hypothesis lies in the presence of hematopoietic precursors within the PMGCT stroma and vessels within the yolk sac tumor component of these tumors. It can be further speculated that expression of hematopoietic growth and differentiation factors in some PMGCT could drive the differentiation of primordial germ cells into hematopoietic progeny. The differentiation factors involved may be responsible for the preferred commitment of the transformed precursors to megakaryocytic and monocytic lineage. Additionally, in a few cases of PMGCT-associated leukemia in which the immunophenotype of the leukemic cells was compared with that of the intratumoral hematopoietic precursors, a comparable result was observed. This suggests a spread of hematopoietic tumor cells from the PMGCT to blood, bone marrow, and/or extramedullary sites. The median time for the development of hematologic neoplasia associated with PMGCT is 6 months (range, 0 to 47 months). The clinical course of the hematopoietic neoplasia is very aggressive with a median survival of 5 months (range, 0 to 16 months) after diagnosis. Hematologic malignancies occurring in patients with PMGCT are thought to be primary, and not therapy related. In some cases, immunohistochemical and cytogenetic evidence (especially presence of 11p chromosome) had previously suggested the clonal relationship between the PMGCT and the hematologic malignancy. As in other previously reported cases, the short interval between the PMGCT and the occurrence of the hematopoietic malignancy argues against a therapy-related origin of the acute megakaryocytic leukemia. There have been two reported cases of PMGCT complicated by acute megakaryocytic leukemia, one presenting with an extradural mass and the other with organomegaly. However, our patient is the first, to our knowledge, to be ever reported in English literature of a PMGCT evolving into an extramedullary acute megakaryocytic leukemia manifesting as a mass causing cord compression. Furthermore, the aggressive course of the acute megakaryoblastic leukemia involving the CNS with sparing of the bone marrow is striking.

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References

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Metastasis of a Histologically Benign—Appearing Meningioma to the Iliac Bone

A 78-year-old woman with a history of recurrent frontal parafalcine meningioma presented with a 10-month history of progressive right hip pain. Meningioma was originally diagnosed at age 69 years, when she presented with an enhancing frontal, parafalcine, dural-based mass on magnetic resonance imaging scan (Fig 1A). She underwent near-total surgical resection followed by 34 fractions of adjuvant external beam radiation therapy. Pathology showed transitional type menigioma with rare foci of necrosis and a few prominent nucleoli but no sheeting, small cells, or evidence of brain invasion, consistent with WHO grade 1 meningioma (Table 1). Eight years later she developed headache and lower extremity spasticity. Magnetic resonance imaging confirmed recurrence of two lobulated, bilateral frontal parafalcine meningiomas (Fig 1B). She underwent a second partial tumor resection. Histological examination again revealed grade 1 transitional-type meningioma. Concurrently with the symptoms of her recurrent meningioma, she developed progressive right hip pain interfering with ambulation. She was diagnosed with trochanteric bursitis and treated with analgesics. Over the ensuing 10 months, her pain gradually worsened, eventually leaving her wheelchair-bound.
Physical examination revealed tenderness of the right groin and hip and weakness of right hip flexion, abduction, and adduction. Imaging showed a well-circumscribed lytic lesion involving the right iliac wing (Fig 2, arrowheads), a pathologic fracture of the superior acetabulum (Fig 2, arrows), and a large soft tissue mass. Immunohistochemical studies of biopsy samples were positive for epithelial membrane antigen and negative for S-100, supporting the diagnosis of meningioma. Histological examination again revealed grade 1 meningioma with prominent whorls (Fig 3A, arrows). The Ki-67 proliferation index was markedly elevated at 10% (Fig 3B, brown nuclei). The patient underwent operative excision. In contrast to the computed tomography biopsy, the resection specimen showed foci of prominent nucleoli, foci of hypercellularity, small cells with high nuclear/cytoplasmic ratios, and some patternless growth. Although mitotic activity did not exceed four cells per 10 high power fields (Table 1), the Ki-67 proliferation index was locally 14% (Fig 3C). These histological features correspond to an atypical meningioma.

