

Intramedullary spinal glioblastoma metastasis from anaplastic astrocytoma of cerebellum: A case report and review of the literature

Keng-Liang Kuo^{1,2}, Ann-Shung Lieu¹, Feng-Ji Tsai^{1,2}, Yi-Ting Chen^{2,3}, Peir-In Liang³

Departments of ¹Neurosurgery and ³Pathology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, ²Department of Medicine, Graduate Institute of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

ABSTRACT

Cerebellar anaplastic astrocytoma is infrequently encountered even nowadays, and drop metastasis with progression into spinal glioblastoma is not reported in the English literature. We report a case of cerebellar anaplastic astrocytoma receiving operation and subsequent concurrent chemoradiotherapy. One year later, progressive weakness of both lower limbs and unsteady gait occurred. Spine magnetic resonance imaging showed cervical and thoracic spine intramedullary tumor. We then performed laminectomy and tumor biopsy. The histopathological report demonstrated primary spinal cord glioblastoma multiforme with positive glial fibrillary acidic protein, high MIB-1 labeling index and negative staining of isocitrate dehydrogenase-1 mutation. After reviewing the English literature to date, most metastatic spinal glioblastoma resulted from previous intracranial glioblastoma, and there are few studies mentioning spinal glioblastoma originating from intracranial low-grade gliomas. Over time, improvement in local control of the primary tumor has raised patient risk of the possibility of spinal metastasis, and clinical physicians should be aware of this aspect so that quicker diagnosis and management will be accomplished, even in patients with lower grade of intracranial gliomas.

Key words: Anaplastic astrocytoma, immunohistochemistry, isocitrate dehydrogenase, spinal glioblastoma

Introduction

Glioblastoma is the most notorious intracranial tumor in adults,^[1] and spinal cord glioblastoma is a rare entity with dismal outcome.^[2] Anaplastic astrocytoma also pertains to aggressive behavior and the potential of malignant transformation into glioblastoma^[1] with 23% 5-year survival rate.^[3] Primary or secondary glioblastoma is diagnosed pending on the clinical course of preexisting, less-aggressive astrocytoma.^[4] Through the improvement in imaging and treatment strategy, life expectancy has increased, and adequate local control of primary intracranial tumor has been achieved more commonly. Spinal glioblastoma is infrequently

encountered, and metastasis from intracranial lesions is mostly thought to result from previous intracranial glioblastoma via the cerebrospinal fluid (CSF) seeding pathway.^[5] We report a rare case of metastatic spinal glioblastoma from previous cerebellar anaplastic astrocytoma, the manifestation of the disease, and further immunohistochemistry (IHC) study of the patient.

Case Report

A 27-year-old male patient without systemic disease came to our clinic owing to progressive unsteady gait. Magnetic resonance imaging (MRI) showed cerebellar mass lesion in the 4th ventricle and obstructive hydrocephalus [Figure 1a]. After brain tumor removal, pathological diagnosis showed anaplastic astrocytoma. After concurrent chemoradiotherapy (CCRT), he was followed up in our neurosurgical clinic. One year later, he returned owing to progressive unsteady gait, urine and stool incontinence and progressive lower limbs weakness, with numbness and paresthesia sensation below the T7-T8 levels. Cervical to thoracic spine and lumbar MRI showed diffusely infiltrating intradural intramedullary tumor over the level of C5-6, T2-6, T9-10, and L1-2 levels with leptomeningeal metastasis [Figure 1c]. After decompressive laminectomy of T2-6, T9-10, and L1-2 level, we incised the dura and the arachnoid membrane, and an intradural intramedullary tumor was seen without infiltration to the

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Address for correspondence:

Dr. Ann-Shung Lieu, Department of Neurosurgical, No. 100, Tzyou 1st Road, Kaohsiung 807, Taiwan.
E-mail: geet810224@yahoo.com.tw

