Case Report:
A Rare Case of a Multifocal Extra-Adrenal Myelolipoma with Markedly Hypocellular Bone Marrow

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Abstract. Extra-adrenal myelolipomas are rare, generally solitary, non-functioning tumors consisting of adipose tissue and hematopoetic elements. These lesions are not known to be associated with underlying hematologic disorders or documented bone marrow abnormalities. We describe the extremely rare occurrence of multifocal, extra-adrenal myelolipomas in a 35-yr-old male. A markedly hypocellular bone marrow is noted, despite normal peripheral blood counts. To our knowledge, this is the first case report of a markedly abnormal marrow examination in a patient with extra-adrenal myelolipoma, and implicates the extra-osseous masses as the driving force behind his normal hematopoesis.

Keywords: myelolipoma, bone marrow hypoplasia, extramedulary hematopoiesis

Introduction

Myelolipomas are rare, benign, nonfunctioning tumors, composed of a mixture of adipose tissue and extramedullary hematopoetic elements, that occur outside the bone marrow. These lesions are almost exclusively located in the adrenal glands, though solitary extra-adrenal myelolipomas have been reported in various locations. Since myelolipomas are typically clinically quiescent, and not associated with hematologic disorders, concomitant bone marrow exams have seldom been reported. We have been able to document fewer than 10 evaluations of bone marrow histology in patients diagnosed with myelolipoma; none of these cases demonstrated a hypocellular marrow.

We report a 30-yr-old male who presented with massive, multifocal, thoracic and retroperitoneal myelolipomatous masses. Interestingly, despite a normal peripheral blood hemogram, bone marrow examination revealed severe hypocellularity, suggesting complete dependence on these extra-adrenal masses for hematopoesis. To the best of our knowledge, this is the first reported case of an extra-adrenal myelolipoma that demonstrated such features.

Case Report

A 30-yr-old African-American male, with no prior medical history, presented complaining of nausea, vomiting, and abdominal pain. Physical examination revealed a healthy appearing man in no acute distress. Abdominal palpation demonstrated left flank fullness, with minimal tenderness. Laboratory tests gave the following results: blood leukocytes 5,200/µl with normal differential cell count; blood hemoglobin 15.9 g/dl with a mean corpuscular volume (MCV) of 103 fl; and blood platelet count 147,000/mm3.

Computed tomographic (CT) scan of the abdomen and pelvis revealed bilateral, solid, fatty masses primarily emanating from the renal sinuses (Fig. 1). An 11.5 cm x 9.7 cm mass emanated from

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the right renal sinus, with fat and soft tissue insinuated between vascular structures. A similar soft tissue mass was noted on the left upper aspect of Gerota’s fascia. No lymphadenopathy was noted. The liver and spleen were normal in size, without focal lesions. CT scan of the chest revealed a heterogeneous, fat, soft tissue mass measuring 7.8 x 4.1 cm in the posterior right mediastinum. Bilateral masses adjacent to the lower thoracic spine were noted (1.74 cm on the right, 2.3 cm on the left).

CT-guided biopsy of the abdominal and mediastinal masses revealed hematopoietic elements and mature adipose tissue, consistent with the diagnosis of myelolipoma (Figs. 2A,2B). Bone marrow biopsy revealed <1% cellularity, composed primarily of adipocytes and scant fibroconnective tissue (Fig. 2C). No hematopoietic cells were noted. There was no evidence of fibrosis, granulomatous inflammation, or cells extrinsic to the marrow. A second bone marrow biopsy confirmed these findings.

Cytogenetic analysis revealed a normal male karyotype. A nuclear medicine bone marrow scan with sulfur colloid revealed increased radionuclide activity in the left kidney, inferior and medial right hemithorax, and mid-sacrum, consistent with extramedullary hematopoeisis. In view of the extensive nature of these masses, surgical intervention was felt to be high-risk, and was therefore not pursued.

The patient has been followed as an outpatient for 4.5 yr. Surveillance CT scans have not revealed any significant change in the mass lesions. Serial hemograms have remained essentially normal. The patient has intermittent flank discomfort that is well controlled with oral analgesics.

Discussion

Myelolipomas are rare, tumor-like lesions composed of a variable mixture of mature adipose tissue and hematopoietic elements resembling bone marrow. These lesions most commonly involve the adrenal glands, constituting <4% of adrenal tumors. In this era of improved noninvasive diagnostic imaging, incidental discovery of myelolipomas has become
increasingly common [1]. While many cases are asymptomatic at diagnosis, local tumor extension may lead to nonspecific complaints including abdominal discomfort, nausea, and vomiting. CT findings vary from high-attenuation areas of predominantly hematopoietic elements to low-attenuation areas of adipose tissue [2]. Although the exact etiology and histogenesis of myelolipomas are disputed, endocrine disorders and/or chronic debilitating diseases are believed to play an important role [3]. Specific therapy of these benign lesions is often not required, as most patients are asymptomatic. In fact, <40 cases of myelolipomas have presented with clinical signs and symptoms that required surgical resection [4]. Resection is generally recommended only in cases where the patient is symptomatic, or where progressive tumor growth occurs with ensuing local compression effects. In asymptomatic patients, follow-up with serial CT scans is appropriate.

