

# Extracranial bone metastases from recurrent anaplastic astrocytoma on FDG PET/CT

## A case report a care-compliant article

Zu-Gui Li, MM<sup>a,\*</sup>, Hai-Yu Mu, MM<sup>b,\*</sup>

### Abstract

**Objective:** Extracranial bone metastases from astrocytoma are rare and frequently detected as part of multiorgan metastases. It is extremely rare for astrocytoma to have extracranial bone metastases alone. The importance of whole-body fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) imaging in evaluating extracranial metastasis (ECMs) has not been described effectively due to the rarity of this event. The purpose of our case report is to emphasize the role of FDG PET/CT in the assessment of tumor recurrence and extracranial bone metastases from anaplastic astrocytoma.

**Methods and materials:** A 25-year-old woman was firstly admitted with a 4-month history of progressive blurred vision, and 2-month history of intermittent headache. Presurgical MRI imaging revealed a large mass in the left trigone of lateral ventricle. Subsequently, she underwent tumor resection, radiotherapy and chemotherapy. A final pathological diagnosis of anaplastic astrocytoma (WHO III) was made. Nearly 12 months after the surgery, the follow-up brain MR imaging revealed a contrast-enhanced lesion in the site of operative region. Whole-body FDG PET/CT imaging was performed to evaluate the situation.

**Results:** Postoperative brain FDG PET/CT showed an abnormal focal FDG uptake corresponding to the contrast-enhanced lesion in the operative area, suggesting a tumor recurrence. Whole-body FDG PET/CT also showed multiple FDG-avid osteosclerotic lesions in the body. It was highly suggestive of extracranial bone metastases. A subsequent open bone biopsy of FDG-avid lesion in right iliac crest was performed. Histopathological and immunohistochemical findings indicated characteristic of glioma. The patient died 1 month later, nearly 13 months after the initial diagnosis.

**Conclusions:** ECMs from anaplastic astrocytoma are extremely rare but they do occur. Whole-body FDG PET/CT imaging with inclusion of brain was valuable in differentiating tumor recurrence from radiation necrosis and in detecting uncommon extracranial bone metastases from anaplastic astrocytoma, which were closely related to prognosis of this disease.

**Abbreviations:** 3D-MIP = 3-dimensional maximum intensity projection, ECM = extracranial metastasis, FDG = fluorodeoxyglucose, FLAIR = fluid attenuated inversion recovery, GFAP = glial fibrillary acidic protein, MRI = magnetic resonance imaging, PET/CT = positron emission tomography/computed tomography, SUV<sub>max</sub> = maximal standard uptake value.

**Keywords:** astrocytoma, CT, extracranial bone metastasis, F-18 FDG, PET

## 1. Introduction

Despite the rarity, extracranial metastasis (ECM) from primary brain tumors has been known for many years since it was originally described in 1928.<sup>[1]</sup> ECMs are known to occur in

patients with several types of primary brain tumors but with an incidence of lower than 0.5%.<sup>[2]</sup> The most frequent metastatic gliomas are medulloblastoma and malignant astrocytoma/glioblastoma, followed by ependymoma.<sup>[3]</sup> ECM of glioma frequently occurred in regional lymph nodes, lungs and pleura, bones, liver, and so on.<sup>[4-6]</sup> It was frequently lethal and related with a poor prognosis.<sup>[5]</sup> Recognizing the patterns of ECMs may lead to the modification of treatment strategies in the patients with primary brain tumors.

As FDG PET/CT yields whole body images and has the ability to identify foci of abnormally high metabolism, it might be a useful method in detecting systemic metastases and identifying local recurrence in brain tumors. However, the report of FDG PET/CT imaging in evaluating ECMs is limited, and the importance of whole-body FDG PET/CT imaging in ECMs has not been well elucidated.<sup>[7,8]</sup> Hence, we presented a rare case of ECMs to emphasize the role of FDG PET/CT in the assessment of tumor recurrence and extracranial bone metastases from anaplastic astrocytoma.

