Congenital Leukemia Cutis Misdiagnosed as Benign Neonatal Hemangiomatosis

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Birth History

- 3600-g female born at 38 1/7 weeks
- G2P0→1 mother via uncomplicated cesarian section (previous myomectomy)
- Numerous violaceous nodules on head, neck, groin > trunk and extremities at birth
- APGAR scores of 9 at 1 and 5 minutes

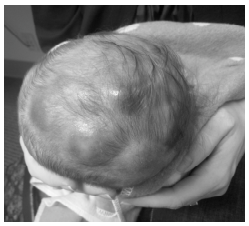
Hospital Course

- Transferred to the NICU for further workup
- Labs:
  - WBC 12.2 _ Liver & renal function, coags normal
  - Hb 19 _ TORCH serologies negative
  - Platelets: 159 _ Neuroblastoma markers (VMA, HVA) negative
- Imaging
  - CXR normal _ MRI head normal
  - Abdominal U/S normal _ ECHO normal

Hospital Course

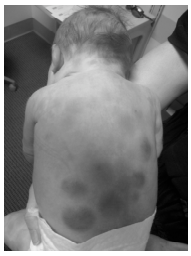
- No dermatology consult obtained
- Presumptive diagnosis of benign neonatal hemangiomatosis given by primary team
- Discharged on 5th day of life
- Presented to UCLA dermatology at day of life 21 with enlarging skin nodules

Physical Examination



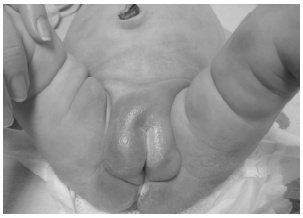
Discrete violaceous nodules on the scalp

Physical Examination



Numerous large violaceous nodules on back, also purpuric patches

Physical Examination

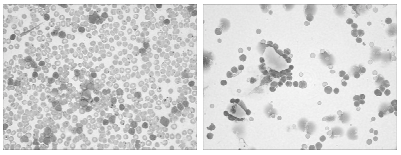


Labia majora with firm violaceous confluent nodules, purpuric macules

Diagnostic Workup

- CBC at 21 days:
  - WBC: 266 with 73% blasts
  - Platelets: 53
- Peripheral smear: 92% blasts
- Flow cytometry:
  - 95% blasts
  - PAX 5 +, CD10 +, CD19 +, CD34 +, CD79 +
  - TdT –, CD117 -
  - + MLL gene rearrangement

Peripheral Smear



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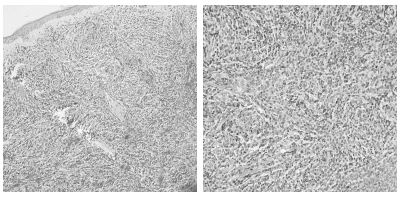
Histology



Skin biopsy of scalp nodule was performed, and showed dermal infiltration by blastic cells c/w precursor b cell acute lymphoblastic leukemia/lymphoma.

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Admission

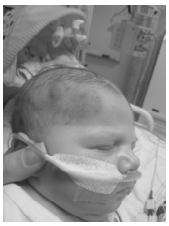
- Diagnosis: Congenital B cell leukemia with leukemia cutis
- CSF: 95% blasts
- Bone marrow: 10% blasts
- Induction chemotherapy:
  - Vincristine, cytoxan, asparaginase, & duanorubicin
  - Intrathecal MTX, cytarabine, hydrocortisone

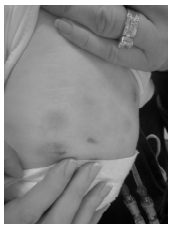
Intrathecal for CNS disease

Hospital Course

- Complicated by tumor lysis syndrome
  - Hyperuricemia, hyperkalemia
  - Required hemodialysis
- Cutaneous lesions began to regress 7 days into induction therapy
- Plan for stem cell transplant

Day 7 of Induction Therapy





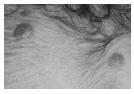
Congenital Leukemia Cutis

Congenital Leukemia

- Presents at birth or within first month of life
- Incidence: 1 per 5 million births
- Fewer than 200 cases reported
- 25% have leukemia cutis
  - Direct infiltration of skin/subQ by malignant cells
- Acute myelogenous leukemia (AML) is most common
  - Acute lymphoblastic leukemia (ALL) represents <10% cases

