Int J Clin Exp Med 2016;9(8):16883-16886
www.ijcem.com /ISSN:1940-5901/IJCEM0025838

Case Report

Glioma progress and extracranial systemic multiple metastasis: a case report

Bingxi Lei*, Wei Xiang*, Meng Yu, Lei Yu, Songtao Qi

*Department of Neurosurgery, Nanfang Hospital, Southern Medical University, Guangzhou, China. *Equal contributors.*

Received February 11, 2016; Accepted June 4, 2016; Epub August 15, 2016; Published August 30, 2016

Abstract: Glioma metastasis outside the central nervous system is rare, and the pathogenesis is not clear. We report a case of glioma progression and extracranial metastasis in a 35-year old man who suffered from glioma and received 2 operations in 16 months because of recurrence. Then, in less than 1 year, PET-CT scan showed multiple bone metastases. Damage in the dura and skull, extracranial invision adjacent to the intracranial lesion and subsequently blood spreading may be the mechanism.

Keywords: Glioma, extracranial metastasis

Background

Glioma is the chiefly primary intracranial tumor. Even though the therapeutic method has improved a lot, most of the patients died of either recurrence or progression inevitably. Progression from low level to high level is the main method of glioma malignant change. Intracranial recurrence and metastasis in the central nervous system are the main causes of death in those diseases. Glioma metastasis outside the central nervous system is rare, and the pathogenesis is unclear. Now we report a case of glioma progression and metastasis outside the central nervous system.

Case report

Patient, male, 35-year old when firstly diagnosed, suffered from repeated headaches for six months, underwent surgical resection in January 2011 after head MRI examination revealed glioma in the right temporal lobe (**Figure 1A1**, **1A2**). Subsequently postoperative MRI shows complete resection of the tumor (**Figure 1B1**, **1B2**), and postoperative pathological examination revealed fat cell type astrocytoma, WHO II grade (**Figure 3A**). Consecutively, the patient underwent synchronous radiation (27 times) and chemotherapy (Temozolamide). In May 2012, the patient underwent the second operation because of recurrence revealed by head MRI (**Figure 1C1**, **1C2**). Afterwards pathological test suggested glioma progression with glioblastoma, WHO IV (**Figure 3B**). Chemotherapy (Temozolamide) and intravenous application of Beacizumab ensued. In March 2013, head MRI examination showed another relapse, with extracranial extension to the right musculus pterygoideus and the maxiliary bone and invasion of the sphenoid sinus and right orbital cavity (**Figure 1E1**, **1E2**). Patient received a local radiotherapy (DT40Gy/20F) in relapse lesions and oral Temozolamide chemotherapy (0.1 g/day) at the same period. During the radiotherapy period, a mass was discovered under the right zygomatic arch (**Figure 1F1**, **1F2**). In April 2013, a mass biopsy was performed under the guide of CT scan, and then was diagnosed with multiform glioblastoma WHO IV (**Figure 3C**). He was then administrated with palliative radiotherapy (DT40Gy/20F) under the right zygomatic arch. Patient complained bone pain during radiotherapy. In June, PET-CT scan showed multiple bone metastases (**Figure 2**), therefore, patient received the first cycle of systematic chemotherapy (teniposide 100 mg and cisplatin 30 mg day 1-4). After chemotherapy, patient suffered from severe IV degree of bone marrow suppression, three lines decreased, and the combination of oral infec-

