



Incidental Bone Lesions in a 78 Year Old Male with History of Grade I Meningioma

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Abstract

The clinical phenomenon of metastatic meningioma is not well described in the literature owing to the relative rarity of its incidence.

We report the case of a 78 year old male with a past medical history notable for successfully resected.

WHO grade I meningioma in June of 2006 who, upon presentation for left thigh pain from a traumatic fall eight years later, was found to have incidental imaging findings of multiple bony lesions in the left iliac crest and spine. Subsequent investigations revealed the diagnosis of WHO grade I meningioma metastatic to the bone. Although its unequivocal rarity would reasonably relegate metastatic meningioma to a diagnosis of exclusion, it is hoped that this case report will prevail upon the reader the importance of keeping this diagnostic possibility on the differential in the appropriate clinical context.

Background

Largely incidental findings from imaging for unrelated reasons, meningiomas account for upwards of 35% of total primary brain tumors. Most are benign, localized, intracranial tumors.

When malignancy occurs in meningioma, this typically connotes a recurrence of the tumor and not metastasis as metastasis outside the cranium is an overall rare occurrence. The latency period for such an event has been reported to be from months to over twenty years. The majority of metastatic meningioma travel to the lungs, intra-abdominal viscera and bone, as was the case in this patient.

Case Report

We report here the case of a 78 year old male who initially presented to the emergency department in March of 2016 with the complaint of left thigh pain and discomfort from an injury sustained after losing balance and falling from a ladder at work. His medical history is notable for a 2.9 cm x 2 cm left parietal occipital falcine meningioma diagnosed in 2006. This was surgically resected successfully that year (Simpson Grade I); subsequent surveillance MRIs of the brain in 2007 and 2008 showed no evidence of recurrence. Between the time of the aforementioned surgical resection and the current presentation, the patient had been overall well, notwithstanding chronic neck and back pain. In the ED on his current presentation, CT scans were done of the left lower extremity and abdomen/pelvis, respectively; the latter was performed due to complaints of pain radiating to the left groin area. The former study was notable for a large hematoma corresponding to findings on physical examination. The latter study, however, had the incidental finding of a large lytic lesion in the right iliac crest and multiple small rounded lucent lesions in the thoracolumbar spine. Shortly after, an MRI of the cervical spine without contrast was performed; this revealed multiple focal lesions in the marrow suggesting metastatic disease to the cervical spine. A CT of the chest done the following month re-demonstrated several lesions at multiple levels of the thoracolumbar spine and also showed a suggested lesion in the sternum. An MRI of the brain done a few days later found an approximately 13 mm circular lesion in the parafalcine region abutting the right parietal lobe, thought to be a recurrence of the original meningioma from 2006.

The patient underwent CT-guided biopsy of the right iliac crest lesion; pathology showed infiltration of the medullary cavity with atypical spindle cells suspicious for metastatic meningioma. Immunohistochemistry of the cells demonstrated: SMA+ (rare), EMA+ (multifocal), Pan-Keratin-, Desmin-, S100-, CD31-, CAMP5.2-, and Pax-8-. Pathology review of specimens from the intracranial meningioma from 2006 and the right iliac biopsied lesion from 2016 confirmed the

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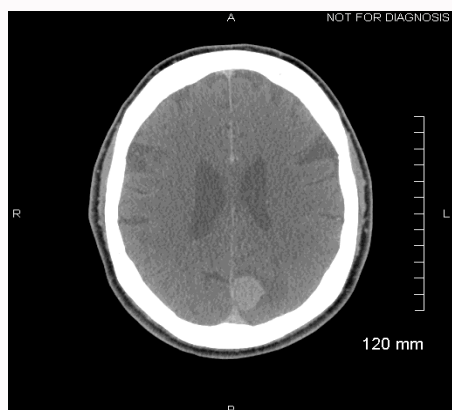


Figure 1: Axial CT image of the head demonstrate a mildly hyperdense left posterior parafalcine mass compatible with a meningioma.

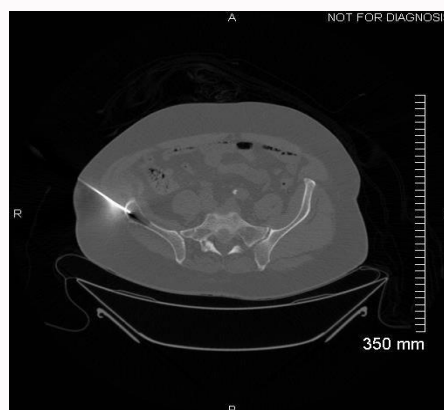


Figure 3: Axial CT image of the pelvis (bone windows) during biopsy demonstrates a biopsy needle within the lytic lesion located in the right iliac crest.