## 2. Case presentations

A 25-year-old woman was firstly admitted with a 4-month history of progressive blurred vision, and 2-month history of intermittent headache. Presurgical MRI imaging revealed a large,

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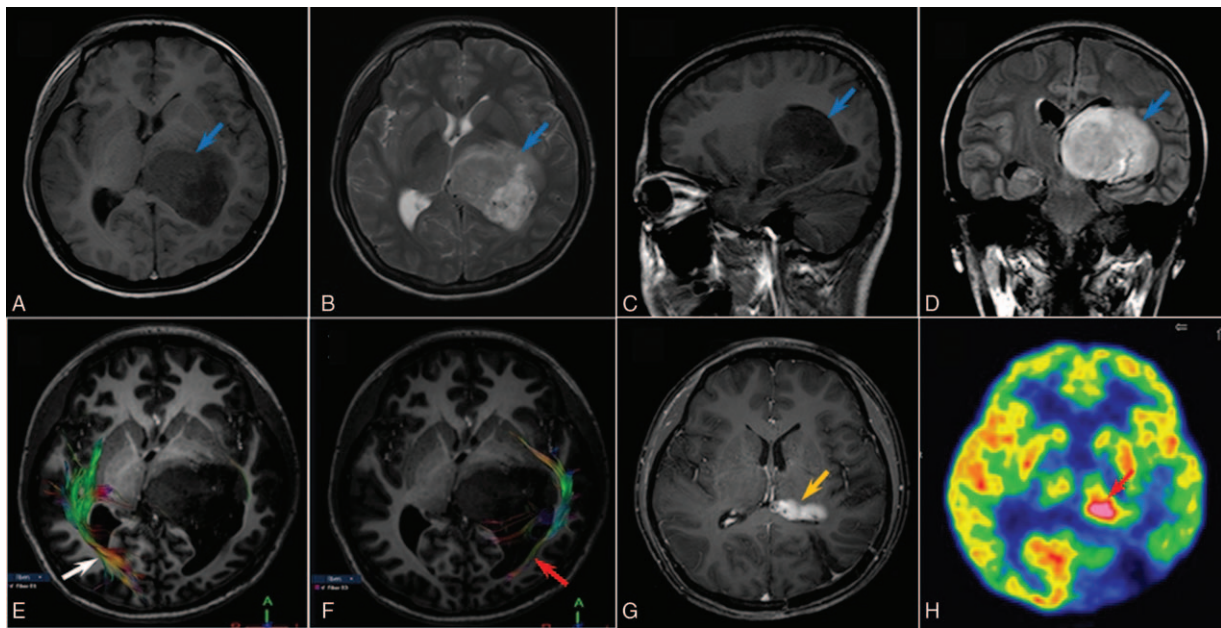
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**Figure 1.** (A–D) Presurgical MR imaging showed a large, round, inhomogeneous 6.3 cm × 5.8 cm × 4.7 cm mass with low signal intensity on T1-weighted images and high signal intensity on T2-weighted and T2 FLAIR images in the left trigone of lateral ventricle (blue arrows). The mass occupied the left lateral ventricle and compress the third ventricle with involving left thalamus. (E,F) Diffusion tensor imaging with fiber tracking also revealed the destruction and compression of left optic radiation fiber tracts (red arrow), as compared with the normal side (white arrow). (G) Follow-up T1-weighted MR image demonstrated that a focal contrast-enhanced lesion in the site of surgical resection (yellow arrow). (H) Postsurgical brain FDG PET/CT imaging showed an increased FDG uptake lesion corresponding to contrast-enhanced lesion in shape and size (red arrow). It was highly suggestive of a recurrent tumor. FDG = fluorodeoxyglucose, PET/CT = positron emission tomography/computed tomography, MRI = magnetic resonance imaging, FLAIR = fluid attenuated inversion recovery.

round, inhomogeneous 6.3 cm × 5.8 cm × 4.7 cm mass in the left trigone of lateral ventricle. The mass occupied the left lateral ventricle and compress the third ventricle with involving left thalamus (Fig. 1A–D). Diffusion tensor imaging with fiber tracking also revealed the destruction and compression of left optic radiation fiber tracts (Fig. 1E and F). The patient underwent a craniotomy with excision of the tumor. Postoperatively, no neurological deficits were detected. A final diagnosis of anaplastic astrocytoma (WHO III) was made based on the histopathological findings. Subsequently, she underwent radiotherapy and chemotherapy with the administration of temozolomide. Nearly 12 months after the surgery, she was readmitted with complaints of right shoulder and back pain for nearly 1 month. The follow-up brain MR imaging revealed a contrast-enhanced lesion in the site of operative region. It was considered to be a tumor recurrence or post-radiation change (Fig. 1G). She was referred for a whole-body FDG PET/CT imaging to differentiate recurrent tumor from radiation necrosis and to evaluate the situation.