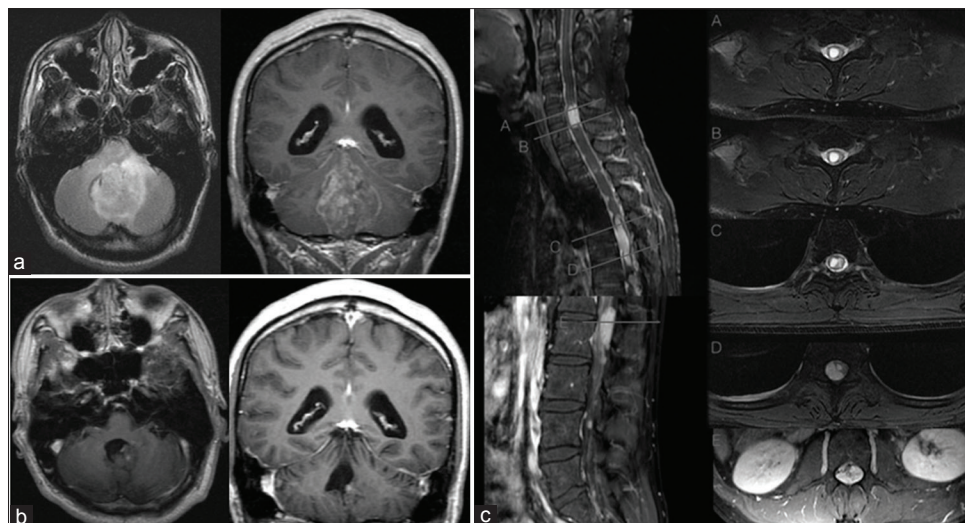


Figure 1: (a) Axial T2-fluid-attenuated inversion recovery image and contrast-enhanced coronal T1-weighted image, (b) Contrast-enhanced axial and coronal T1-weighted image, (c) Contrast-enhanced sagittal T1-weighted image, intramedullary tumor seen between C5 and C7 levels, T4 to T6 levels, and L1-2 levels. (Section A: C5-6; Section B: C6-7; Section C: T4-5; Section D: T6-7; Section E: L1-2 level)

dura. The tumor is centrally located within the spinal cord, and we approached the tumor from the midline posteriorly. Spinal tumor biopsy of both thoracic and lumbar part was then performed, and the patient remained paraplegic with incontinence postoperatively. Spinal glioblastoma was the final diagnosis, and from both thoracic and the lumbar parts, showed typical features of glioblastoma inclusive of nuclear atypia, high mitotic index, necrosis and microvascular proliferation. IHC study showed positive glial fibrillary acidic protein (GFAP), high Ki-67 labeling index (30%), positive tumor protein p53 (TP53) mutation and negative finding of isocitrate dehydrogenase-1 (IDH-1), compared to the brain anaplastic astrocytoma [Figures 2 and 3].

Aside from previous radiotherapy (5940 cGy/33 fractions) of the intracranial lesion, the patient then received radiotherapy over the spine (3750 cGy/15 fractions) and further chemotherapy, with the regimens of carboplatin, vincristine and bevacizumab.

Discussion

In the spinal cord tumors, astrocytoma accounts for 6–8%, and one-third of these tumors are high-grade. Spinal cord glioblastomas account for only 1–3% of all spinal cord tumors and 1–5% of all glioblastomas.^[6] This may be explained by the nature of scarce proportion of neuroglia cells in the spinal cord. Otherwise, dismal outcome is also noted in spinal cord glioblastoma with mean survival from 6 to 18 months.^[2]

Glioblastoma, categorized by the clinical course, can be diagnosed as primary and secondary glioblastomas. The definition relies on whether preexisting, less-aggressive astrocytoma is present. Through improvement and understanding on a molecular basis, TP53, epidermal growth

factor receptor (EGFR), phosphatase tensin homolog, and the marker of IDH-1, there are still limitations in differentiating primary or secondary glioblastoma.^[4] For our patient, according to his history of previous cerebellar anaplastic astrocytoma and subsequent spinal cord glioblastoma, secondary glioblastoma was impressed. Followed up brain MRI, 1-year later post-CCRT showed cerebellar tumor shrinkage but with leptomeningeal enhancement [Figure 1b]. IHC study of anaplastic astrocytoma showed positive GFAP, EGFR, and p53 with negative expression of IDH-1; and the same finding for spinal glioblastoma except for Ki-67 expression [Figures 2 and 3]. Otherwise, there was no significant difference of the IHC staining between the lumbar and thoracic glioblastoma. This finding implies that cerebellar anaplastic astrocytoma and spinal glioblastoma arise from the same origin with different proliferation potential, and secondary glioblastoma can be confirmed with assurance.

According to the literature, most secondary glioblastomas come from previous intracranial glioblastomas. Intracranial anaplastic astrocytoma with malignant transformation into glioblastoma is less frequent and mostly locally recurrent or along the white matter tract. Drop metastasis is a possible mechanism of secondary spinal glioblastoma through the CSF pathway.^[5] For our patient with previous cerebellar anaplastic astrocytoma, the patient suffered subsequent spinal glioblastoma rather than in the intracranial region, which implies that one should not ignore the possibility of spinal lesion if the patient expresses contributory discomfort. Otherwise, since the progress of health care and treatment strategies, patient life expectancy has increased, and the possibility of spinal secondary glioblastoma increased, even though the primary intracranial lesion might not present as a glioblastoma. Early diagnosis and adequate management for

