EXTRAMEDULLARY ACUTE MYELOID LEUKEMIA: TESTICULAR MYELOID LEUKEMIA, LEUKEMIA CUTIS WITH LEPTOMENINGEAL INVOLVEMENT

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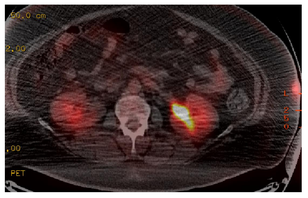
INTRODUCTION

Myeloid sarcoma also called granulocytic sarcoma, myeloblastoma, or chloroma is an extramedullary tumor of immature granulocytic cells. Extramedullary soft tissue manifestations are relatively rare in hematological malignancies. One of the rarest manifestations is myeloid sarcoma (MS). MS develops as part of acute myeloid leukemia, myeloproliferative neoplasm, or myelodysplastic syndrome or at relapse, especially following allogeneic hematopoietic stem cell transplant. Demographically, it has a slight male predominance with a male to female ratio of 1.2: 1. It may occur at any age and any site in the body leading to very varied clinical presentations. We report a rare case of extra medullary myeloid sarcoma appearing in testes and skin with leptomeningeal involvement.

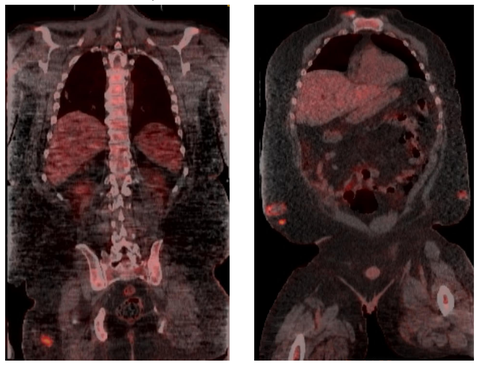
Patient Description

44-year-old Caucasian male with past medical history of morbid obesity, hypertension, hyperlipidemia and diabetes mellitus type 2.
-Family history of colon cancer in mother and uterine cancer in sister.

Clinical, Histopathology & Radiology images



PET scan post orchiectomy soft tissue nodules within the subcutaneous tissues of the abdominal wall on the left exhibit increased tracer activity.



PET scan post induction chemotherapy showing multiple areas of hypermetabolic foci involving nodular densities of bilateral lower anterior abdominal wall and subcutaneous stranding of bilateral buttock. Relatively homogeneous FDG uptake throughout the marrow compartment of visualized osseous structures. A focal uptake involving right proximal clavicle compatible with active metastatic disease.

Initial Presentation with Extramedullary Testicular mass

Month 1- Right Testicular pain

- Patient presented with right testicular pain and swelling and underwent radical orchiectomy.
- Pathology reported seminoma and received adjuvant carboplatin for pT3 disease.

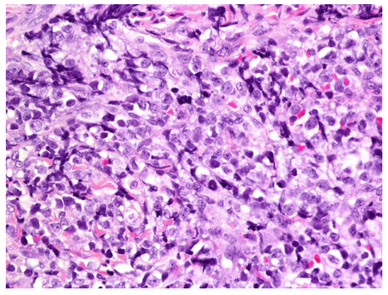
Month 3- Left Testicular pain

- Patient underwent left radical orchiectomy the following month.
- Pathology reported CD4(+), CD56(+) high grade hematopoietic neoplasm. Scattered nonspecific CD68, CD14, CD123 and diffuse CD163 and CD33 expression. Negative for morphologic evidence of a seminoma. Sent for review at NCI (Jaffe): Immature hematopoietic neoplasm most consistent with myeloid sarcoma with monoblastic features. UNC pathology concurred with myeloid sarcoma. Repeat evaluation of Right testicular specimen was CD45+.
- Myeloid mutation screening by NeoType Analysis identified a mutation of known or likely clinical significance in NRAS G13D; pertinent negatives include FLT3, IDH1, and IDH2

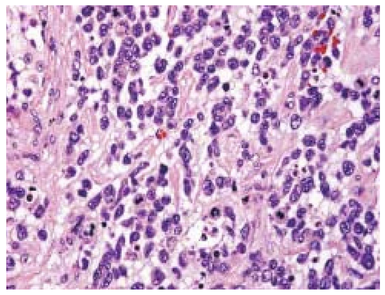
Initial Diagnosis AML, extramedullary, leptomeningeal disease

Month 5- Month 7

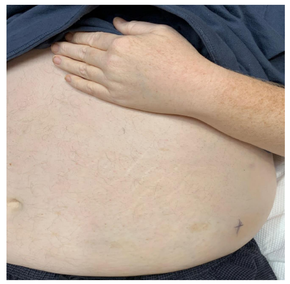
- Admitted with severe pain in bilateral lower extremities and inability to bear weight with numbness in buttocks and anal area. MRI L-spine showed evidence of diffuse leptomeningeal metastatic disease. Bony metastases at T12 and L3. Extraosseous extension of metastatic lesion in the right L3 posterior elements. 3.8 x 2.9 cm
- Bone marrow biopsy showed normocellular marrow with multilineage hematopoiesis. Negative for evidence of myelodysplasia, myelo or lymphoproliferative or acute leukemia.
- PET scan revealing 8.0 SUV focus of hyper metabolic activity in the right hemi scrotum concerning for locally recurrent disease. There were widespread osseous areas of increased uptake, consistent with metastatic disease. 3 soft tissue nodules within the subcutaneous tissues of the abdominal wall on the left exhibit increased tracer activity.
- FNA of the subcutaneous nodule showed CD56 positive monocytoid cells.
- Induction chemotherapy with 7+3 (Cytarabine 100 mg/m2, Daunorubicin 90mg/m2) with Gemtuzumab ozogamicin 3mg/m2 on day 1, 4, 7 was completed.
- Cerebrospinal fluid studies showed monoblastic/monocytic proliferation and patient received intrathecal (IT) chemotherapy alternating between methotrexate and cytarabine every week. CSF studies were cleared after 2 IT chemotherapy. Patient underwent placement of ommaya reservoir.
- Patient remained in the hospital for 87 days due to poor count recovery and developed pulmonary embolism. He required inpatient rehab for 12 days prior to being discharged to begin his next chemotherapy cycle.