Although the natural history of myelolipomas has not been clearly defined, these tumors have demonstrated the potential for variable growth and a risk for bleeding. Acute hemorrhage, the most clinically significant complication of these otherwise benign lesions, may present as a sudden onset of pain in the flank or back, nausea, vomiting, hypotension, or rapidly worsening anemia. A study of myelolipomas at the Armed Forces Institute of Pathology by Kenney et al [1] identified 86 lesions in 74 patients. Nine of the patients presented with evidence of acute hemorrhage. The mean tumor diameter in the cases was 14.2 cm. Of the 9 patients with acute hemorrhage, 8 had tumors >10 cm in greatest diameter. The authors suggested that increasing tumor size may be a predictive factor of bleeding risk.

Extra-adrenal myelolipomas (EAML) are infrequent, with an incidence of 0.4% at autopsy, and fewer than 40 cases reported [5]. The typical lesion is a solitary, well-defined mass within the abdomen, commonly in the retroperitoneal presacral area (comprising approximately half of reported cases). Less common sites of involvement include pelvic and hepatic regions, with sporadic cases in thoracic and gastric locations [6]. To our knowledge, only 3 prior cases of multifocal EAML have been reported [1,6]. The sizes of EAML have been reported to range from 4 to 15 cm, with a mean diameter of 8.2 cm [7]. EAML occurs more commonly in women, with a male:female ratio of 1:2. The median age at diagnosis is 66.5 yr.

Extra-adrenal myelolipomas are distinct from true bone marrow in that no reticular sinusoids or bone spicules are present. A strong association of EAML with underlying inflammatory disorders, diabetes, and cardiovascular disease has been described, similar to that seen with adrenal myelolipomas. In Fowler and coworkers’ series of 13 cases of EAML, all were solitary tumors, and usually located within the abdomen [7]. Grossly, these tumors were characteristically well circumscribed, and yellow in color (consistent with a predominance of adipose tissue). Microscopically, mature adipose tissue and hematopoietic cells, including myeloid, erythroid, and megakaryocytic elements, were visualized. Increased aggregates of lymphoid cells have been reported as well, though the nature of these lymphoid cells is not well-established. For instance, in Fowler and coworkers’

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<thead>
<tr>
<th>Epidemiology</th>
<th>Females &gt; males, median age 67 yr</th>
<th>Males &gt; females, median age 44 yr</th>
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<tbody>
<tr>
<td>Clinical characteristics</td>
<td>Well circumscribed, usually in abdomen</td>
<td>Multifocal, propensity for mediastinal involvement, hepatosplenomegaly</td>
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<tr>
<td>Associated conditions</td>
<td>Inflammatory diseases, endocrinopathies</td>
<td>Thalassemias, chronic hemolytic anemias, myeloproliferative disorders</td>
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<tr>
<td>Histopathology</td>
<td>Adipose tissue often predominant, (+) lymphoid aggregates</td>
<td>Erythroid hyperplasia, (-) lymphoid aggregates</td>
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review [7], 8 of 13 cases of EAML were noted with lymphocyte abundance or aggregates on histologic examination. Saboorian et al [8] performed flow cytometric analysis of a presacral extra-adrenal myelolipoma specimen. They reported increased lymphoid aggregates with unremarkable T cells, polyclonal B cells, and a small fraction of NK cells. The authors concluded that these lymphoid aggregates are a benign finding, without phenotypic aberrations or B-cell monoclonality.

The differential diagnosis of EAML depends on the anatomic site of tumor involvement. However, extramedullary hematopoietic tissue (EHT) warrants special mention here. This entity can be difficult to distinguish from EAML, clinically, radiographically, and even histologically in some cases. EHT typically occurs as a secondary or compensatory event in response to underlying hematologic disease, such as hemoglobinopathies, myeloproliferative disorders, or severe skeletal diseases. These patients are often younger than those with EAML (median age 43.7 yr in one series). Seen in the clinical setting of anemia and marked bone marrow hyperplasia, these tumors are often multifocal. Unlike EAML, unexplained splenomegaly (80%) and hepatomegaly (58%) are common [9]. On histologic examination, EHT typically demonstrates higher cellularity, with erythroid hyperplasia universally present. These lesions consist of scattered, poorly circumscribed foci of marrow elements in the spleen, liver, and mediastinum. A predominance of the hematopoietic component (with less fat), and absence of lymphoid aggregates are characteristic; these features are in direct contrast to those of EAML. Several key clinical characteristics that distinguish EHT from EAML are highlighted in Fowler and coworkers’ review [7]. In this series, diagnosis of EAML required exclusion of: (a) known anemia, (b) diffuse extramedullary hematopoiesis in other tissues, or (c) unexplained splenomegaly (see Table 1).

Several features of our case stand out as rare or unique from those previously reported in the myelolipoma literature. Very rarely have extra-adrenal myelolipomas been reported to occur with a multifocal distribution. The most unusual feature of our case, however, centers around the accompanying bone marrow findings. Bone marrow analysis has been performed in a limited number of myelolipoma cases; these marrows were all essentially normal or unremarkable. Our case is the first reported patient with markedly hypocellular bone marrow in association with a myelolipoma or extramedullary hematopoiesis. The exact classification of this patient remains unclear, as does the underlying etiology. Further assessment of cases of myelolipomas and extramedullary hematopoietic tumors, particularly with bone marrow analysis, may be helpful in the future.

References