Case Report

Extracranial metastasis of anaplastic oligoastrocytoma: a case report and review of the literature

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Abstract: Glioblastoma multiforme (GBM) is the most common and aggressive primary intracranial tumor. The tumor metastases outside the CNS are rare, so therapeutic experience with these types of tumors is limited. We present a case of a 20-year-old female with a history of left temporal anaplastic oligoastrocytoma, who was found to have biopsy proven metastases to the lung. In April 2014, the patient presented with intermittent headache for 4 months. Physical examinations confirmed no obvious abnormalities. Computed tomography (CT) scan and magnetic resonance image (MRI) scan of the brain showed a large mass with ring-like enhancement in left temporal lobe. She underwent craniotomy to resect the intracranial tumor. The pathological investigation showed the lesion to be a classical anaplastic oligoastrocytoma with focal necrosis and a Ki-67 labeling index of 10-30%. After operation, the patient received radiotherapy and chemotherapy. Two years later, the patient readmitted due to chest discomfort. A chest X-ray and CT showed a mass in the right lung. The lesion was confirmed to be a metastatic malignant glioma via pulmonary bronchoscopy biopsy. In conclusion, as the life expectancy is gradually increasing for GBM patients with newer therapies, the incidence of extracranial metastases may increase and this rare phenomenon may become more common and clinically relevant.

Keywords: Oligoastrocytoma, extracranial metastasis, case report

Introduction

Glioblastoma multiforme (GBM) is the most aggressive brain tumor with poor prognosis; patients with GBM have a median survival time of about 14 months. The extracranial metastases of high grade gliomas rarely occur in less than 2.0%, although GBMs account for approximately two thirds of the neuroepithelial tumors that metastasize extracranially [1]. Several explanations for the rarity of extracranial GBM metastases are as shown: Firstly, there is insufficient time for glioblastoma cells to establish metastasis in extracranial organs because of extremely shortened survival of patients; Secondly, the unique blood-brain barrier, a thickened basement membrane of blood vessels, prevents hematogenous spread; In addition, the absence of a lymphatic system, the thickened dura mater, the lack of extracellular matrix, and the sparse connections between the subarachnoid space and extracranial lymphatic vessels, prevent lymphatic spread. Moreover, suppression of extracranial growth of glioblastoma cells by the immune system is also important [2]. Herein, we present a case of anaplastic oligoastrocytoma with lung metastasis. The potential pathogenetic mechanisms and their main routes of spread to extracranial sites are discussed.

Case report

In April 2014, a 20-year-old female with right-handed manual has presented with intermittent headache for 4 months. Her medical history and family history were non-contributory. Physical examinations confirmed no obvious abnormalities. Computed tomography (CT) scan and magnetic resonance image (MRI) scan showed a large mass with ring-like enhancement in left temporal lobe. Peritumoral edema
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was obvious. No other focal lesion was identified (Figure 1A and 1B). The results of preoperative investigations including standard blood tests and a chest X-ray were within normal limits. The left frontal temporal approach was performed to resect the intracranial tumor. During hospitalization the patient had not received any blood transfusion. The histopathology showed the lesion to be a classical anaplastic oligoastrocytoma with focal necrosis and a Ki-67 labeling index of 10-30% (Figure 1C). The tumor cells were immunopositive for glial fibrillary acid protein (GFAP). Following an uneventful postoperative recovery, the patient received a full course of radiotherapy and chemotherapy synchronously. Subsequently, a temozolomide chemotherapy for 6 courses was administrated. At that time, the patient’s initial symptoms had clinically resolved. But in April 2016, the patient complained of chest discomfort. A chest X-ray and CT showed a mass in the right lung. (Figure 2A). The lesion was confirmed to be a malignant neoplasm via pulmonary bronchoscopy biopsy. Immunohistochemical staining for glial revealed positive for GFAP (Figure 2B and 2C). Anaplastic oligoastrocytoma with metastasis the lung was suspected. The patient accepted the treatment of Vemurafenib and radiotherapy. In October 2016, cervical lymph nodes became enlargement. The patient rejected cervical lymph nodes biopsy. At present, the patient can take care of herself without headache or nameless aphasia. The brain MRI shows the postoperative-state of left temporal-lobe without signs of recurrence.

Figure 1. A. Computed tomography (CT) scans shows a large mass in left temporal lobe. Peritumoral edema was obvious (red arrows). B. Contrast-enhanced T1-weighted axial image shows a large mass with ring-like enhancement in the left temporal lobe (red arrows). C. H&E stained sections of the patient’s original brain surgery demonstrating a high grade glioma (×100).