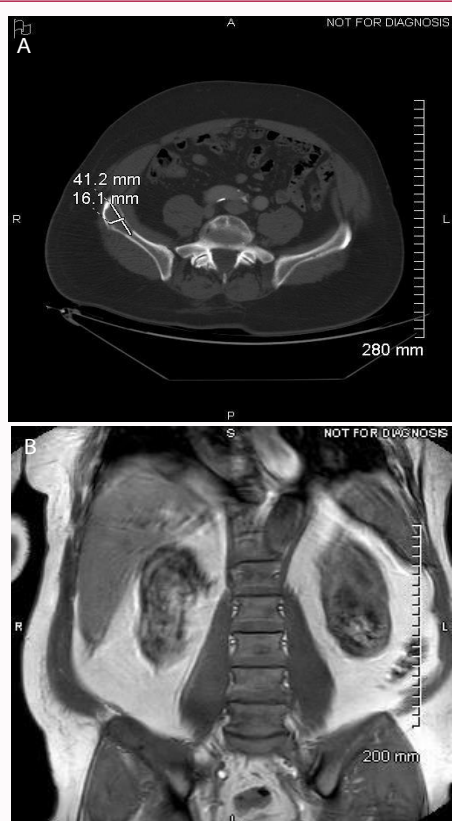


Figure 2: A) Axial CT image (soft tissue windows) of the abdomen/pelvis demonstrates a mildly expansile and lytic lesion in the right iliac crest with calipers super imposed on the lesion. B) Coronal localizer MRI image demonstrates low marrow signal in the right iliac crest.

diagnosis of grade I meningioma. Given the fact that the patient was minimally symptomatic from the meningioma the decision was made to monitor only and no medical intervention was initiated.

Discussion

Among all of the primary CNS tumors, meningiomas are the most common, numbering roughly one in every three primary tumors found in the brain and spinal cord [1]. Meningiomas have a gender predilection for females, the female to male ratio being about 2-3:1 [2]. The incidence of meningioma also has a positive correlation with the advancement of age, with the median age at diagnosis being 65 years.

Multiple investigations have been undertaken to establish possible etiologies for the development of meningioma. The most prominent etiologic association is history of CNS exposure to ionizing radiation, including radiation therapy used to treat other primary malignancies [3,4]. Our patient has no such history.

Less commonly, there are certain genetic mutations implicated in the development of meningioma. The most well established is mutation of the NF2 tumor suppressor gene that results in neurofibromatosis type 2 (NF2) [5]. As a consequence of this mutation, patients with this syndrome are typically found to develop distinct simultaneous malignant entities, predominantly vestibular schwannomas and gliomas [6]. As many as 50% of these patients have at least one meningioma but are oftentimes afflicted with multiple tumors [5]. There are other less prominent risk factors which include hormonal factors, the concomitant presence of breast cancer, obesity and head trauma [7,8,9].

Meningiomas are classified by the WHO based on morphology and histopathological characteristics; the latest iteration was rendered in 2007 [10]. Meningiomas are delineated into 3 broad groups: Grade I (benign), Grade II (atypical), and Grade III (malignant). The vast majority (90%) of meningiomas are Grade I tumors [11].

There are distinct clinical characteristics and behaviors that distinguish Grade II and III meningiomas from Grade I meningiomas; these are: increased proclivity for invasion into local brain parenchyma, an increased likelihood of recurrence following initial treatment, and a shorter overall survival [12]. All three characteristics are seen to the greatest degree in grade III meningiomas and to a lesser extent in grade II meningiomas [13,14]. Grade I meningiomas, on the other hand, infrequently recur, do not exhibit invasion into surrounding brain structures, and have a considerably longer overall survival and better prognosis [15]. The risk of recurrence after initial treatment rises successively with increasing tumor grade and atypical histopathological features which include high cellularity, tumor necrosis, high mitotic rate and vascular invasion [16].

The present case defies these general conventions insofar as the patient had an indolent recurrence of his original grade I tumor after complete surgical resection.