The patient fasted >6 hours before the tracer injection and received an intravenous injection of 5.55 MBq/kg (0.15 mCi/kg) of F-18 FDG. The blood glucose level was measured immediately at the time of FDG injection and it was <150 mg/dL. She was instructed to rest in a quiet dim room without talking during the subsequent 1 hour of the FDG uptake period and was allowed to breathe normally during image acquisition without specific instructions. Whole-body PET/CT scans including a separate 3-dimension mode acquisition of brain was performed using a PET/CT scanner (Discovery ST-16; General Electric Medical Systems, Milwaukee, WI). The images were viewed on Xeleris and AW workstation. The maximal standardized uptake value ( $SUV_{max}$ ) was measured semiquantitatively using lean-body-mass-index correlated based on a ROI-analysis. She

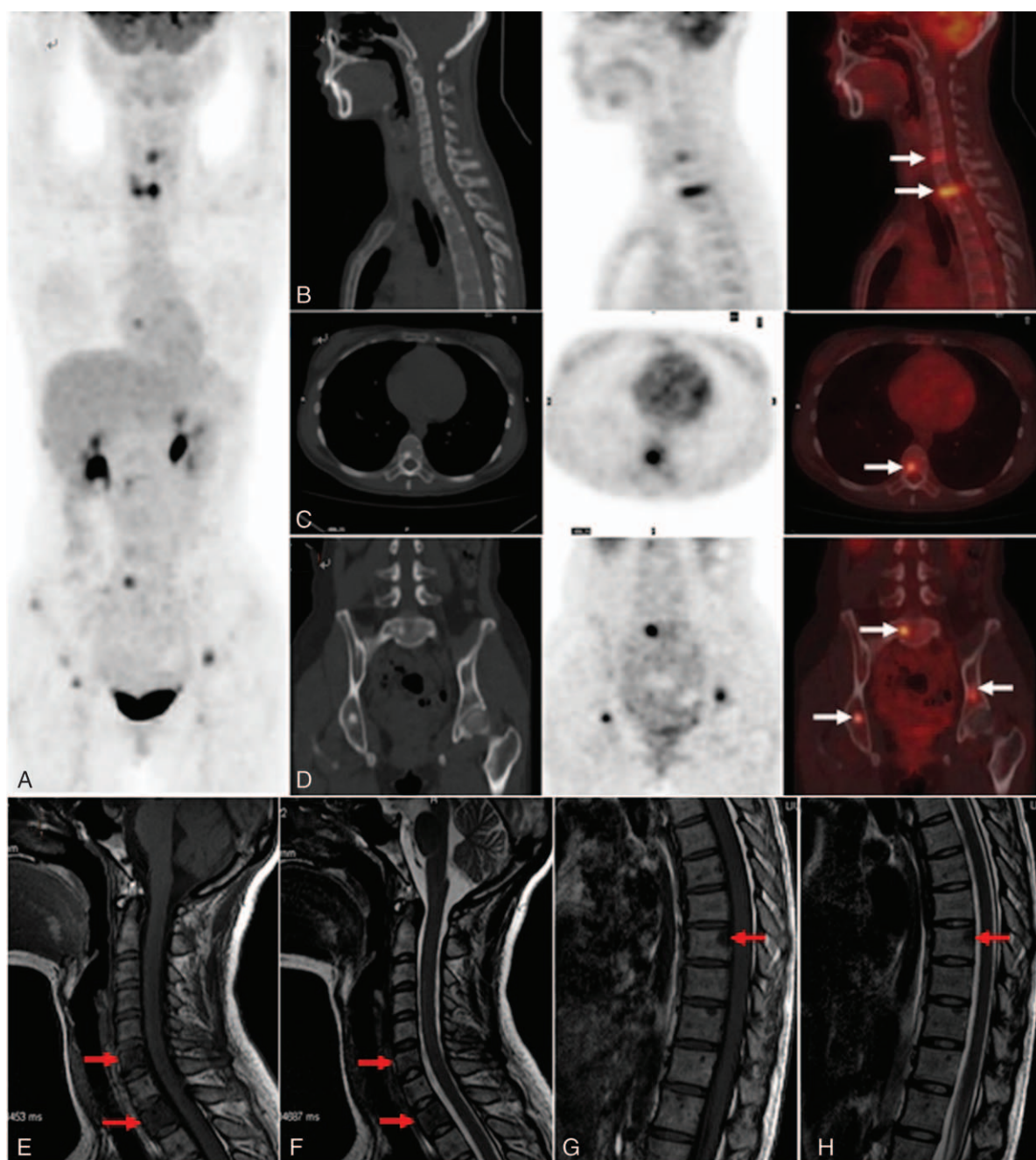
did not have the history of diabetes mellitus and a second primary history of malignancy.