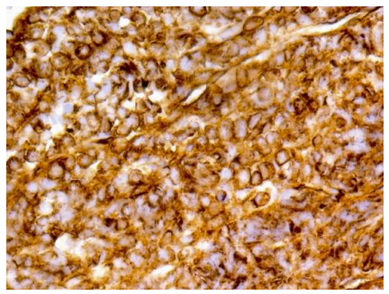
Leukemia cutis, or myeloid sarcoma of the skin. Low power magnification demonstrating an infiltrate of atypical cells with round to irregular nuclear contours, fine chromatin, conspicuous nucleoli, and pale cytoplasm.



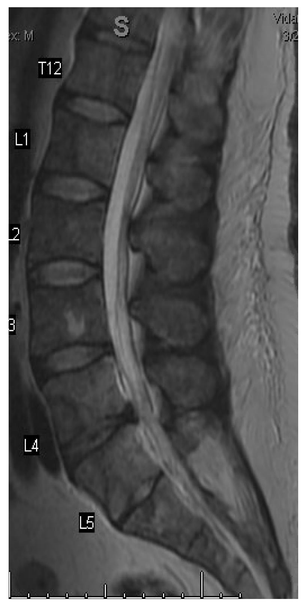
Myeloid sarcoma involving testes, neoplastic cells have folded nuclei and abundant cytoplasm



Left lower abdominal wall, subcutaneous nodule marked by x.



CD56 immunohistochemical staining identifies the neoplastic cells (100×)



MRI Lumbar spine showing marked interval progression of bony metastatic disease. No pathologic fracture. Mild interval progression of intradural metastatic disease.

Consolidation Therapy

Month 8- Month 9

- He was started on high dose cytarabine (HiDAC) for consolidation. Repeat PET scan showed 7 areas of hypermetabolic foci involving nodular densities of bilateral lower anterior abdominal wall and subcutaneous stranding of bilateral buttock. Biopsy of these lesion were negative.
- He completed 2 cycles of HiDAC but had repeated hospital admissions and therapy was switched to azacytidine and venetoclax.
- Patient was seen by bone marrow transplant team and plan was for haplo (if possible) or MMUD Match: 9/10 available from registry,2 half siblings were being typed.

Month 10- Month 11

- Patient presented with severe throbbing lower back pain associated with bilateral lower extremity heaviness and weakness. He had also developed cellulitis at the site of ommaya reservoir.
- MRI brain showed new patchy T2/FLAIR hyperintense signal in the adjacent right frontal white matter/corpus striatum and minimal, smooth ependymal enhancement in the lateral ventricles. Increased number and size of marrow replacing lesions throughout the visualized skeleton concerning for metastatic disease.
- Patient underwent right iliac bone biopsy that showed >90% marrow involvement of previously diagnosed myeloid sarcoma (sheets of infiltrative cells with identical phenotype). Cytology is small round blue cells with somewhat eccentric cytoplasm and a degree of maturation characterized by variable nuclear complexity. Positive for CD56 (>90% of marrow cellularity), CD4 and lysozyme. Possible small subset for CD68. Negative for: synaptophysin, chromogranin, S100, CD117, CD34, CD20, CD3, CD8, MPO, CD138.
- Hospital course was complicated with acute kidney injury, electrolytes imbalance concerning for spontaneous tumor lysis syndrome. He became hemodynamically unstable and transferred to critical care for vasopressor support.
- Once patient was stabilized, discussions were held for re-induction of chemotherapy with CLAG (G-CSF 300 mcg sc, cladribine 5 mg/m^2 over 2 hours, and cytarabine 2 gm/m^2 over 4 hours beginning 2 hours after cladribine, all daily times 5 days) vs palliative care consult.
- Patient made the decision of pursuing comfort care collectively with his family and forego any aggressive treatment. He was transferred to palliative floor and passed away peacefully.

DISCUSSION

This case highlights a rare unique presentation of AML as myeloid sarcoma of testis with normal bone marrow. Misdiagnosis is not uncommon and can delay the appropriate treatment. Extra medullary involvement from leukemia is very aggressive and needs high suspicious and prompt treatment. Systemic chemotherapy using AML-like regimens should be commenced early, even in non leukemic disease. Allogeneic hematopoietic stem cell transplantation has demonstrated promising results, particularly in patients who achieved complete remission with AML-induction protocols, and recent advances in genetic profiling may enable the development of novel targeted therapies. Prospective multicenter controlled trials are required to further refine management decisions and investigate the role of novel targeted therapies.

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