Case 10

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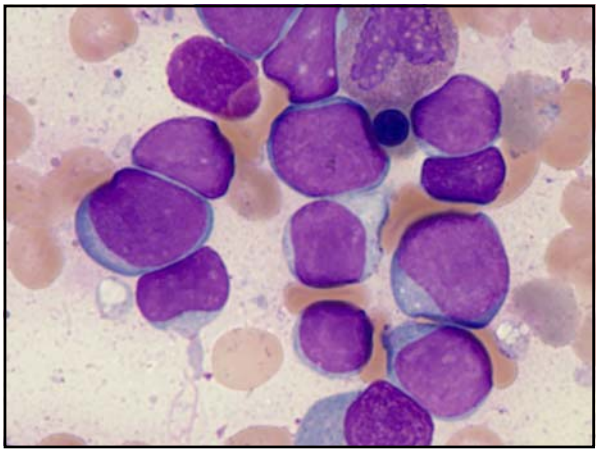
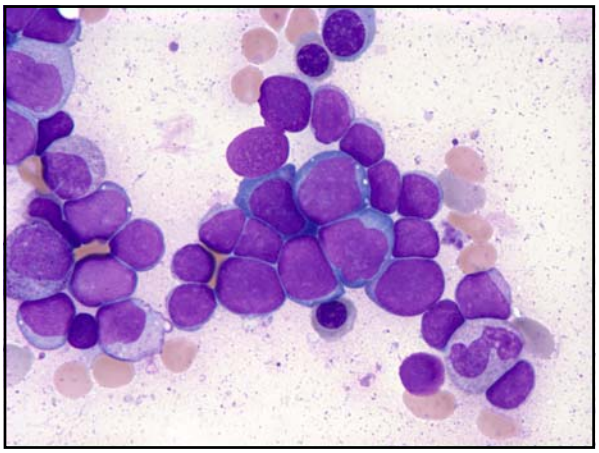
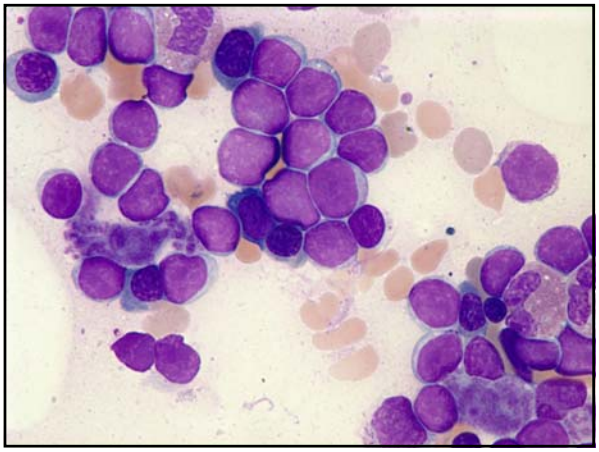
History

- A 3-month-old girl was referred to the pediatric hematology-oncology service for persistent neutropenia. She had been born premature at 32 weeks gestation, with time in NICU. At birth she had a white blood cell count of $9x10^9$/L and an absolute neutrophil count of $1.5x10^9$/L (both within reference range). Over the following 3 months her neutrophil count decreased to as low as $0.5x10^9$/L. A bone marrow aspiration was performed.







Findings

- Acquired anemia/ neutropenia in an infant
- Numerous immature cells in marrow
- Leukemia?

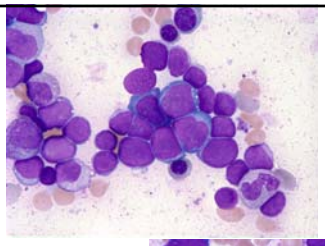
Acute Leukemia in Children

- Signs and symptoms (variable among patients)
  - Fatigue
  - Pallor
  - Petechiae
  - Cytopenias
  - Organomegaly
  - Lymphadenopathy

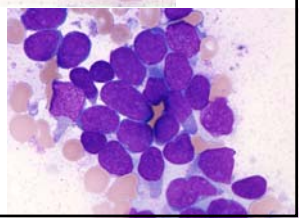
Leukemia?

- Pros
  - Persistent idiopathic cytopenias (neutropenia, anemia)
  - Marked increase in immature cells in marrow (>20%)
- Cons
  - Normal platelet count
  - No leukocytosis (O.K. for A.L.L. but uncommon in infant A.L.L.)
  - Clinically stable, not acutely ill

Our Patient



A.L.L.



