# Metastatic meningioma presenting as cancer of unknown primary

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## Abstract

We describe a case of anaplastic meningioma presenting in an extracranial osseous location, initially diagnosed as cancer of unknown primary. Although anaplastic meningioma comprise 3% of all meningiomas, this subtype is more likely to be associated with metastases. The increased degree of dedifferentiation in anaplastic meningioma makes diagnosis difficult, especially if characteristic imaging findings of meningioma are not identified. Adequate tissue for diagnostic purposes and appropriate imaging studies may help in establishing a definitive diagnosis.

## Case Report

A 72-year-old Caucasian male patient was admitted to our hospital for excision of the metastatic adenocarcinoma of the skull vertex. It was diagnosed at an outside facility as carcinoma of unknown primary. He was initially diagnosed four years ago, when he presented to his primary care physician for worsening left hip pain, which was accompanied by mild muscular atrophy. A computerized tomographic (CT) scan demonstrated mixed sclerotic and lytic lesions in the left iliac wing. A bone scan demonstrated increased activity in the left sacroiliac joint. Magnetic resonance imaging (MRI) of lumbar spine showed abnormal signal in the left sacrum and ilium, consistent with metastatic disease. This area was biopsied and showed a metastatic poorly differentiated carcinoma, diffusely positive for wide-spectrum cytokeratin and negative for TTF1. Restaging studies did not demonstrate any other lesions. He was subsequently evaluated by radiation oncology and underwent radiation therapy to the left hip. The patient did well over the next 18 months, when he returned with an enlarged skull mass and received site directed radiation therapy. No biopsy of the skull mass was performed at this visit. He presented again in 6 months with a left tibial lesion for which he was treated with palliative radiation. A biopsy performed at this presentation did not demonstrate any neoplasm. Six-months later, he presented with increasing size of the skull mass and was initiated on chemotherapy with a regimen consisting of carboplatin and etoposide. He did have a moderate response to treatment. However, on follow-up, he was noted to have CT evidence of invasive and enlarging osseous metastasis measuring six centimeters (cm) involving the right frontal bone along with mild localized mass effect on the right frontal lobe. Consequently, he underwent another series of treatment with radiation therapy to the skull mass with a total dose of 35 grays (Gy). Despite an initial response to therapy, he subsequently had further progression of the calvarial mass including cutaneous breakdown, and presented to our institution for care.

A nuclear medicine PET/CT of trunk showed an intensely FDG avid mass in the posterior left pelvis involving soft tissue and left iliac bone. Additionally, he underwent a subtotal resection of the skull mass, demonstrating anaplastic meningioma (Figure 1). A CT guided biopsy of left iliac mass also revealed metastatic anaplastic meningioma. An octreotide scan (Figure 2) was performed revealing significant uptake in the left hip and right distal femur for which palliative radiation therapy was recommended, which was administered locally. However, he presented to a local ER soon after completion of radiation therapy with worsening left-sided weakness with CT evidence of cerebral edema. MRI revealed enhancing mass at the site of prior partial resection consistent with progressive disease (Figure 3). He was no longer a candidate for surgery. Salvage radiation was attempted, but the patient continually to decline, and was ultimately enrolled in hospice for end of life care.

## Discussion and Conclusions

Meningiomas are the most common adult CNS tumors, accounting for up to 30% of all cases. They are often discovered during autopsies, especially in elderly population. The classical presentation of meningioma is an incidentally discovered lesion arising within the central nervous system (CNS), often monitored by serial imaging and seldom necessitating immediate intervention.[1] The overwhelming majority of meningiomas are intracranial in nature.[2] Distant metastases with meningioma remain rare. The World Health Organization (WHO) classifies meningioma into benign (WHO grade I), atypical (WHO grade II) and anaplastic meningioma (WHO grade III), comprising 90%, 7% and 3% of all meningiomas, respectively.[3] The anaplastic meningiomas are characterized by increased proliferation rate, high mitotic index (≥20 mitoses) and areas of necrosis.[4]

