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A Leukemic Presentation of Alveolar Rhabdomyosarcoma in a 52-Year-Old Woman Without an Identifiable Primary Tumor

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Abstract

A 52-year-old woman presented with fatigue and thrombocytopenia. Imaging studies were unremarkable with the exception of a positron emission tomography scan, which demonstrated intense F-18 fluorodeoxyglucose uptake fusing to the marrow. A bone marrow aspirate was notable for large discohesive cells with basophilic cytoplasm, and flow cytometric analysis identified a population of phenotypically unusual cells that coexpressed CD56 and CD71. Immunohistochemical findings in the marrow biopsy demonstrated that the neoplasm was alveolar rhabdomyosarcoma, further supported by the presence of a t(2;13). This unusual case demonstrates that leukemic presentations of rhabdomyosarcoma can occur in older adults in the absence of an identifiable primary tumor.

Keywords

alveolar rhabdomyosarcoma; bone marrow; immunohistochemistry; flow cytometry; cytogenetics

Introduction

Rhabdomyosarcoma (RMS) is the most common soft-tissue tumor of childhood but is rare in adults. The alveolar subtype of rhabdomyosarcoma (ARMS) is most frequently seen in adolescents, and characteristically involves the sinuses, breast, and soft tissue of the extremities, with approximately 23% exhibiting metastasis to the marrow.^{1,2} Here we report an unusual case of ARMS in an older adult that lacked an identifiable primary tumor and mimicked acute leukemia.

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Declaration of Conflicting Interests

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Case Report

A 52-year-old woman presented with fatigue, easy bruising, and a petechial rash, and was found to be thrombocytopenic. She was treated with steroids for presumed idiopathic thrombocytopenia, but subsequently developed disseminated intravascular coagulation. Additional studies showed a leukocytosis with left-shifted granulocytes and circulating nucleated red blood cells. Imaging studies were unremarkable with the exception of a positron emission tomography/computed tomography (PET/CT) scan, which demonstrated intense diffuse F-18 fluorodeoxyglucose (FDG) uptake fusing to the marrow with no other evidence of abnormal focal FDG uptake (Figure 1A). The bone marrow was biopsied, and a cytospin preparation of the aspirate (Figure 1B) showed large atypical cells with round nuclei, fine chromatin, 1 or more nucleoli, and a moderate amount of agranular basophilic cytoplasm. Some of the atypical cells contained cytoplasmic vacuoles, and the cytoplasmic borders were ruffled with occasional blebs. Flow cytometric analysis of the aspirate revealed that 13% of the cells expressed CD56 and CD71, but were negative for CD34, CD117, myeloid, B-cell, T-cell, erythroid and megakaryocytic markers (Figure 1C and D). The marrow space was largely replaced by atypical cells with relatively scant cytoplasm, and thin fibrous septa were seen (Figure 1E). Immunohistochemical stains demonstrated that the tumor cells diffusely expressed CD56, myogenin and desmin, but were negative for CD45, CD43, CD123, AE1/AE3, Cam5.2, CK7, CK20, TTF-1, synaptophysin, chromogranin, and S100 (Figure 1F and G). Cytogenetic studies showed a complex karyotype in 2 of 20 cells: 50,XX,+2,der(2)t(2;13)(q35;q14)x2,add(4)(p16),+5,del(8)(q?11.2q?13),+10,der(13)t(2;13),-20,+mar1,+mar2. The patient was treated with chemo-therapy, but the disease recurred and the patient died approximately 1 year after diagnosis.

Discussion

Very few leukemic presentations of RMS have been reported in patients older than 21 years, and these cases typically show marrow involvement in the setting of a tissue mass.³⁻⁹ Patients with leukemic presentations of RMS often demonstrate cytopenias and can also develop disseminated intravascular coagulation.⁸ The increased FDG uptake throughout the axial skeleton seen on PET/CT scan in this case suggests either bone marrow activation or pathology, and may be seen in profound anemia, thalassemia, myelodysplastic syndrome, leukemia, metastatic marrow infiltration, or after recent administration of chemotherapy or hematopoietic growth factors. In patients who lack such a history, bone marrow biopsy is indicated.

On aspirate smears, the neoplastic cells of ARMS are morphologically similar to leukemic blasts, particularly acute myeloid leukemia (AML) with megakaryocytic differentiation. The cells of ARMS are discohesive and can be detected by flow cytometry. Most cases express CD56, which is also expressed on other neoplasms that involve the bone marrow, including AML, blastic plasmacytoid dendritic cell neoplasm, plasma cell myeloma, peripheral T-cell lymphoma, small cell carcinoma, Merkel cell carcinoma and primitive neuroectodermal tumor/Ewing sarcoma.^{10,11}

On core biopsy, ARMS resembles lymphoma; however, the fibrous septa of ARMS suggest a diagnosis of RMS, which is confirmed by immunohistochemical stains. Diffuse myogenin labeling and expression of desmin and muscle specific actin are characteristic of ARMS. Of note, immunohistochemical studies have demonstrated that several markers that are characteristically associated with hematopoietic neoplasms can be positive in RMS, including ALK-1, Pax-5, and CD20.^{12,13} The occasional aberrant expression of cytokeratins or neuroendocrine markers in ARMS is useful in differentiating RMS from hematopoietic neoplasms; however, it does create potential for a mis-diagnosis of ARMS as small cell carcinoma, which can be resolved if muscle markers are performed.

Cytogenetic testing may also aid in the diagnosis of ARMS. The translocation t(2;13)(q35;q14) is seen in approximately half of ARMS, an alternate t(1;13)(p36;q14) is present in about 20% of cases, and the remainder of morphologically defined ARMS cases lack these translocations.¹⁴ ARMS often contains numerous additional chromosomal aberrancies, which can mimic the complex karyotypes seen in AML.

To our knowledge, this case represents the first case of extensive bone marrow involvement by ARMS in an older adult without an identifiable primary site. Marrow involvement by ARMS is a potential diagnostic pitfall in bone marrow biopsies, and it is important for pathologists and clinicians to be aware of this unusual presentation.

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Figure 1.

A positron emission tomography (PET) scan at the time of diagnosis (A) demonstrates intense F-18 fluorodeoxyglucose (FDG) uptake fusing to the marrow with no other evidence of abnormal focal FDG uptake in a maximum intensity projection. A cytopsin preparation of the aspirate contains scattered large atypical cells with large round nuclei and agranular cytoplasm with occasional vacuoles (1000×) (B). Flow cytometric analysis of the bone marrow shows that the atypical cells (pink) are negative for CD45 with moderate side scatter (C) and CD56 expression (D). The marrow space is largely replaced by medium to large atypical cells with scant to moderate amounts of cytoplasm that are separated by occasional thin fibrous septa (E). The atypical cells express CD56 (F) and myogenin (G).