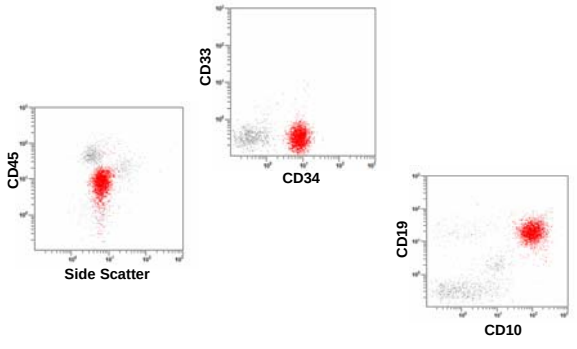
Flow Cytometry

- A.L.L. in children:
  - CD19+, CD10+, CD20+/-, CD22+/-, CD34+/-, CD38+, TdT+

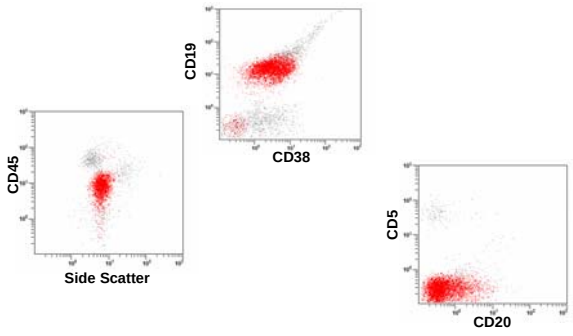
Flow Cytometry

- Our patient:
  - CD19+, CD10+, CD20+/-, CD22+/-, CD34+/-, CD38+, TdT+

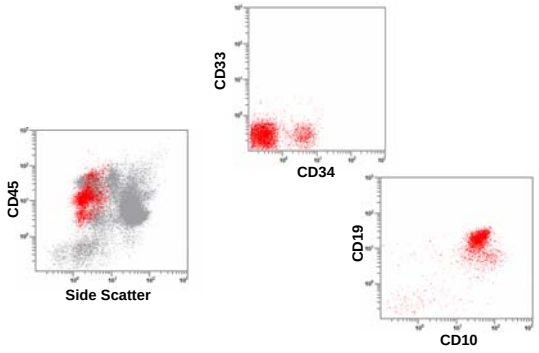
Flow Cytometry – A.L.L.



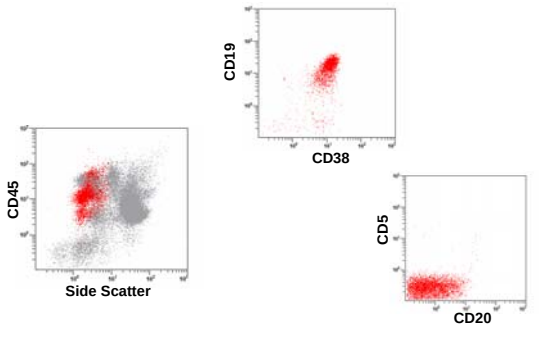
Flow Cytometry – A.L.L.