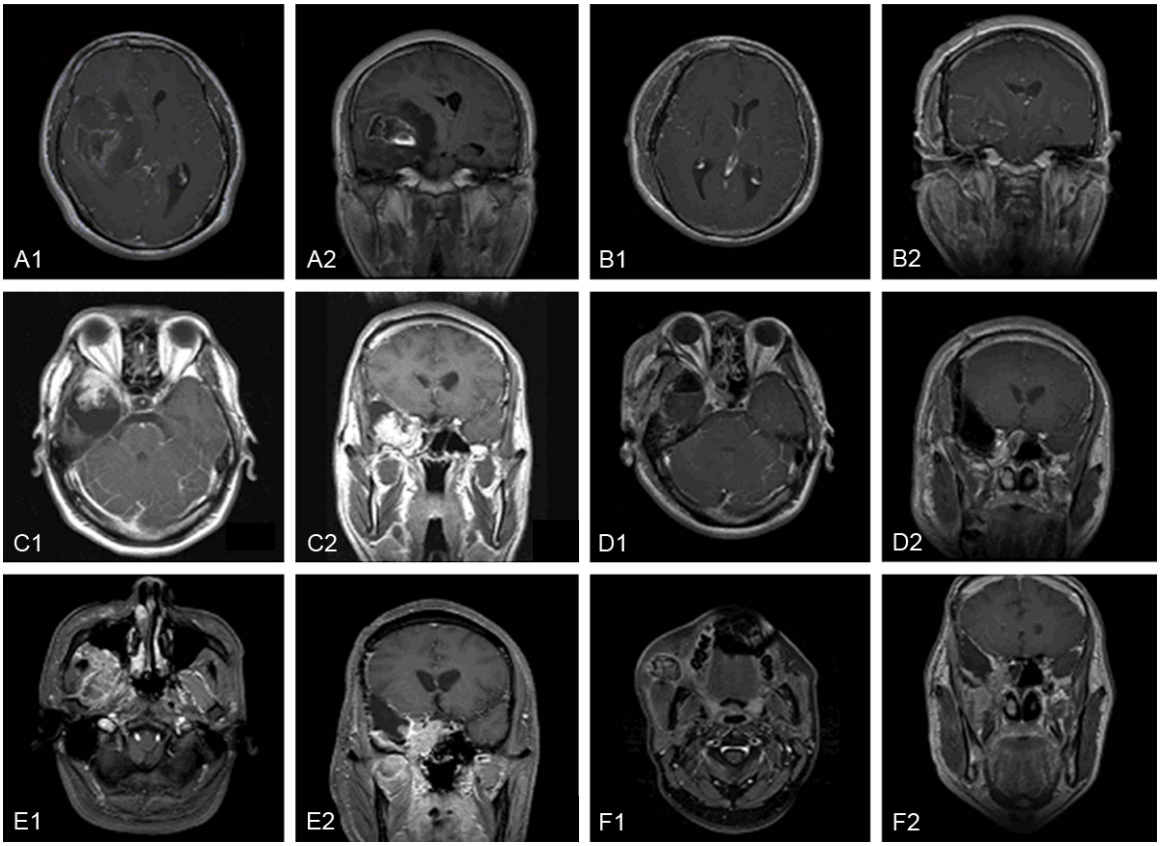

Figure 1. A1 and A2: MRI images before the first operation; tumor with bleeding located in the right temporal lobe. B1 and B2: MRI images after the first operation; tumor was completely resected and the ventricular was not entried. C1 and C2: MRI images before the second operation; heterogeneously enhancing lesion in the right temporal lobe revealed the tumor recurrence the first time in situ. D1 and D2: MRI images after the second operation; tumor was completely resected again. E1 and E2: Tumor recurrence the second time with extracranial extension to the right musculus pterygoideus and the maxiliary bone and invasion of the sphenoid sinus and right orbital cavity. F1 and F2: The extracranial tumor developed and involved right zygomatic arch.

tion, low serum albumin and electrolyte disorder.

Discussion

Glioma is the most commonly primary tumor in the central nervous system (CNS), and comprehensive treatments including surgical resection, radiotherapy and chemotherapy are the standard method nowadays. Unlike extracranial cancers, patients suffered from glioma usually died of intracranial hypertension and brain function failure due to local intracranial recurrence or intracranial metastasis and nerve damage, but it rarely metastasizes outside the CNS [1]. One explanation of the rarity of extracranial metastasis is that the blood-brain barrier and lack of a lymphatic drainage system in the CNS prevent glioma cells from infiltrating and metastasizing beyond the central nervous axis [2, 3]. Additionally, the short survival period of patients died of malignant glioma causes insufficient time to establish extracranial metastasis. However, with the improvement in survival duration and better neuro-imaging techniques, more and more attentions are paid to the extracranial metastasis of malignant glioma [4, 5].

The mechanisms of glioma extracranial metastasis are still not well known. Several reports of extracranial glioma metastases show correlations between such phenomenon and operations including aggressive surgical resection, biopsy, and ventriculoperitoneal shunting, which lead to tumor cells depositing into the blood system or to surgical damages in the dura and skull [3, 6]. Such operations provide opportunities for glioma cells vascular invasion and cerebrospinal fluid dissemination, thereby increas-

