

# A Rare Case of Bone Marrow Metastasis of a Splenic Angiosarcoma

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## Citation

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## Abstract

We report a rare finding of bone marrow metastasis from an angiosarcoma of the spleen with secondary involvement of the liver. The patient was a 43-year-old woman who initially presented with anemia, thrombocytopenia, and a high-grade angiosarcoma of the spleen with focal metastasis to liver. She was later treated with chemotherapy but continued to be anemic and thrombocytopenic. Bone marrow biopsy revealed moderate infiltration by angiosarcoma with typical features of spindle tumor cells and anastomosing vascular channels. Immunohistochemical studies revealed the tumor cells to express the endothelial markers CD31, CD34, and factor VIII. Angiosarcomas are rare and aggressive tumors. Although angiosarcomas frequently metastasize to the solid organs, bone marrow metastasis has been rarely documented. However, in view of several other reported cases of angiosarcoma of the spleen with metastasis to the bone marrow, it has been proposed that angiosarcomas have a rare propensity for bone marrow infiltration.

## INTRODUCTION

Metastasis of solid tumors to the bone marrow is a common occurrence that occurs via the bloodstream. Micrometastases have been demonstrated in the bone marrow of 30- 75% of patients with common malignancies.<sup>1</sup> The solid tumors most frequently detected in bone marrow in adults are carcinomas of the breast, prostate, lung, and gastrointestinal tract, while neuroblastoma, rhabdomyosarcoma, and Ewing sarcoma account for the majority of cases in children.<sup>1,2</sup>

Angiosarcomas are rare neoplasms, comprising only about 1-2% of all soft tissue sarcomas, and bone marrow metastasis is rarely documented. Primary angiosarcomas can develop at any site in the body, but the most common sites are the skin and superficial soft tissues, followed by breast, liver, spleen, and bone.<sup>3,4</sup> Similar to the primary solid tumors, the common sites of metastasis of angiosarcomas are the lungs, liver, and lymph nodes.<sup>3,4</sup> Angiosarcoma metastasizing to the bone marrow has rarely been documented but may result in a variety of outcomes. Micrometastases may occur and remain undetected by conventional staging methods. Conversely, the tumor cells may grow and alter the structure of the bone marrow, resulting in clinically significant metastases. Metastases to the cortical bones often present with bony pain, pathologic fracture, and hypercalcemia, while infiltration of the bone marrow or reactive marrow fibrosis may compromise

hematopoietic functions. The hematologic abnormalities suggestive of marrow infiltration are peripheral cytopenia and/or leukoerythroblastic changes. We report here a patient with primary angiosarcoma of the spleen with liver and bone marrow involvement who had persistent anemia and thrombocytopenia.

## REPORT OF A CASE

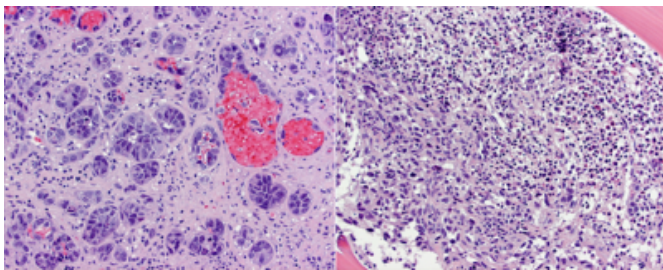
The patient is a 43-year-old woman with history of hepatitis C and intravenous drug abuser who presented with anemia, thrombocytopenia, and an abdominal mass localized to the left upper quadrant. Physical examination revealed abdominal tenderness and splenomegaly. An ultrasound confirmed the enlarged spleen. The liver demonstrated cirrhotic changes with an echogenic mass in the liver. Splenectomy with liver biopsy was carried out for tissue diagnosis and therapeutic purpose. The diagnosis of an angiosarcoma of the spleen was rendered from histologic and immunochemical evaluation of the tissue. However, since the patient continued to have anemia and thrombocytopenia, a bone marrow biopsy was carried out after 2 weeks post-splenectomy.

The splenic parenchyma was extensively effaced by high-grade angiosarcoma morphologically similar to that found in the liver and bone marrow. The tumor infiltrate had solid areas of spindled and polygonal cells and abundant vascular

spaces. The vasoformative process included focal spongiform architecture and large lumina containing blood cells (Fig. 1a). The vascular spaces were lined by a row of plump and protruding endothelial cells. There were occasional large multinucleated cells and mitotic figures (Fig. 1a). The diagnosis of angiosarcoma was confirmed by positive immunohistochemical stains for CD31, CD34, and Factor VIII. Metastatic angiosarcoma was also noted within the liver in portal vasculature and hepatic sinusoids. Extramedullary hematopoiesis was also found in the liver.

