

Case Report

Metastatic Alveolar Rhabdomyosarcoma with Extensive Bone Marrow Replacement in an Older Adult

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Keywords

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Abstract

Rhabdomyosarcoma is extremely rare in adults. Metastatic rhabdomyosarcoma can resemble other malignancies, which can delay diagnosis and prompt treatment. This case illustrates an example of metastatic alveolar rhabdomyosarcoma with concurrent bone marrow infiltration. A 67-year-old woman presented with epistaxis and diffuse bone pain. She developed progressive thrombocytopenia requiring platelet transfusions. The patient was initially thought to have leukemia. She was found to have a large sinonasal mass with extensive metastatic disease and bone marrow infiltration. The patient was ultimately diagnosed with metastatic alveolar rhabdomyosarcoma. She was started on chemotherapy with vincristine, actinomycin, and cyclophosphamide. Unfortunately, she died prior to discharge home. Alveolar rhabdomyosarcoma can resemble a primary bone marrow malignancy when it infiltrates the bone marrow. Further investigation is needed to clarify its clinical behavior and expedite diagnosis and treatment.

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Introduction

Rhabdomyosarcoma is exceedingly rare in adults, and it is more common in children [1]. In children, the most common sites of presentation include the head and neck, the genitourinary region, and the extremities [2]. In adults, the most typical site of presentation is the extremities, but initial presentation can occur within the head and neck region [3, 4]. This case demonstrates a unique presentation of metastatic alveolar rhabdomyosarcoma with widespread disease and complete bone marrow infiltration. To date, there are no reported cases of metastatic alveolar rhabdomyosarcoma with concurrent bone marrow infiltration documented in an older adult.

Case Presentation

A 67-year-old woman presented with subacute epistaxis and diffuse bone pain. Her past medical history included poorly differentiated triple-negative infiltrating ductal carcinoma of the left breast and melanoma of the upper lip. Both malignancies were diagnosed and treated 20 years prior to her current presentation. For her breast cancer, she underwent left modified radical mastectomy followed by chemotherapy with doxorubicin and cyclophosphamide and then paclitaxel. Her breast cancer was successfully treated with no evidence of recurrent disease. For her melanoma, she underwent resection but no systemic therapy afterward. There were no other records regarding the details of her melanoma treatment, and no genetic workup appeared to be performed for inherited cancer predispositions.

The patient presented to her outpatient medical oncologist, who treated her for breast cancer, to further evaluate her symptoms. Her labs included a white blood cell count of $13.6 \times 10^3/\mu\text{L}$, hemoglobin 9.4 mg/dL, and platelet count $22,000/\text{mm}^3$. Her platelet count was normal approximately 5 months prior to presentation. Complete blood count differential showed absolute neutrophil count $2,900/\mu\text{L}$, lymphocytes $3,800/\mu\text{L}$, eosinophils $100/\mu\text{L}$, and increased monocytes $2,200/\mu\text{L}$. There were also increased metamyelocytes ($1,000/\mu\text{L}$), myelocytes ($700/\mu\text{L}$), and immature blasts ($400/\mu\text{L}$). Differential diagnosis for her anemia and thrombocytopenia included chemotherapy-related pancytopenia, hemolytic anemia, rheumatological disease, and vitamin deficiency. Serological workup for these differentials was unremarkable, so bone marrow biopsy was performed. Preliminary results of the bone marrow biopsy demonstrated small-round-blue-cell tumor (shown in Fig. 1, 2).

She was subsequently admitted to the hospital due to concern for acute leukemia, especially given her prior chemotherapy. However, initial bone marrow biopsy results showed replacement of the bone marrow by metastatic tumor with expression of neuroendocrine markers (INSM1, CD56, synaptophysin, and chromogranin). Further evaluation of the bone marrow showed diffuse staining for muscle markers (myogenin and desmin), strongly favoring an alveolar rhabdomyosarcoma with some neuroendocrine differentiation. Noncontrast CT of the head demonstrated a large trans-spatial infiltrative mass in the left nasosinal cavity. Further advanced imaging, including MRI of the brain, noted that this mass extended into the skull base and cavity along with widespread lymphadenopathy. CT of the chest, abdomen, and pelvis demonstrated diffuse metastatic disease, including along the spine, thoracic rib cage, lungs, adrenal glands, and spleen. Nuclear bone scan demonstrated heterogeneous appearance of the marrow in the bilateral humeri and proximal femurs.