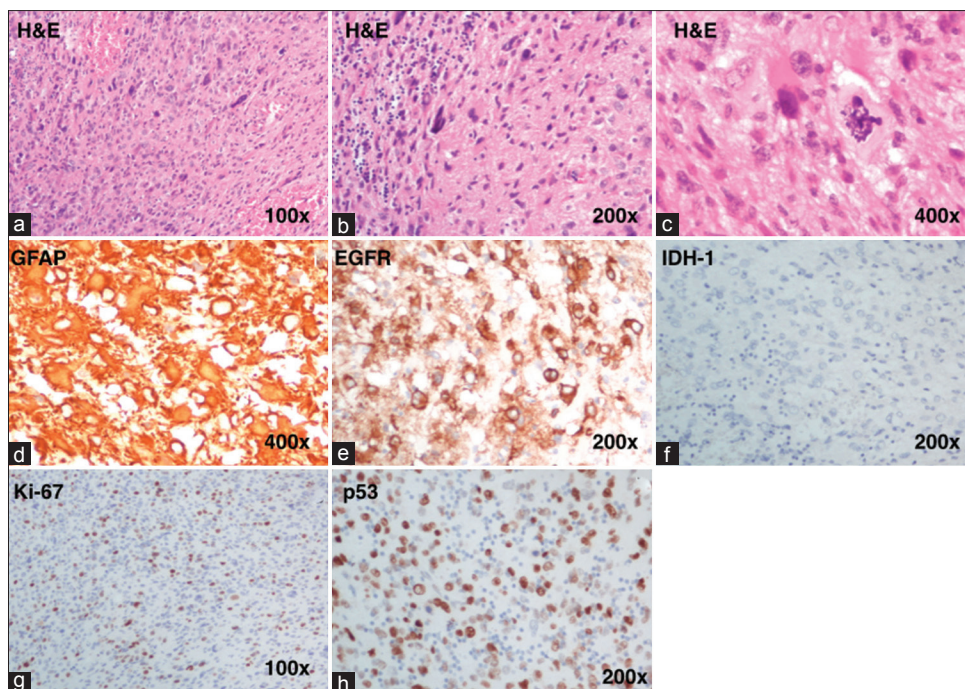


Figure 2: Permanent pathology of cerebellar anaplastic astrocytoma. (a and b) The low-power image displays hypercellularity of neoplastic cells, (c) The high-power image shows tumor cells featuring hyperchromatic, nuclear pleomorphism and increased mitotic activity. Atypical mitosis is also identified, (d-h) These tumor cells are immunoreactive for glial fibrillary acidic protein, epidermal growth factor receptor and p53 but negative for isocitrate dehydrogenase-1 and synaptophysin. The Ki-67 labeling index is about 5–10%

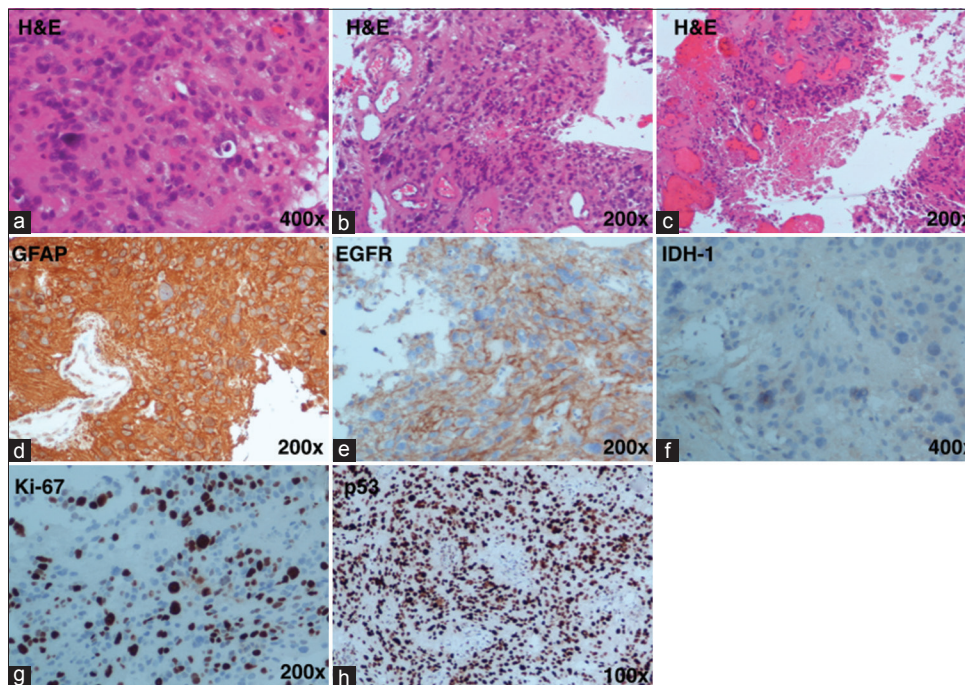


Figure 3: Permanent pathology of spinal cord glioblastoma, (a) tumor cells with increased cellularity and frequent mitoses, (b and c) Florid proliferation of blood vessels and tumor necrosis, (d–f) Tumor cells are immunoreactive to glial fibrillary acidic protein, epidermal growth factor receptor, but negative to isocitrate dehydrogenase-1, (g and h) The Ki-67 labeling index is high, up to 30% focally. The p53 immunostain is positive

patients with spinal metastasis ensure better outcome and quality of life, and clinical physicians should not ignore the possibility of spinal secondary glioblastoma, since secondary

glioblastoma will occur in patients with intracranial primary glioblastoma as well as in intracranial anaplastic astrocytoma, like our case of cerebellar anaplastic astrocytoma.

Conclusions

We share a case of secondary glioblastoma from cerebellar anaplastic astrocytoma. Since the progress of treatment strategies and management, clinical physicians should not ignore the significance that secondary glioblastoma might ensue even in patients with lower grade gliomas.

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