### Figure 1

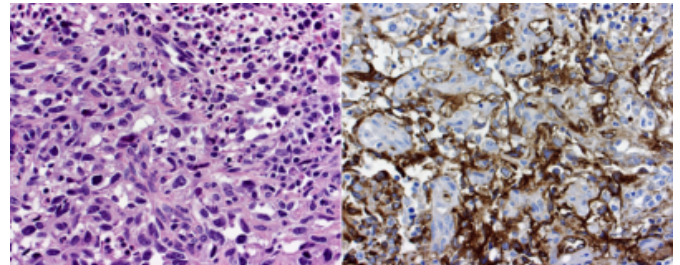
Fig. 1a (left). Primary angiosarcoma of the spleen shows massive infiltrate and vascular luminal formation lined by a row of plump and protruding neoplastic endothelial cells. The spleen was almost completely replaced by high grade angiosarcoma (hematoxylin-eosin, original magnification x200). Fig. 1b (right). Posterior iliac crest bone marrow biopsy effaced by an infiltrate of metastatic angiosarcoma with solid areas of tumor cells and vasoformative process (hematoxylin-eosin, original magnification x200).



The bone marrow core specimen was obtained by trephine biopsy from the posterior iliac crest. The biopsy was adequately decalcified. The bone marrow was hypercellular with an overall marrow cellularity exceeding 90%. The marrow space was extensively fibrotic and effaced in many areas by non-discrete clusters and sheets of pleomorphic neoplastic cells (Fig. 1b). The tumor morphology was characterized by spindled or polygonal epithelioid cells with elongated nuclei, open and clumped chromatin, and small nucleoli with several atypical mitotic figures (Fig. 1c). These tumor cells were forming vascular channels. Immunohistochemical stains were positive for CD31, CD34, and Factor VIII (Fig. 1d). The remaining hematopoietic elements showed normal maturation. The bone marrow aspirate contained frequent cohesive clusters of atypical cells with regular nuclei, fine nuclear chromatin, inconspicuous nucleoli, and abundant deeply basophilic cytoplasm. Normally maturing trilineage hematopoietic cells were admixed with the metastatic tumor cells.

### Figure 2

Fig. 1c (left). Higher magnification of the metastatic angiosarcoma in the bone marrow biopsy (hematoxylin-eosin, original magnification x400). Fig. 1d (right). Immunohistochemical staining of the bone marrow biopsy for CD31 showing strong positive staining of the tumor cell cytoplasm (original magnification x400).



### COMMENT

Angiosarcomas are high-grade, clinically aggressive tumors with a substantial incidence of high local recurrence and distant metastasis. The patient in this report had a history of hepatitis C with liver cirrhosis and developed angiosarcoma of the spleen with metastasis to the liver and the bone marrow. Both the primary tumor of the spleen and metastasis in the bone marrow were characterized by solid areas of poorly differentiated endothelial cells and a vasoformative process. The diagnosis of metastatic angiosarcoma was confirmed by immunohistochemical evaluation of the bone marrow biopsy.

Primary splenic angiosarcoma is a rare highly aggressive neoplasm in which metastases tend to occur early and spread widely. For example, metastatic disease was reported in 69% of the patients in one reported series, 83% in another, and 100% in a third study.<sup>5-7</sup> The incidence of bone marrow involvement in patients with primary splenic angiosarcoma is unclear as bone marrow procedures are not routinely performed in all patients, and the sensitivity of the bone marrow evaluation for metastatic disease is dependent upon the sample volume and other factors. A high incidence of bone marrow metastasis might be expected from the common occurrence of cytopenia in these patients. For example, in a study of forty patients with splenic angiosarcoma, Falk et al. reported a 91% incidence of cytopenia, including anemia (50%), thrombocytopenia (33%), and pancytopenia (22%).<sup>5</sup> Metastases to the bone or bone marrow were found in seven (17%) of these patients. The literature contains many other reported cases of angiosarcoma metastatic to the bone marrow, the majority of which originated from a primary splenic angiosarcoma.<sup>8-11</sup> The clinical and laboratory presentation was similar in many

patients, with the common occurrence of massive splenomegaly and leukoerythroblastic anemia. Raffel and collaborators recently reported a similar patient with splenic angiosarcoma who presented with thrombocytopenia and had extensive lytic bone lesions but a negative bone marrow biopsy. It has been suggested that splenic angiosarcoma may have an apparent propensity to metastasize to the bone marrow, perhaps because of the expression of specific adhesion receptors by the tumor cells.<sup>11</sup> Pathologists should be aware of the existence of this entity, particularly in patients with cytopenia and splenomegaly.

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