A Rare Cutaneous Harbinger of Acute Leukemia: A Case Report

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A Rare Cutaneous Harbinger of Acute Leukemia: A Case Report

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Background

- Acute myeloid leukemia (AML) is arrested maturation and uncontrolled proliferation of a group of hematopoietic progenitor cells.[1] Clinical presentation varies (Table 1).
- Leukemia cutis(LC) is invasion of neoplastic precursors into different layers of the skin commonly associated with underlying systemic disease, first described in 1895 by Hindenberg and Hirschlaff.[5-6]
- If LC develops prior to blasts appearing in peripheral blood or bone marrow, it is aleukemic leukemia cutis (ALC). ALC is extremely difficult to diagnose clinically and early recognition is essential for initiation of treatment.

Table 1. Clinical Presentaiton of AML [2-4]

• Pancytopenia complications
  • Anemia: fatigue, weakness, skin pallor
  • Thrombocytopenia: gingival bleeding, ecchymosis, epistaxis, petechiae
  • Leukopenia: varying degrees of infections

• Extramedullary sites
  • Gingival infiltrates
  • Cutaneous lesions: vasculitis, **Leukemia Cutis**
  • Myeloid sarcoma: intestines, mediastinum, uterus, ovary, lymph nodes, orbit

• Bone Pain/Arthralgias
• CNS involvement: headache, facial nerve palsies, motor deficits
• Fever: infection > leukemia
• Adenopathy: palpable and significant enlargement is rare
• Organomegaly

Case Presentation

- A 59 year-old-female presents with **generalized weakness, low grade fevers and weight loss** over 2 months with bilateral ankle arthralgias and **maculopapular, nonpruritic rash on abdomen** (Image 1) developing after ~1.5 months.
- **Peripheral blood** (image 2)showed **leukocytosis with 70% monocytes** but flow cytometry showed **fully mature cells** with no aberrant phenotype. Comprehensive rheumatologic, infectious and endocrine work-ups were negative.
- **Skin biopsy** (image 3) showed a mononuclear cell infiltrate, with round/slightly convoluted nuclei, moderately dispersed chromatin consistent with **leukemia cutis**.
- **Bone marrow biopsy** (image 4) showed **82% blasts** expressing monocytic markers consistent with **acute monoblastic (M5) leukemia,** +FLT3-ITD, NPM1 and -CEBPA, CD34.
- Right sided facial droop developed. LP negative for leukemic involvement.
- **7+3 induction chemotherapy** with idarubicin and cytarabine initiated. In remission at 3 month follow-up. To bridge for **allogeneic stem cell transplant,** 2 cycles of high dose cytarabine and 1 cycle decitabine were administered.

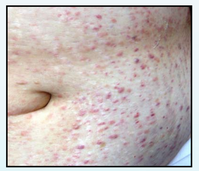

Image 1. Maculopapular, erythematous/violaceous, non-pruritic rash that erupted gradually on patient abdomen and back prior to spreading to the extremities. Rash did not improve with systemic steroids but resolved with 7+3 induction chemotherapy.

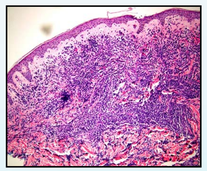

Image 2. Peripheral blood smear shows large amount of mature monocytes with no evidence of dysplasia (A). Smear was taken same time as skin biopsy. Flow cytometry indicates the large monocyte population (B).

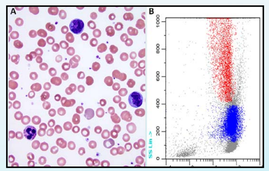

Image 3. Skin biopsy shows monocytic infiltrate consistent with leukemia cutis with the dermis exhibiting overwhelming immature monocytic infiltrates positive for MPO,CD68, CD45, CD33, CD68, CD4. Biopsy was performed after 3 weeks of maculopapular rash present with a peripheral blood smear that showed only mature monocytosis.

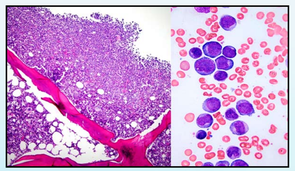

Image 4. Bone marrow biopsy with 82% monoblasts with diminished maturation. +CD56 and –CD117 assist with the M5 AML diagnosis. +FLT3 ITD, NPM1 and – CEBPA, confirming with a poor prognosis and aggressive disease.

Discussion:

- AML is the clinical expansion of >20% myeloid blasts in peripheral blood or bone marrow that involve one or all myeloid lineage.[7]
  - Classified into favorable, intermediate, and unfavorable based on cytogenetics.[1]
- Skin manifestation of AML are rare, occurring 5-15% adults and more common in M5 with ~10-30% skin involvement.[7-8]
  - LC is more common in systemic disease, occurring aleukemic in 7%.[5]
    - ALC : skin infiltration prior to appearance in blood or bone marrow by~1 month.[5]
- Skin lesions vary making diagnosis difficult without a biopsy. (Table 2)
  - LC represent aggressive disease, higher tumor burden with poor prognosis, but shorter time to remission.[7-9]
  - Increase risk for relapse and new skin lesions require re-biopsy.[9]
  - CD markers associated with AML M5 with LC are + CD45, 56, 33, 4 and – CD117, 68, 34, MPO.[7]
- ALC should prompt bone marrow biopsy and chemotherapy initiation irrespective to bone marrow status.
  - Stem cell transplant considered in first remission with other prognostic factors.[9]
  - Chemotherapy may induce remission in bone marrow but not with LC.[9]
  - Palliative radiation can help with pruritus.[9]

Table 2. Leukemia Cutis Characteristics[5,7-9]

Size/Shape		Color	Distribution
Macules	Solitary	Red	Lower Extremity
Papules	Multiple	Brown	Upper Extremity
Plaques		Violaceous	Trunk/Face
Nodules		Blueberry (infants)	
Ulcers			• Areas of inflammation/trauma • Physiologic response to specific chemotactic factors

Conclusion:

AML should be suspected in patients presenting with skin lesions, low grade fevers, weight loss and leukocytosis despite lack of leukemic cells in peripheral blood. Treatment should not be delayed and initiated based on skin biopsy.

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