This case is unique in two respects. Firstly, metastatic meningioma is exceedingly rare, especially with appendicular osseous involvement as the presenting site. Other extracranial sites of metastatic disease reported in the literature include lungs,[5] blood vessels,[6] esophagus,[7] and skin.[8] Secondly, the initial biopsy finding at the outside institution was suggestive of poorly differentiated carcinoma, and the primary site was not identified. Therefore, the primary site remained unidentified four years after initial presentation. To the best of our knowledge, this is the first reported case of anaplastic meningioma with initial presentation in the extracranial osseous tissue without an obvious visualized primary site. He was consequently treated as carcinoma of unknown primary. A definitive diagnosis was made after a surgical resection of the calvarial lesion was attempted. Anaplastic meningioma was not identified in previously performed biopsies, which may be secondary to paucity of tissue obtained via biopsy. An octreotide scan may assist in making the diagnosis. The somatostatin receptors are commonly expressed in meningiomas, and enable visualization with a radiolabeled somatostatin analog, which may be offered in initial diagnosis, identifying metastatic sites and follow-up.[9,10] In this case, an octreotide scan did reveal additional foci of disease in the right distal femur.

The primary modality of treatment for meningiomas is surgical resection for symptomatic disease. Radiation therapy is offered in poor surgical candidates or remnant tumor as in subtotal resection. No standard of care exists for systemic therapy. Both cytotoxic as well as targeted therapy has been evaluated in meningiomas. Confounding data exists regarding efficacy of hydroxyurea. The

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Key words: meningioma, metastasis, unknown primary.

Contributions: the authors contributed equally.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 28 August 2013.
Accepted for publication: 8 September 2013.


*Rare Tumors 2013; 5:e59*
*doi:10.4081/rt.2013.e59*

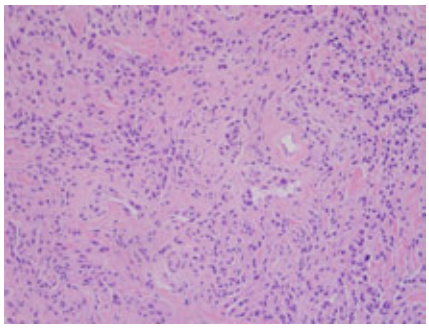

**Figure 1. Representative images from skull mass revealing anaplastic meningioma.**

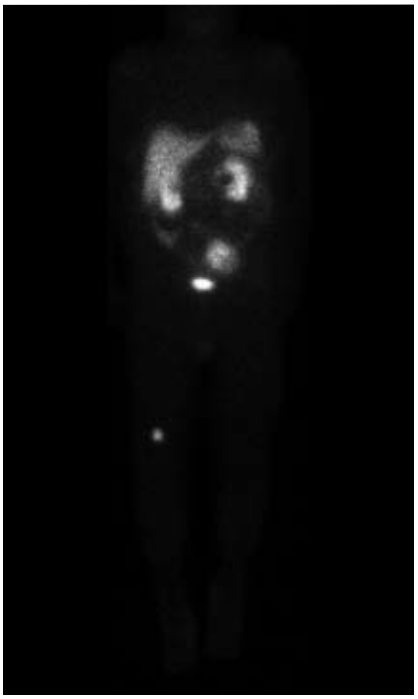

**Figure 2. Octreotide Scan showing uptake in right distal femur.**

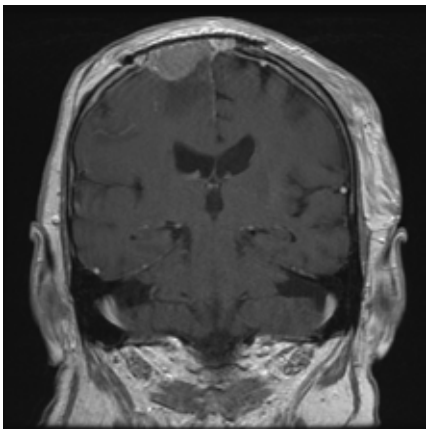

**Figure 3. Magnetic resonance imaging head showing recurrent anaplastic meningioma.**

somatostatin analogues have demonstrated efficacy in unresectable or recurrent meningiomas.[11] The management of recurrent or anaplastic meningiomas is complicated by aggressive tumor growth and refractoriness to cytotoxic therapies.[12] Responses to temozolomide[13] and irinotecan[14] in clinical trials have been disappointing so far. Trials with signal transduction inhibitors are underway. However, the low incidence of atypical and anaplastic meningiomas limits such efforts.

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