Figure 2. (A) Contrast-enhanced computed tomography reveal a large irregular mass in the right middle lobe of lung and right hilus pulmonis (red arrows). (B) Pulmonary bronchoscopy biopsy demonstrate anaplastic oligoastrocytoma with metastasis the lung on hematoxylin and eosin (H&E) staining (magnification, ×40) and (C) nests of metastatic glioma on immunohistochemical staining for glial fibrillary acidic protein (GFAP) (magnification, ×40).
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Discussion

Malignant gliomas account for approximately two-thirds of all primary brain tumors in adults, and can be separated into four types-anaplastic astrocytoma (AA), anaplastic oligodendroglioma (AO), anaplastic oligoastrocytoma (AOA) and glioblastoma multiforme (GBM) -on the basis of histology [3-5]. AOA with necrosis (grade III) was described as GBMs with oligodendroglioma component (GBMO) (grade III) in the 2007 WHO classification of tumors in the central nervous system (CNS) [6]. But, according the 2016 WHO classification of tumors in the central nervous system (CNS), the pathology about this case was assigned NOS designations due to the absence of molecular testing. There are less than 2% of GBM present extracranial metastases, despite in 1926 when Bailey and Cushing stated that distant metastasis from primitive brain tumors do not exist [1].

Several patterns of intracranial tumor emigration outside have been reported, as follows: (i) Cerebrospinal Route: Oligodendrogliomas are prone to extracranial metastasis through cerebrospinal fluid (CSF). Onda et al. have suggested that lesser differentiated tumor cells and a lower rate of GFAP expression contribute to a higher tendency to spread into the CSF [7]. In addition, the migration of GBM cells may spread to the peritoneum or pleura via the movement of CSF through shunts. (ii) Hematogenous Pathway: The hypoxic and proliferative zone of glioblastoma result in angiogenesis-related breakdown of the blood-brain-barrier [8]. The operation destroys the natural defense system of CNS. Thus, tumor cells can directly migrate into the systemic circulation, arrest and adhere to a target organ site. (iii) Lymphatic metastasis: lymphatic in the nasal mucosa and dural lymphatics were associated with the subarachnoid space [9-13]. In 1912, It was demonstrated that the channel connect the subarachnoid space with lymphatic vessels in the nasal mucosa via the cribiform plate of the ethmoid bone in human. In the 1980s, Cserr et al. first documented the interstitial fluid from the brain drains to cervical lymph nodes [10]. Above all, in 2015, Antoine L et al. discovered functional lymphatic vessels lining the dural sinuses. These structures are able to carry both fluid and immune cells from the CSF, and are connected to the deep cervical lymph nodes. Therefore, malignant gliomas maybe migrate in the extracranial organs through the lymphatic vessels. (iv) Genetic alterations: Molecular differences may underlie the rare occurrence of systemic metastasis of glioblastoma. In 2000, Park et al. reported four cases of extracranial metastasis of GBM with TP53 mutations. This phenomenon demonstrated that TP53 mutations maybe promote glioblastoma extracranial metastasis [14]. Manolo P et al. suggested a decrease of DNA-PK genetic expression, which is a DNA-dependent protein kinase involved in DNA repair mechanisms, contributes to the malignant transformation of the glioma.

In the course of spreading, the target organ produces local factors; i.e., growthfactors, cytokines, genetic composition of the malignant glioma cell, extra-cellular matrix components, adhesion molecules, enzyme action, cell motility and the cytoskeleton [15]. In the role of local factors, tumor cells migrate away from the original site, arrive in the host organ and rapidly proliferate. The site of metastasis most frequently appears in the lung and pleura (60%), in addition there are lymph nodes (51%), particularly in the cervical group, liver, spleen, skeleton (31%), where vertebral bodies are the most involved [15-20]. A recently published meta-analysis of 88 cases of extracranial GBM demonstrated that the overall survival (OS) had a median of 10.5 months, the median time from diagnosis to detection of extracranial metastasis was 8.5 month, and from detection of extracranial metastasis to death was 1.5 month. All of the metastasis sites, lung metastasis stood out as having the worst prognosis [21]. In the present case, the patient was thought to intracranial tumor cells metastasize to the lung. Histopathologic confirmation obtained via pulmonary bronchoscopy biopsy revealed highly cellular pleomorphic cells similar to that seen in the primary cerebral anaplastic oligoastrocytoma.

The patient was diagnosed with extracranial metastasis 24 months after anaplastic oligoastrocytoma, which was confirmed. She is still alive with a KPS of 70 scores recently. The survival interval of the current case is longer than the recently published meta-analysis, which may be ascribed to the presence of some oligodendroglial elements in tumors. The tumor tissue contains necrosis elements, but was still considerably longer than the OS time of patients with conventional GBM. The longer the patient survived, the more favorable the target organs.
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developed the microenvironment to facilitate the survival and proliferation of tumor cells. At the same time there is sufficient time for tumor cells to escape the immune system and adapt to the different microenvironmental conditions of extracranial organs.

Conclusions

Although the mechanism of malignant gliomas extracranial metastasis is not fully understood, it suggests that if we collect the rare cases carefully and review the literatures constantly, we will illuminate the mechanisms of extracranial metastasis in the near future. As the life expectancy is gradually increasing for GBM patients with newer therapies, the incidence of extracranial metastases may increase and this rare phenomenon may become more common and clinically relevant.

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Written informed consents were obtained from the patients for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

Disclosure of conflict of interest

None.

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