Case Report

An Unusual Case of Glioblastoma Multiforme, Presenting as Skeletal Superscan

Abstract

Extracranial metastases of glioblastoma multiforme (GBM) are very rare. The estimated incidence is <2%. We report a case of a 49-year-old woman, who was a known case of GBM in the left temporo-occipital lobe. She was operated and had received radiotherapy and adjuvant chemotherapy for the same. Subsequently, the patient underwent bone scan. On 99 m-Tc methylene diphosphonate (MDP) bone scan, homogenously increased tracer uptake was noted in the axial and appendicular skeletal system, suggesting metastatic skeletal superscan.

Keywords: *99 m-Tc MDP bone scan, bone metastasis, extracranial metastases, glioblastoma multiforme, superscan*

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Introduction

In adults, glioblastoma multiforme (GBM) is the most common malignant primary brain tumor.[1] Grade IV is the highest grade in the WHO classification of brain tumors defined by histopathologic features of endothelial proliferation and necrosis.[2] The incidence of GBM is 3.19 cases/100,000 person years. It has a very poor prognosis with a 5-year survival rate of 4%–5%, and the survival rate at 2 years is only 26%–33%.[3-6] In the younger age group, specific point mutation of isocitrate dehydrogenase (IDH) 1 or 2 genes are seen to be associated.[7] It has a more favorable outcome. The IDH wild-type is seen in the majority of the GBM.[8,9] The molecular changes in glioblastoma typically include mutations in genes regulating receptor tyrosine kinase/rat sarcoma/p53/phosphoinositide 3-kinase.[10] Majority of the patients present with a clinical history of 3–6 months. If tumor develops from a low-grade astrocytoma, the symptoms, however, may span over a long period.[11,12] Occasionally, the symptoms might be mistaken for a stroke.[13] By direct effect, there is necrosis of brain tissue, which gives rise to symptoms depending on the involved region of the brain. About 40%–60% of patients present with focal neural deficit and cognitive impairments. 20%–40% of patients have frontal lobe involvement causing a personality change.[11,12] Large tumors can lead to gait impairment and incontinence.[13] There is increased intracranial pressure and surrounding edema due to gradual increase in tumor size. This leads to a shift in intracranial contents, resulting in headaches. Headache is a characteristic feature in 30%–50% of GBM patients.[11,12] Unilaterally localized headache with no specific pain pattern is seen and is often associated with vomiting and papilledema.[13] 20%–40% cases may have seizures depending on the location of tumor cases. It is usually a focal onset episode. This can be simple partial, complex partial, or generalized seizures.[11-13] Extracranial metastases of GBM are rare with incidence of <2%.[14,15] The GBM may spread by the hematogenous and lymphatic route.[16] In some cases, direct extension of tumor can be the mode of spread. The rarity of metastatic GBM can be explained by the absence of lymphatics in the central nervous system and the lack of communication between intracranial and extracranial perivascular spaces.[17] Furthermore, the shorter survival time of patients, and the metastatic disease which is still undiagnosed can be the cause.[18] The most commonly affected organ systems extracranially are bones, lymph nodes, and lungs. Although extracranial GBM does not shorten the survival time of patients drastically, the physicians should be aware of its presence. If there are any symptoms