Meningiomas are the most common benign tumors of the brain, representing 20% to 30% of all intracranial tumors. Local invasion and distant metastasis of intracranial meningiomas have been described in the medical literature, but are rare. Access to the blood is thought to occur through the system of dural venous sinuses. Approximately 75% of meningioma metastases are associated with prior intracranial surgery or direct invasion of a venous sinus. The lungs are the most common site for meningioma metastasis, followed by liver, bones, pleura, mediastinum, and lymph nodes. Our patient had metastatic spread of meningioma to the iliac bone. To our knowledge, this is the first case of metastasis to the extra-axial bony pelvis reported in the medical literature. The route of metastasis in our patient is unclear, but may have been through the superior sagittal sinus and caval system given the parafalcine location of her primary tumors and history of prior intracranial surgery. The recently updated 2007 WHO classification scheme (Table 1) divides meningiomas into three grades based on histology. Greater than 90% of grade 3 tumors exhibit aggressive behavior (local invasion and/or distant metastasis).

<table>
<thead>
<tr>
<th>WHO Grade</th>
<th>Histologic Subtypes</th>
<th>Specific Histologic features</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (benign)</td>
<td>meningothelial, fibroblastic, transitional, angiomatous, microcystic,secretory, lymphoplasmacytic,metaplastic,psammomatous</td>
<td>Does not meet criteria for II or III</td>
</tr>
<tr>
<td>II (atypical)</td>
<td>chordoid, clear cell</td>
<td>≥ 4 mitotic cells per 10 hpf or 3 or more of the following: increased cellularity, small cells, necrosis, prominent nucleoli, sheeting, and brain invasion</td>
</tr>
<tr>
<td>III (anaplastic/malignant)</td>
<td>papillary, rhabdoid</td>
<td>≥ 20 or more mitoses per 10 hpf or tumor cells resemble malignant carcinoma, sarcoma, or melanoma</td>
</tr>
</tbody>
</table>

Abbreviation: hpf, high power fields.
Grade 1 tumors almost never metastasize or invade adjacent structures. However, as this case demonstrates, a subset of grade 1 meningiomas can have malignant potential. One potential predictor of aggressive meningioma is the Ki-67 index, a marker of cell proliferation. The Ki-67 proliferative index (PI) has been identified as an independent predictor of both survival and tumor recurrence in meningiomas, but is not part of the WHO staging system. In a retrospective study by Ohta et al., recurrent meningiomas had a mean PI of 5.7%, metastatic meningiomas had a mean PI of 14.7%, and non-recurrent, non-metastatic meningiomas had a mean PI of 1%. In addition to PI, primary tumor appearance on imaging may be useful. One study indicated that multiple lobulations and a "mushrooming" appearance may correlate with malignant potential. Based on these criteria, our patient’s initial imaging studies (Figs 1A and 1B) may have been an early clue to the aggressive nature of her disease, though the prolonged time course between initial surgery and symptoms of recurrent disease is not compatible. In summary, most meningiomas are benign and never undergo malignant transformation. However, a small subset of meningiomas, usually those with atypical histological features, can metastasize. For this reason, we emphasize the importance of considering the possibility of metastasis in patients with a history meningioma who present with symptoms that cannot be explained solely by tumor mass effect in the brain. This is especially true for patients with recurrent meningiomas. The clinician should also consider performing additional tests, like staining for Ki-67, to identify those histologically benign-appearing meningiomas with increased malignant potential.

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**AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

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**REFERENCES**


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**Small-Cell Lung Carcinoma Presenting With Otalgia and Hearing Impairment**

A 79-year-old male presented to the department of otorhinolaryngology due to progressive right otalgia and hearing impairment for 3 months. Pure-tone audiogram revealed increased hearing threshold of the right ear. Local examination disclosed one yellowish round tumor at right external auditory canal. Punch biopsy of the tumor was performed. The pathological examination revealed tumor cells with scant cytoplasm, finely granular nuclear chromatin, and absence of nucleoli (Fig 1A, hematoxylin and eosin staining). Immunohistochemically, the tumor cells are reactive to synaptophysin (Fig 1B), cytokeratin, and thyroid transcription factor 1.