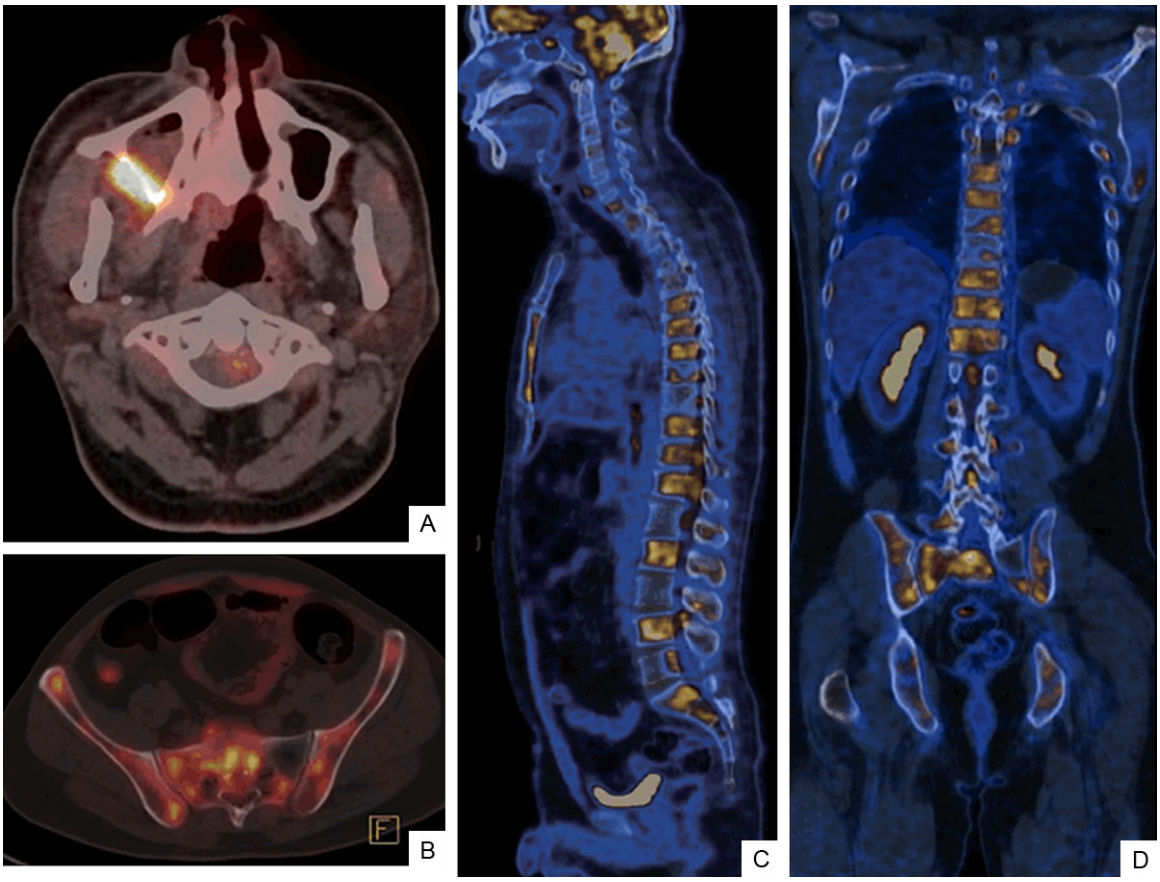

Figure 2. PET-CT images of multiple bone metastases. A: Lesions of the right maxillary sinus posterior wall. B: Lesions of the sacrum and bilateral iliac. C and D: System bone metastasis; Most of the whole body bone metabolism increased significantly.

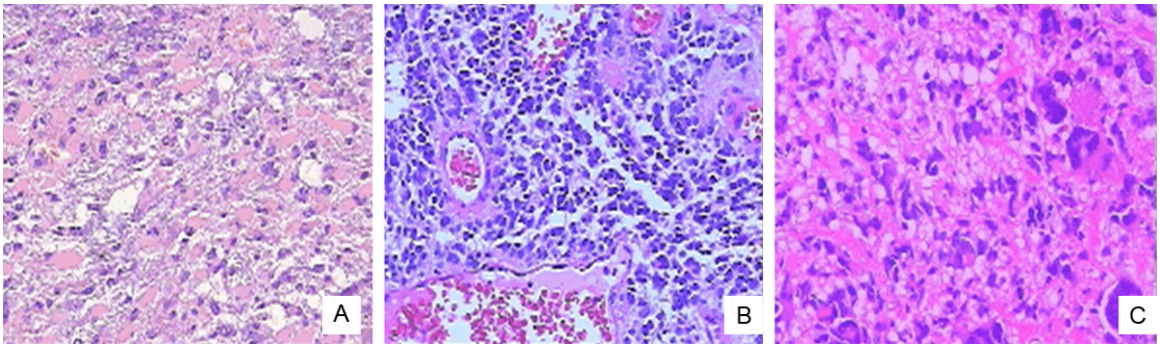

Figure 3. A: Pathological examination of the tumor for the first operation (H&E, 200×); gemistocytic astrocytoma, WHO grade II. The tumor cells scatter in distribution and have no heteromorphism and less caryocinesia. The tumor vasculature is inconspicuous. B: Pathological examination of the tumor for the second operation (hematoxylin and eosin staining, 200×); glioblastoma, WHO grade IV. Histologic examination reveals high cell density, polymorphism of the nuclei of the tumor cells, proliferated blood vessels and necrosis. C: Pathological examination of the tumor under the right zygomatic arch of the patient (H&E, 200×); glioblastoma, WHO grade IV. A number of tumor giant cell, polymorphism of the nuclei of the tumor cells.