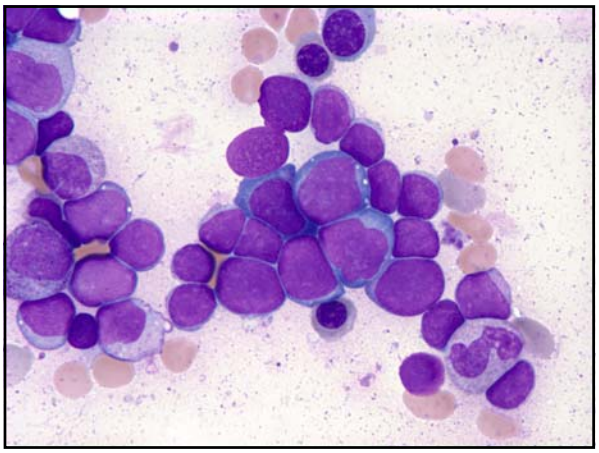


Flow Cytometry – Our Patient

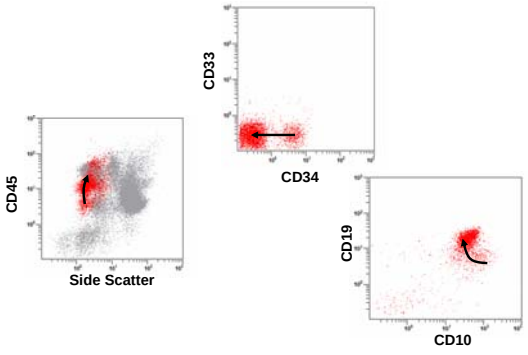


Flow Cytometry – Our Patient

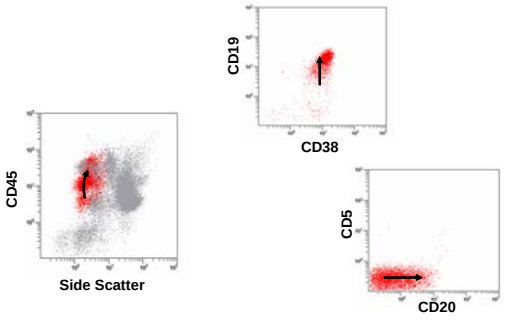




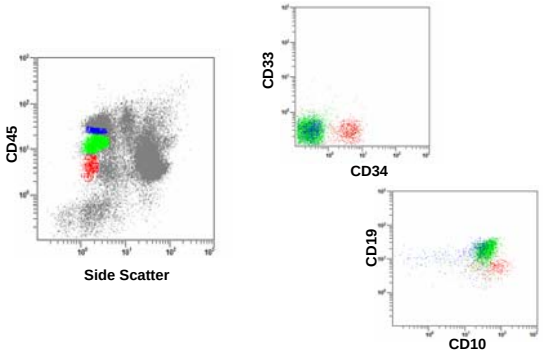
Flow Cytometry – Our Patient



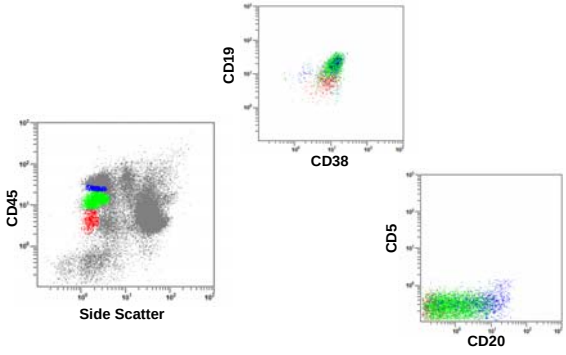
Flow Cytometry – Our Patient



Flow Cytometry – Our Patient



Flow Cytometry – Our Patient



Diagnosis

Hematogone Hyperplasia

Hematogones

- Physiologic B-cell precursors
  - "Mystery Cells"
  - Normal counterpart to B-precursor lymphoblasts
- Substantially resemble leukemic lymphoblasts, both morphologically and immunophenotypically

Hematogones

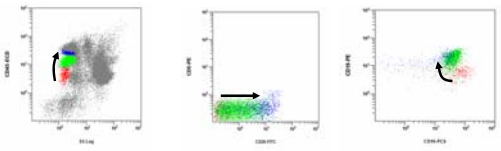
- Proliferate in a variety of reactive states, most notably in children
  - Autoimmune cytopenias (ITP, etc)
  - Recovery from chemotherapy (including A.L.L. therapy)
  - Hematogone hyperplasia usually <10% of nucleated cells in marrow, but occasionally much higher, raising differential diagnosis with acute leukemia

Hematogones

- May be distinguished from leukemic lymphoblasts by a characteristic pattern of maturation, both morphologically and immunophenotypically

Hematogones

- Maturation pattern by flow cytometry *very consistent and reproducible-- readily distinguishable from lymphoblasts*
  - Analysis should be *iterative*, based on known patterns at each stage of maturation
  - Evaluate *patterns* not lists of markers
  - Avoid simple "gate and analyze" approach
  - Treat as *data* not as dot-plots



Hematogones-immunophenotype

- CD45 dim in early forms, brighter in later forms
- Low side angle light scatter
- CD19 increases slightly with maturation
- CD10 bright in early forms, slightly dimmer in later forms, negative in mature B-cells
- CD20 increases progressively with maturation
- CD34 uniformly positive in earliest forms, then negative (no gradual progression)
- CD38 uniformly positive in early and later forms, then variable in mature B-cells (no gradual progression)
- TdT expression mirrors CD34 expression
- **No expression of myeloid antigens**

Summary

- Hematogones are physiologic B-cell precursors; normal counterpart to B-lineage lymphoblasts
- May become hyperplastic in numerous reactive conditions, especially in children
- Often seen in recovery from anti-leukemic therapy
- May be present in high enough percentage to mimic overt leukemia
- Readily distinguished from lymphoblasts by careful morphologic and immunophenotypic assessment