The follow-up brain FDG PET/CT imaging demonstrated an abnormal focal FDG-uptake with  $SUV_{max}$  of 10.6, which was corresponding to the area of enhancement in shape and size on MR images (Fig. 1H). It was highly consistent with a tumor recurrence. Whole-body FDG PET/CT imaging also showed multiple osteosclerotic lesions with intense FDG-uptake with  $SUV_{max}$  of 10.8 in bones without any other abnormally high metabolism in the body, suggesting multiple extracranial bone metastases (Fig. 2A–D). Subsequently, cervical and thoracic spine MR images revealed that multiple hypointense lesions on both T1-weighted and T2-weighted images, which were thought to be consistent with osteosclerotic metastases (Fig. 2E–H). As extracranial bone metastases are extremely rare, a subsequent biopsy of FDG-avid lesion in right iliac crest was performed to make a confirmative diagnosis. Histopathological findings indicated characteristic of glioma (Fig. 3A). Immunohistochemically, the diagnosis was further confirmed by the expression of glial fibrillary acidic protein (GFAP) (Fig. 3B). The patient died 1 month later, nearly 13 months after the initial diagnosis.

The institutional review board (Pingjin Hospital) approved this work and informed consent was given by patient. The authors of this manuscript have no conflicts of interest.

### 3. Discussion

Extracranial metastasis from astrocytoma is rare but frequently lethal, and related with a poor prognosis. It has been suggested that the median time from diagnosis to detection of ECM is 8.5 months and the time from ECM to death is only 1.5 months.<sup>[5]</sup> In our case, the time from diagnosis to detection of

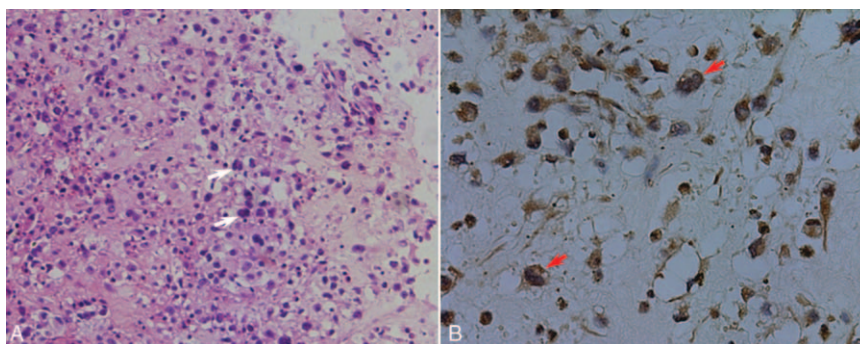


**Figure 2.** (A) Postsurgical whole-body FDG PET/CT anteroposterior 3D-MIP image images showed multiple focal abnormal FDG-avid regions in the body. (B–D) Selected PET/CT images revealed multiple osteosclerotic lesions with intense FDG-uptake in cervical and thoracic vertebra, sacral and iliac bones (white arrows). (E–H) The MRI images showed that multiple focal lesions with low signal intensity on sagittal T1-weighted and T2-weighted images (red arrows), which were consistent with osteosclerotic metastases. FDG=fluorodeoxyglucose, PET/CT=positron emission tomography/computed tomography, MRI=magnetic resonance imaging, 3D-MIP=3-dimensional maximum intensity projection.

ECMs is 12 months, but the time from ECM to death is only 1 month. Earlier diagnosis and treatment may improve the prognosis. Thus, the clinician caring for patients with astrocytoma should be alerted to this possibility.

A greater understanding of the pathogenesis of systemic metastases is necessary before more effective measures of prevention can be designed. But the mechanism of extracranial spread of malignant gliomas is still unclear. It might be explained by the following reasons: (1) the absence of lymphatic vessels; (2) the lack of communicating channels between the intracerebral

perivascular space and extracerebral fluid space; (3) the connections between the subarachnoid space and extracranial lymphatic vessels are very sparse; (4) the walls of intracerebral veins are too thin and collapse before any tumor penetration; (5) dural veins are protected by a dense connective tissue; (6) the immunological response of the host organ to neuroglial tumour cells may prevent their growth outside the central nervous system.<sup>[4,9,10]</sup> A further explanation could be the short life span of patients with high-grade tumors who do not survive long enough to develop metastases.<sup>[11]</sup> Despite of this, the possible



**Figure 3.** (A) Histologic examination (hematoxylin and eosin staining, original magnification  $\times 200$ ) demonstrated high cellularity and nuclear pleomorphism of the tumor cells (white arrows). (B) Immunohistochemical result (original magnification  $\times 400$ ) revealed that the tumor cells were positive for GFAP (red arrows). GFAP = glial fibrillary acidic protein.

mechanisms of extracranial spread could be described as follows: (1) hematogenous spread via the vessels of the primary tumor; (2) hematogenous spread after tumor invasion of the dural veins; (3) hematogenous and/or lymphogenous spread after infiltration of the skull and extracranial soft tissues; (4) spread via the cerebrospinal fluid; (5) spread via ventriculoatrial or ventriculo-pleural shunts.<sup>[4]</sup> In our presented case, she developed multiple extracranial bone metastases in the body. We considered that the main pathway of ECM might be the hematogenous spread because the patient had undergone a craniotomy with tumor resection.