Another telling difference that distinguishes Grade I meningioma from Grade II/III meningioma is the likelihood of extracranial

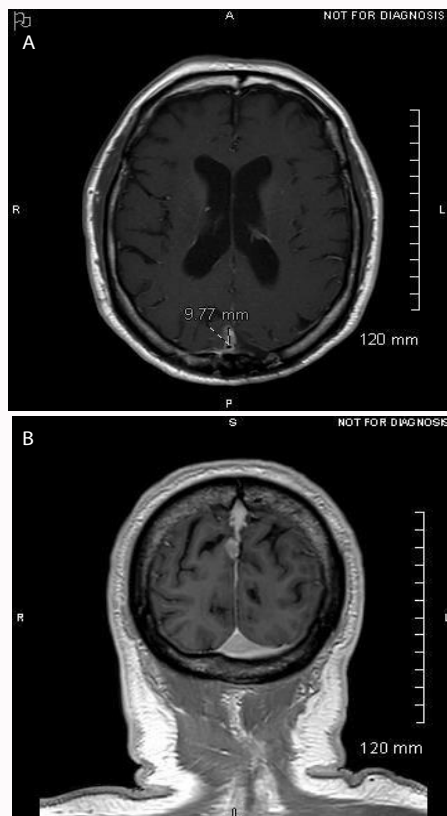


Figure 4: A) Axial T1 W post-contrast MRI image demonstrates post surgical changes of the posterior parietal calvarium. Calipers are placed on a 9.77 mm avidly enhancing nodule along the posterior falx cerebri suspicious for recurrent meningioma in the post-surgical bed. B) Coronal T1W post-contrast MRI image demonstrates the same lesion as in (A.) and better demonstrates its relationship to the superior sagittal sinus, which is situated just above and slightly more posterior to the mass.

metastasis. Overall, extracranial metastasis is rare and is estimated to occur in less than 0.1% - 0.2% of all patients diagnosed with meningioma [16]. However, for the patients with grade II and grade III tumors, extracranial metastasis can occur in as many as 5% and 30% of patients, respectively [10].

It is estimated that roughly 60% of extracranial metastases go to the lungs, 34% go to the abdomen and liver, and 18% go to the cervical lymph nodes and surrounding glandular tissue [16]. It is thought that in these situations, tumor cells travel through venous channels from which they enter the right-sided circulation and end in one of the three sites specified. Less commonly, metastatic meningioma tumor cells may access the vertebral venous system by which they may travel to other distinct sites in the body [17]. In order of decreasing incidence, these sites of metastasis are: the long bones, pelvis and skull (11%); pleura (9%); vertebrae (7%); and mediastinum (5%) [16].

That metastasis is so exceedingly rare for grade I meningiomas and of itself makes this case being discussed remarkable. Moreover, as outlined above, it is rare to find metastases of meningiomas to the bone as in this case.

As discussed, the goal for the initial treatment of meningioma is complete surgical resection with or without adjuvant radiation therapy [18]. Surgical resection is frequently curative for grade I meningioma [6]. Adjuvant radiation therapy is more commonly used to treat grade II and always grade III meningioma; this is

because of invasion into surrounding tissue that makes complete surgical resection implausible and the higher likelihood of recurrence [19,20,21]. For grade II tumors that are incompletely resected, radiation therapy is also standard [22]. It is less clear when it comes to considering adjuvant radiation therapy for grade II meningiomas for which complete surgical resection is achieved. Radiation therapy is more likely to be incorporated in the treatment plan if the tumor possesses features that portend for recurrence or progression and if the predicted morbidity from therapy is low [23,24].

At this time, there is no demonstrated benefit to the use of systemic chemotherapy after surgery and radiation therapy for treatment refractory tumor burden, recurrent meningiomas or malignant meningiomas. There have been a number of chemotherapeutic agents tried for treatment of recurrent or malignant tumors; amongst these are hydroxyurea, temozolomide, cyclophosphamide, doxorubicin and vincristine [25-28]. Results have been disappointing as there is no conclusive evidence that any of these agents have significant potential in altering the biology of the tumor(s) and improving clinical outcomes.

Other medical strategies that have attempted to exploit specific aspects of the biology of recurrent or metastatic grade II and grade III tumors do not as yet appear to have demonstrated benefit. These include use of estrogen/progesterone receptor inhibitors, EGFR tyrosine kinase receptor inhibitors, the angiogenesis inhibitor bevacuzimab, interferon alfa-2b, and somatostatin analogs [25,29,30-32].

Immunotherapy is a novel approach that appears to have promise for systemic treatment of recurrent and metastatic meningiomas. It attempts to change the mechanisms by which high grade meningiomas inhibit the immune response in the immediate area of tumor growth. Studies have demonstrated that PD-L1 expression is increased with atypical meningioma cells and may correlate with its more aggressive behavior and poorer prognosis.

Further advances in the understanding and unraveling of the complex and sophisticated biologic profile of meningioma raise hope that soon this will translate into more promising therapeutic applications.

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