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referable to these areas of spread, they should be evaluated by the physicians. The approximate median OS for patients with GBM is 12–15 months.[19] Reportedly, cases with local intracranial recurrence have a median OS of 7.5 months.[20] Local continuous growth is the most common form of GBM recurrence which is seen within 2–3 cm from the border of the original lesion.[21-23] Original tumor location recurrence occurs in more than 90% of the patients with glioma. In 5% of cases, multiple lesions develop after treatment.[24] Rarely, GBM cases may develop new parenchymal lesions which do not exhibit continuous growth patterns, ventricular spread, or dissemination.[25] Uncommon relapse patterns can be seen in midline tumors or those which infiltrate both hemispheres.[26] Subtotal resections are sometimes done in an attempt to preserve neurological function and maintain patient quality of life. This may later lead to residual tumor growth which is seen on imaging scans or manifest as new symptoms. The appearance of residual tumor growth is also defined as tumor recurrence. The term "tumor progression" is considered synonymous with "tumor recurrence" because of the spectrum from which new lesions can develop. The treatment of recurrent GBM is multimodal including surgery, radiotherapy, chemotherapy, and antiangiogenic therapy. Surgical resection of GBM reduces the metastasis risk, and chemotherapy and radiotherapy in metastatic GBM are considered helpful in prolonging survival.[14] Further knowledge in the field of underlying tumor biology, gene therapy, antiangiogenic antagonists, and immunotherapies may help in developing more promising treatment plans.[27]

We report an unusual case in which a patient presented with skeletal superscan and further investigations helped in the diagnosis.

Case Report

A 49-year-old female patient, who was a known case of GBM in the left temporo-occipital lobe for which she had craniotomy. Following which the patient had received adjuvant chemotherapy (temozolomide) and radiotherapy treatment. Subsequently, the patient presented with left-sided body pain. In suspicion for skeletal metastases, the patient was referred for bone scan. Whole-body bone scan was done with IV administration of 20 mCi of 99 m-Tc MDP. Anterior and posterior images [Figure 1a & b representing anterior and posterior images, respectively] showed homogenously increased tracer uptake in the axial and appendicular skeleton system with increased bone soft tissue ratio and very faint visualization of the kidneys, suggesting of metastatic superscan. Magnetic resonance imaging spine was also done which showed multiple hyperintense bony lesions in all lumbar vertebrae, bilateral iliac bones and sacrum, favoring skeletal metastases. Subsequently, to look for other visceral metastasis, contrast-enhanced computed tomography (thorax, abdomen, and pelvis) was done, which showed extensive sclerotic lesions in multiple vertebrae, sternum, and bilateral pelvis.

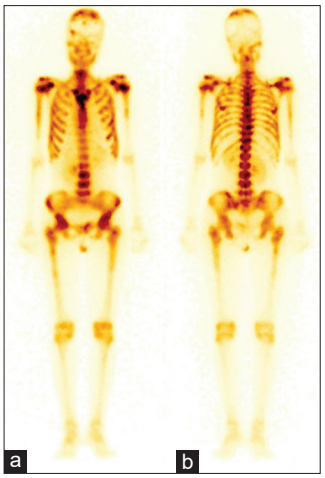

Figure 1: Figure a & b represent anterior and posterior bone scan images respectively, which show homogeneously increased tracer uptake in the axial and appendicular skeleton with increased bone to soft tissue ratio and very faint visualization of the kidneys, suggestive of metastatic super-scan

Bone marrow biopsy later confirmed the diagnosis and the diagnosis of GBM with diffuse skeletal metastases was made. However, before commencement of any therapy patient succumbed to the disease.

Discussion

The natural history of GBM metastases is still not completely defined. The knowledge of clinical factors which promote GBM metastases may explain the mechanisms of tumor cell invasion in the brain. Although extracranial GBM does not decrease the survival time of patients with GBM, the awareness regarding its existence leads to better management of patients. There are very few case reports published, showing skeletal metastases from GBM and only one case report showing presentation as skeletal superscan.[28] In a study done by Manohar *et al*., the overall incidence of superscan in different types of cancers was 1.3%. It was most commonly seen in patients with prostate cancer followed by breast and lung cancer.[29] The case discussed above is of a patient with GBM who presented with skeletal superscan. A bone scan with diffusely increased skeletal radioisotope uptake relative to soft tissue in association with absent or faint renal activity ("absent kidney sign)" is known as a superscan.[30,31] Recurrence is also not uncommon and is treated with a multimodal approach including surgery, radiotherapy, chemotherapy, and antiangiogenic therapy. However, further understanding of underlying tumor biology is essential in developing more effective therapies.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not

be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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