Rare

Presentation



- Hyperleukocytosis
- Hepatosplenomegaly
- Central nervous system involvement
- Leukemia cutis
  - 'Blueberry muffin baby'
    - Multiple firm violaceous nodules on head and trunk
    - Purpura, petechiae, echymoses

Pathogenesis of Congenital Leukemia

- Mixed lineage leukemia (MLL) gene
  - Chromosome 11 band q23
  - Role in hematopoiesis
  - Most commonly involved gene
  - Rearranged in 80% congenital ALL, 60% AML
- + MLL translocation → poorer prognosis

MLL: encodes a 431 Kda protein.
MLL rearrangements are rare In noninfant leukemias, but are seen in leukemias treated with chemo agents that target topoisomerases II
Maternal consumption of products that inhibit topoisomerases may contribute to the development of congenital leukemia

Differential Diagnosis Blueberry Muffin Baby

- Induction of neonatal dermal erythropoiesis
  - Congenital infections
    - Rubella
    - Coxsackie virus
    - Cytomegalovirus
    - Toxoplasmosis
  - Hemolytic disease
    - ABO or Rh incompatibility
    - Hereditary spherocytosis
- Infiltrative cutaneous processes
  - Leukemia cutis
  - Metastatic neuroblastoma
  - Malignant histiocytosis
  - Langerhans cell histiocytosis
- Transient myeloproliferative disorder

Neuroblastoma: blue firm nodules with persistent blanching after rubbing 2/2 local catecholamine release
LCH: can present as nodules and purpura, but more commonly is diffuse blisters and pustules leading to erosions

Congenital Leukemia Diagnostic Criteria

1. Presentation at birth or within first 4 weeks of life
2. Proliferation of immature white blood cells
3. Infiltration of immature white blood cells into extrahematopoietic tissue
4. Absence of other diseases mimicking leukemia cutis

Must meet all 4 diagnostic criteria

Treatment

- 3 phases:
  - Remission-induction phase
    - Glucocorticoid, vincristine, asparaginase, & an anthracycline
  - Consolidation phase
    - High-dose MTX, 6-mercaptopurine
  - Continuation therapy
    - Intrathecal MTX Q 3 months, vincristine Qmonth, 6-MP Qday & MTX Qweek
- Stem cell/bone marrow transplant
- Prevention of tumor lysis syndrome
  - Hyperuricemia, hyperphosphatemia, hypocalcemia, hyperkalemia

goal of induction is to achieve remission or less than 5% blasts in the bone marrow. Induction therapy generally consists of 3-4 drugs

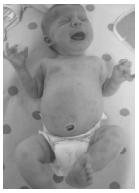
Anthracycline = duanorubicin

Consolidation therapy is given soon after remission is achieved to further reduce the leukemic cell burden before the emergence of drug resistance and relapse in sanctuary sites (ie, testes, CNS). In this phase of therapy, the drugs are given at doses higher than those used during induction or the patient is given different drugs (ie, high-dose MTX and 6-mercaptopurine [6-MP]), epipodophyllotoxins with cytarabine, or multiagent combination therapy. Consolidation therapy also appears to improve the long-term survival of patients with standard-risk disease

Prognosis

- 23% survival at 24 months
- + MLL rearrangement → worse prognosis
- Must have high index of suspicion and low threshold to biopsy
- Consider other etiologies of 'blueberry muffin baby'
- Early cytogenetic analysis

Our Patient…



- Recurrence of scalp nodule 3 months after induction chemotherapy
  - Biopsy proven leukemia
- Failed re-induction chemotherapy with higher doses of same regimen
- Now on comfort care measures

THANK YOU!

References

1. Congenital acute lymphoblastic leukemia: report of a case with leukemia cutis. Akcakus M, et al. Clin Pediatr (Phila). 2004 Jun;43(5):487-90.
2. Congenital leukemia cutis. Fender AB, et al. Pediatr Dermatol. 2008 Jan-Feb;25(1):34-7.
3. Congenital leukemia cutis with subsequent development of leukemia. Zhang IH, et al. J Am Acad Dermatol. 2006 Feb;54(2 Suppl):S22-7.