The biopsy from the left sinonasal mass revealed a malignant epithelioid neoplasm growing deep to the respiratory mucosa (shown in Fig. 3). There were irregular, pleomorphic nuclei with nuclear hyperchromasia and a variable amount of cytoplasm (shown in Fig. 4). A minor population of the cells had eccentrically located eosinophilic cytoplasm, imparting a

Fig. 1. Bone marrow biopsy demonstrating complete infiltrating with small-round-blue-cell tumor (hematoxylin and eosin. $\times 100$).

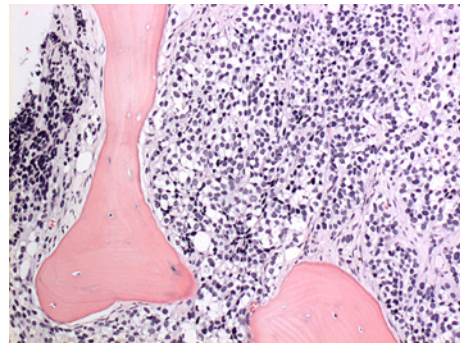


Fig. 2. Higher power of bone marrow biopsy further characterizing small-round-blue cells (hematoxylin and eosin. $\times 400$).

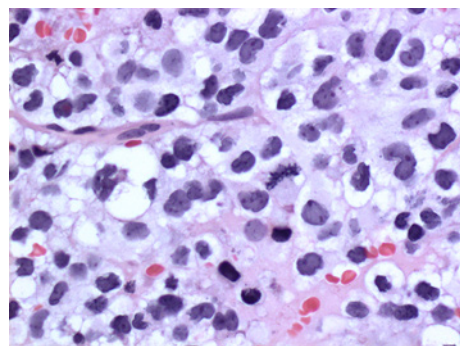
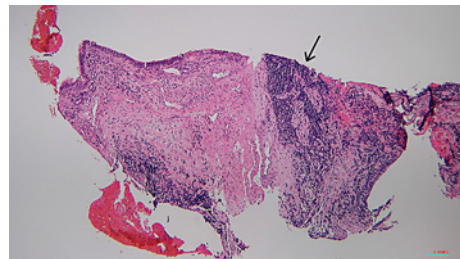


Fig. 3. The biopsy from the left sinonasal mass revealed a malignant epithelioid neoplasm growing deep to the respiratory mucosa (hematoxylin and eosin. $\times 40$; the arrow points to the malignant tumor).



rhabdoid appearance. The tumor cells had strong nuclear expression of myogenin (shown in Fig. 5) and membrane expression of desmin (shown in Fig. 6). FISH and molecular testing on the bone marrow, performed at an outside institution, demonstrated a FOXO1 gene rearrangement, consisting of a PAX3-FOXO1 fusion. Altogether, these findings confirmed the diagnosis of stage IV alveolar rhabdomyosarcoma.

Due to the widespread nature of her disease, she was started on chemotherapy with vincristine (1.5 mg/m^2), actinomycin-D (0.045 mg/m^2), and cyclophosphamide ($1,200 \text{ mg/m}^2$) (VAC) once the PAX3-FOXO1 fusion returned positive. It was approximately 2 weeks between initial bone marrow biopsy and positivity for the fusion study before treatment was initiated. She remained persistently thrombocytopenic, which was complicated by epistaxis and melena during her hospitalization and required multiple transfusions of platelets. The patient experienced acute hypoxic respiratory failure secondary to mucus plugging and aspiration requiring transfer to the intensive care unit. At that point, she declared that she wanted to stop all treatment and proceed with hospice care. Unfortunately, she died prior to discharge home.

Fig. 4. The tumor cells have irregular, pleomorphic nuclei with nuclear hyperchromasia and a variable amount of cytoplasm (hematoxylin and eosin, $\times 400$; the arrow points to a prototypical tumor cell).