The current diagnostic criteria for diagnosing ECMs were firstly established by Weiss in 1955, which included: (1) the clinical history of primary brain tumor; (2) the metastatic lesion has to meet the histological characteristics of a primary brain tumor; (3) a complete autopsy must be performed to exclude the possibility of any other primary tumor; and (4) the presumed extracranial metastases.<sup>[12]</sup> As FDG PET/CT yields whole-body imaging and has the ability to identify foci of abnormally high metabolism, it is possible to exclude a potential undiscovered primary tumor other than primary brain tumor. Therefore, a complete postmortem examination is not necessary today, as whole-body FDG PET/CT imaging is widely used.<sup>[7,8]</sup> In this case, she had a history of anaplastic astrocytoma. Then, a tumor recurrence in operative area was identified by the combination of postsurgical brain FDG PET/CT and contrast-enhanced MRI images. Interestingly, whole-body FDG PET/CT also revealed that multiple FDG-avid osteosclerotic lesions without any other primary malignant in the body. The following pathological results of biopsy indicated the characteristic of glioma. Immunochemically, GFAP-positivity indicated that the tumor could originate from intracranial astrocyte, which is of great importance for the diagnosis of metastatic intracranial glioma. Thus, this patient fulfilled these criteria of ECMs.

In the clinical setting, presurgical brain FDG PET/CT was frequently used in the evaluation and management of patients with primary brain tumors including the grading of tumors, determination of prognosis, and the differentiation of recurrent tumor from radiation necrosis. As a rule, areas located outside the brain, however, are not scanned in routine brain PET/CT. Moreover, whole-body FDG PET/CT inclusion of brain was usually used in patients with suspected intracranial metastases to identify the extracranial primary tumor sites. However, the use of presurgical whole-body FDG PET/CT in primary brain tumors is limited, either because presurgical MR imaging performed well or ECMs are not taken into account due to the scarcity of this

event. Without that information, it is not possible to exclude spontaneous distant metastasis of primary brain tumor,<sup>[7,13–15]</sup> and it is difficult to know the exact time of the presence of ECM. Further and detailed investigation of presurgical evaluation in ECMs with whole-body FDG PET/CT imaging (including brain) is required in our future study.

Extracranial bone metastases from astrocytoma can be differentiated in lytic or sclerotic lesions on neuroimaging, and they are frequently accompanied by the involvement of other locations in the body. It is relatively rare for astrocytoma to have extracranial bone metastases alone. Interestingly, in our presented case, whole-body FDG PET/CT revealed multiple FDG-avid osteosclerotic metastases which were finally confirmed by the pathological and immunohistochemical results. It is reported that osteosclerotic metastasis is more commonly caused by prostate, breast, and lung together accounting 80% of such metastasis, followed by thyroid, urinary bladder, renal, and stomach as primary sites.<sup>[16]</sup> However, the report of osteosclerotic metastasis from anaplastic astrocytoma is relatively rare with only a few reports in previous literatures.<sup>[6,7,17,18]</sup> As multiple extracranial osteosclerotic metastases can easily present as a carcinoma of unknown primary, especially in absence of obvious CNS symptoms, an origin of primary brain tumor should not be ignored. We emphasize that ECMs of astrocytoma should be kept as a differential diagnosis in a case of occult primary with osteosclerotic metastasis.

#### 4. Conclusions

In summary, ECMs from primary brain tumors, albeit rare, do occur. The neuro-oncologists should pay attention to the systematic survey for ECMs from astrocytoma. We proposed that whole-body FDG PET/CT imaging with inclusion of brain should be incorporated into the diagnostic algorithm of ECM to give a comprehensive assessment of this rare event. The roles of FDG PET/CT imaging in evaluating ECM from primary brain tumors possibly include: (1) to exclude a potential second primary malignancy in the diagnosis of ECMs; (2) to give a thorough search for the possible metastases which are related to prognosis; (3) to differentiate tumor recurrence from radiation necrosis.

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