ing the risk of systemic spread and extracranial tumor metastasis [8, 9]. However, Anzil [7] suggested that early hematogenous spread may be another mechanism based on the finding of more than 10% of all such extracranial metastasis occurred in the absence of prior surgical

intervention. He believed that aggressive operations are not prerequisites for extracranial metastasis of glioma. Another mechanism of extracranial glioma metastasis indicates the existence of circulating glioma cells in the blood system. Therefore, the fraction of glioma cells in the circulation may provide an opportunity for early detection and genetic analysis of intracranial glioma [10]. Park [11] considered that the metastatic potential of the GBM might be associated with P53 gene mutations and differential clone selection, which may provide some targets for glioma extracranial metastasis. For this case, the extracranial metastasis may arise from the operation or irradiation damage in the dura and skull, followed with extracranial invision adjacent to the intracranial tumor, and subsequently blood spreading.

Although extracranial metastasis of malignant glioma remains rare, neurosurgeons should realize how to perform a protective surgical treatment to reduce the possibility of extracranial metastasis as its adverse outcome. The total tumor resection or extended resection in necessity is the base of all treatment strategy, non-tumor resection outside the boundary is necessary, and the integrity of dura and skull should be affirmed in the operation. Additionally, exploring prospective detection means for the genetic and molecular feature of extracranial metastasis is an important subject for future study in the field of glioma.

Disclosure of conflict of interest

None.

Address correspondence to: Songtao Qi, Department of Neurosurgery, Nanfang Hospital, Southern Medical University, Guangzhou, China. E-mail: qisongtaonfyy@126.com

References

[1] Kalokhe G, Grimm SA, Chandler JP, Helenowski I, Rademaker A, Raizer JJ. Metastatic glioblastoma: case presentations and a review of the literature. J Neurooncol 2012; 107: 21-7.

[2] Santos AV, Saraiva PF, Santiago B. Extracranial metastasis of glioblastoma multiforme. Acta Med Port 2003; 16: 209-11.

[3] Figueroa P, Lupton JR, Remington T, Olding M, Jones RV, Sekhar LN, Sulica VI. Cutaneous metastasis from an intracranial glioblastoma multiforme. J Am Acad Dermatol 2002; 46: 297-300.

[4] Mirzayan MJ, Samii M, Petrich T, Börner AR, Knapp WH, Samii A. Detection of multiple extracranial metastases from glioblastoma multiforme by means of whole-body [18F] FDG-PET. Eur J Nucl Med Mol Imaging 2005; 32: 853.

[5] Piccirilli M, Brunetto GM, Rocchi G, Giangaspero F, Salvati M. Extra central nervous system metastases from cerebral glioblastoma multiforme in elderly patients. Clinico-pathological remarks on our series of seven cases and critical review of the literature. Tumori 2008; 94: 40-51.

[6] Wakabayashi T, Yoshida J, Kageyama N, Mutsuga N, Takeuchi Y. Extraneural metastasis of malignant glioma through a ventriculoperitoneal shunt: growth in peritoneal cavity as ascitic form. No Shinkei Geka 1985; 13: 547-52.

[7] Anzil AP. Glioblastoma multiforme with extracranial metastases in the absence of previous craniotomy. Case report. J Neurosurg 1970; 33: 88-94.

[8] Frank S, Kuhn SA, Brodhun M, Mueller U, Romeike B, Kosmehl H, Regenbrecht CR, Ewald C, Reichart R, Kalff R. Metastatic glioblastoma cells use common pathways via blood and lymphatic vessels. Neurol Neurochir Pol 2009; 43: 183-90.

[9] Thorsen F, Tysnes BB. Brain tumor cell invasion, anatomical and biological considerations. Anticancer Res 1997; 17: 4121-6.

[10] Adamczyk LA, Williams H, Frankow A, Ellis HP, Haynes HR, Perks C, Holly JM, Kurian KM. Current Understanding of Circulating Tumor Cells - Potential Value in Malignancies of the Central Nervous System. Front Neurol 2015; 6: 174.

[11] Park CC, Hartmann C, Folkerth R, Loeffler JS, Wen PY, Fine HA, Black PM, Shafman T, Louis DN. Systemic metastasis in glioblastoma may represent the emergence of neoplastic subclones. J Neuropathol Exp Neurol 2000; 59: 1044-50.