap confirmed a markedly elevated intracranial pressure of 65 cmH2O. The cell count of CSF was 11 per microliter, whereas the protein and glucose levels were 400 mg/dL and 50 mg/dL, respectively. CSF cytology identified only a few lymphocytes with atypia.

In spite of repetitive CSF examinations and MRIs, the etiology was not determined. However, MRI performed 2 months later revealed an enlargement of the pons (Fig. 2A–C) and extensive leptomeningeal dissemination over the cerebrospinal axis (Fig. 2C–F). Biopsy through a hemilaminectomy of the T9 identified a subdural tumor that was grayish in color, elastic hard, and moderately vascular. Microscopically, the tumor comprised highly atypical cells with prominent pleomorphism (Fig. 3). Immunohistochemically, the tumor cells were diffusely positive for glial fibrillary acidic protein. The MIB-1 index was 30%. O6-methylguanine-DNA methyltransferase promoter methylation was present, whereas mutations in isocitrate dehydrogenase 1 and isocitrate dehydrogenase 2 were not identified. These were consistent with GBM. The patient underwent chemoradiation therapy postoperatively.

Discussion

Based on the clinical and pathologic findings, the present case was thought as leptomeningeal GBM sustaining communicating hydrocephalus and nonenhancing pontine tumor. Such nonenhancing parenchymal tumors are a rare entity, charac-
terized by faster progression than common low-grade gliomas and formidable outcome [11,12]. In our case, the affected pons rapidly expanded for 2 months. In the present case, leptomeningeal dissemination and a nodular lesion on the thoracic cord rapidly spread as enhancing tumors. In contrast, the pontine tumor was consistently nonenhancing. Given that the appearance on neuroimaging and the mode of progression were quite different between these extrinsic and intrinsic tumors, they seemed to be independent with each other.

Even low-grade gliomas can manifest leptomeningeal dissemination [13]. Furthermore, the arachnoids in patients with NF1 may be abnormally thickened to disturb CSF flows that cause a misleading appearance on neuroimaging, which does not reflect the actual intracranial pressure [14]. Therefore, histologic diagnosis should be made as early as possible when patients with NF1 simultaneously sustain communicating hydrocephalus and nonenhancing parenchymal tumor.

Fig. 2 - Axial T1- (A) and T2-weighted images, (B) postcontrast sagittal T1-weighted image of the brain (C), and postcontrast sagittal T1-weighted images of the spine (D-F) after 2 months showing extensive leptomeningeal dissemination and enlargement of the pons (A arrow). Spinal dissemination is thickest between the T8 and T9 levels (D arrow).

Fig. 3 - Histologic appearance of the tumor showing highly atypical cells with prominent pleomorphism. Hematoxylin and eosin stain, ×200.
Conclusion

Histologic diagnosis should be made as early as possible when patients with NF1 simultaneously manifest communicating hydrocephalus and nonenhancing parenchymal tumor.

REFERENCES

[1] Alexander VM, Cloughesy TF. Adult glioblastoma. J Clin Oncol 2017;35:2402–9.
[2] Ostrom QT, Gittleman H, Wu J, Kromer C, Wolinsky Y, Kruchko C, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2009-2013. Neuro Oncol 2016;18:v1–75.
[3] Lawton CD, Nagasawa DT, Yang I, Fessler RG, Smith ZA. Leptomeningeal spinal metastases from glioblastoma multiforme: treatment and management of an uncommon manifestation of disease. J Neurosurg Spine 2012;17:438–48.
[4] Maria BL, Cafferty LL, Singer HS, Epstein JI, Carson BS. Diffuse leptomeningeal seeding from a malignant spinal cord astrocytoma in a child with neurofibromatosis. J Neurooncol 1986;4:159–63.
[5] Wheen LC, Anderson NE, Baker PC, Singh VK, Synek BJ. Leptomeningeal infiltration as the presenting manifestation of a malignant glioma. J Clin Neurosci 2006;13:298–301.
[6] Bathla G, Gupta S, Moritani T. Primary leptomeningeal glioblastoma with systemic metastases-case report and review of literature. Clin Imaging 2015;39:672–6.
[7] King JA, Halliday W, Drake JM. High-grade primary diffuse leptomeningeal gliomatosis in a child with neurofibromatosis Type 1. J Clin Oncol Pediatr 2008;2:402–5.
[8] Arkadir D, Felling Y, Gomori MJ, Linetsky E, Shalom E, Lossos A. Aggressive leptomeningeal gliomatosis in neurofibromatosis type 1. J Clin Oncol 2012;30:e269–70.
[9] Huttner AJ, Kieran MW, Yao X, Cruz L, Ladner J, Quayle K, et al. Clinicopathologic study of glioblastoma in children with neurofibromatosis type 1. Pediatr Blood Cancer 2010;54:890–6.
[10] Roth J, Ber R, Wisoff JH, Hidalgo ET, Limbrick DD, Berger DS, et al. Endoscopic third ventriculostomy in patients with neurofibromatosis type I: A multicenter international experience. World Neurosurg 2017;107:623–9.
[11] Lasocki A, Gaillard F, Tacey MA, Drummond KJ, Stuckey SL. The incidence and significance of multicentric noncontrast-enhancing lesions distant from a histologically-proven glioblastoma. J Neurooncol 2016;129:471–8.
[12] Pope WB, Sayre J, Perlina A, Villablanca JP, Mischel PS, Cloughesy TF. MR imaging correlates of survival in patients with high-grade gliomas. AJNR Am J Neuroradiol 2005;26:2466–74.
[13] Perilongo G, Garrè ML, Giangaspero F. Low-grade gliomas and leptomeningeal dissemination: a poorly understood phenomenon. Childs Nerv Syst 2003;19:197–203.
[14] Kang YS, Park EK, Kim YO, Kim JS, Kim DS, Thomale UW, et al. Altered cerebrospinal fluid dynamics in neurofibromatosis type 1: severe arachnoid thickening in patients with neurofibromatosis type 1 may cause abnormal CSF dynamic. Childs Nerv Syst 2017;33:767–75.