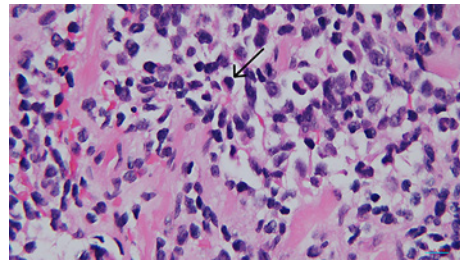


Fig. 5. A minor population of the cells have eccentrically located eosinophilic cytoplasm, imparting a rhabdoid appearance. The tumor cells have strong nuclear expression of myogenin (myogenin immunohistochemistry, $\times 400$; the arrow highlights a tumor cell nucleus with positive nuclear expression).

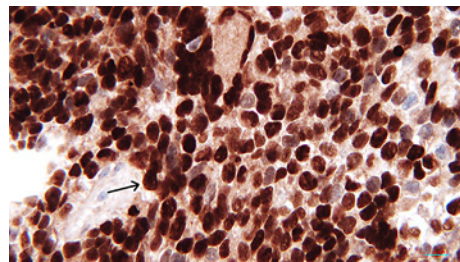
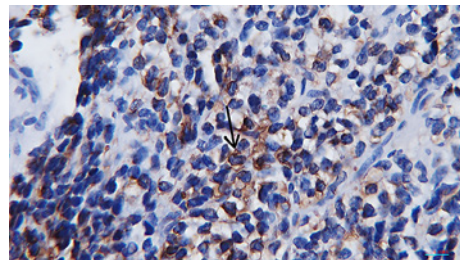


Fig. 6. The tumor cells have strong membrane expression of desmin (desmin immunohistochemistry, $\times 400$; the arrow points to a tumor cell with a thin layer of membrane expression).



Discussion/Conclusion

This report illustrates a case of metastatic rhabdomyosarcoma in an older adult, who initially presented with anemia and severe thrombocytopenia manifested by epistaxis and bone pain due to complete bone marrow infiltration. Prior case reports have demonstrated metastases from initially diagnosed alveolar rhabdomyosarcoma, but they were not concurrent with the initial diagnosis [5, 6]. Bone marrow involvement of alveolar rhabdomyosarcoma is very common in pediatric patients [7, 8]. Alveolar rhabdomyosarcoma has the propensity to invade the bone marrow, so it can be difficult to distinguish from a primary bone marrow process [9].

Previous cases have utilized CD56 positivity and CD45 negativity to differentiate rhabdomyosarcoma from leukemia, but the RNA fusion study for PAX3-FOXO1 was not confirmed in these patients prior to initiating treatment [6, 10, 11]. These reports were also documented in younger to middle-aged patients rather than an older adult as in the present case. Additionally, Aida and colleagues [11] utilized a treatment regimen with vincristine, doxorubicin, and cyclophosphamide due to lack of access to actinomycin-D. The VAC regimen, however, is recommended for high-risk rhabdomyosarcoma patients [12]. Given the propensity to confuse bone marrow involvement from rhabdomyosarcoma with leukemia, confirmation of the diagnosis was prioritized prior to initiating treatment in this patient. For this patient, the RNA fusion study for PAX3-FOXO1 required 2 weeks to result, which led to a delay in

initiation of treatment. However, the patient's prognosis at the time of diagnosis was poor and may have not been changed with earlier treatment initiation. A prior systematic review with meta-analysis has associated the PAX3-FOXO1 fusion with poor prognosis and overall survival [13].

Alveolar rhabdomyosarcoma is a rare diagnosis in adults, and bone marrow replacement is even more uncommon. The clinical behavior of alveolar rhabdomyosarcoma in adults and older adults requires more investigation. Treatment options are primarily based on studies in pediatric patients, so it is difficult to extrapolate efficacious therapies to adults, especially older patients. Future research is needed to clarify these ongoing questions.

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Statement of Ethics

Written informed consent for publication of the case was obtained from the patient's next-of-kin for publication of the details of the medical case and accompanying images. This case was determined to be exempt from approval by the Wake Forest School of Medicine Institutional Review Board.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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There was no funding relevant to this study.

Author Contributions

All authors (J.J.C., R.T.M., P.D.S., and R.K.P.) made substantial contributions to the conception or design of the work, drafting the work, or revising it critically for important intellectual content; made final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability Statement

Data are not readily available due to potential compromise of the identity of the subject.

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