**Dr Narender Tejwani**
**Consultant Hematopathologist**
**Department of Laboratory Services**
**RGCI & RC**

# CASE HISTORY

- 1 year 8 month old male baby
  - Anemia requiring 1 transfusion
  - Platelet type bleed: Thrombocytopenia
  - Worked up outside where he was found to have extreme leukocytosis and was diagnosed as JMML
  - There is no history of fever

# CLINICAL FINDINGS

- General Physical Examination
  - Alert, active and well oriented child
  - Pallor was severe withPetechial spots at dependent parts
  - No fever, No Lymphadenopathy
- Systemic Examination
  - **Splenomegaly 4cm below costal margins**

# CLINICAL DIAGNOSIS

**Acute Leukemia**: In view of anemia requiring transfusion with platelet type bleeding and splenomegaly in a young child

# INVESTIGATIONS

- Hb: 5.6gm%
- Platelets: 6000 per cumm
- TLC: 93000 per cumm
  - 73% lymphocytes, few appear immature
  - 8% Monocytes, Morphologically normal
  - 19% neutrophils
- TORCH and EBV workup was negative

# INVESTIGATIONS

- Bone Marrow Aspirate
  - Showed infiltration by small to intermediate lymphoid cells similar to that in PS
  - Myeloid maturation was normal and erythroid were normoblastic, No megakaryocyte was seen
  - No malarial parasite/LD body was seen
- Bone Marrow Biopsy
  - showed infiltration by lymphoid cells interstitially
  - No megakaryocyte was seen
  - No Granuloma was seen

D/D: Acute Leukemia Vs NHL

# FLOWCYTOMETRY

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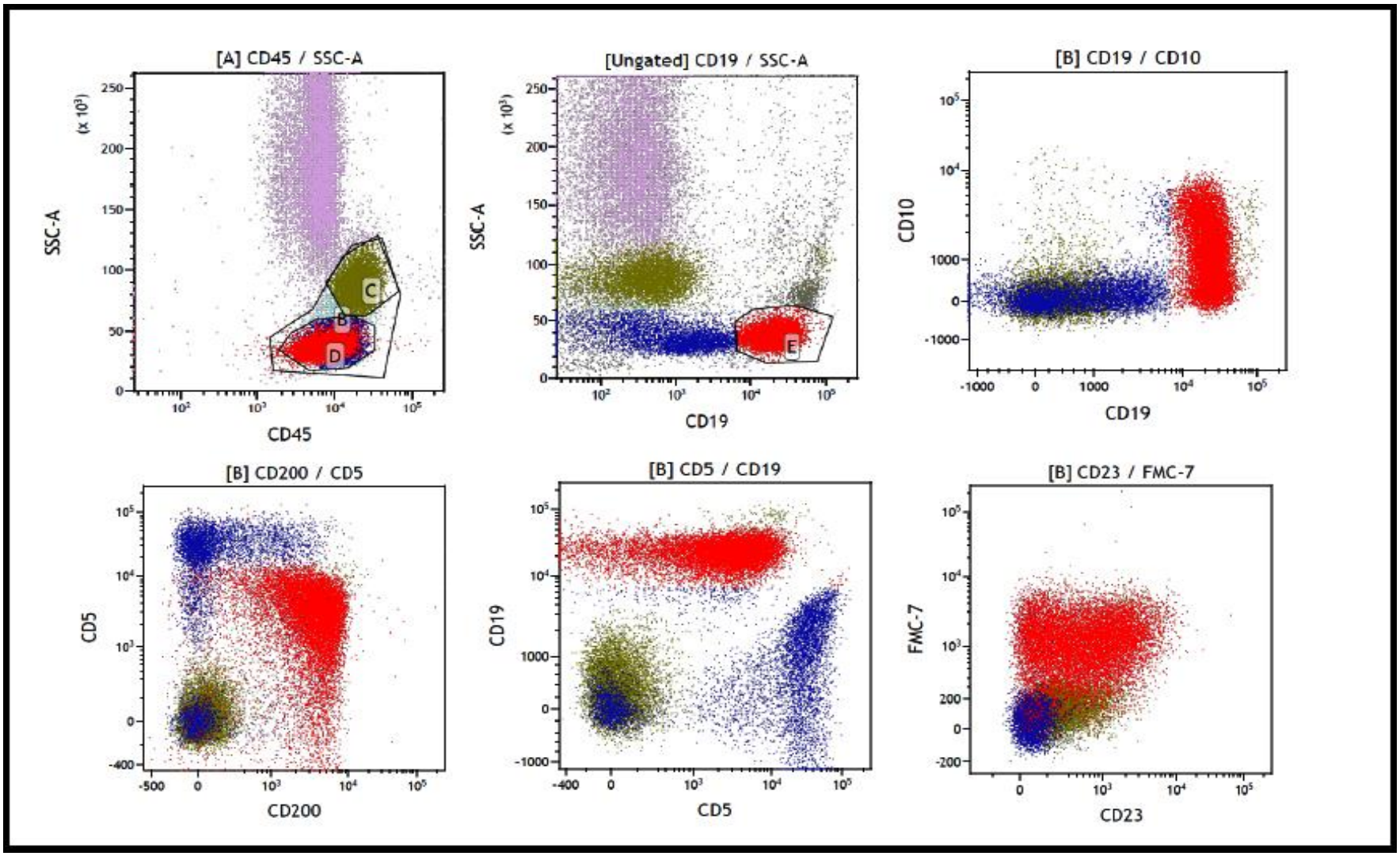
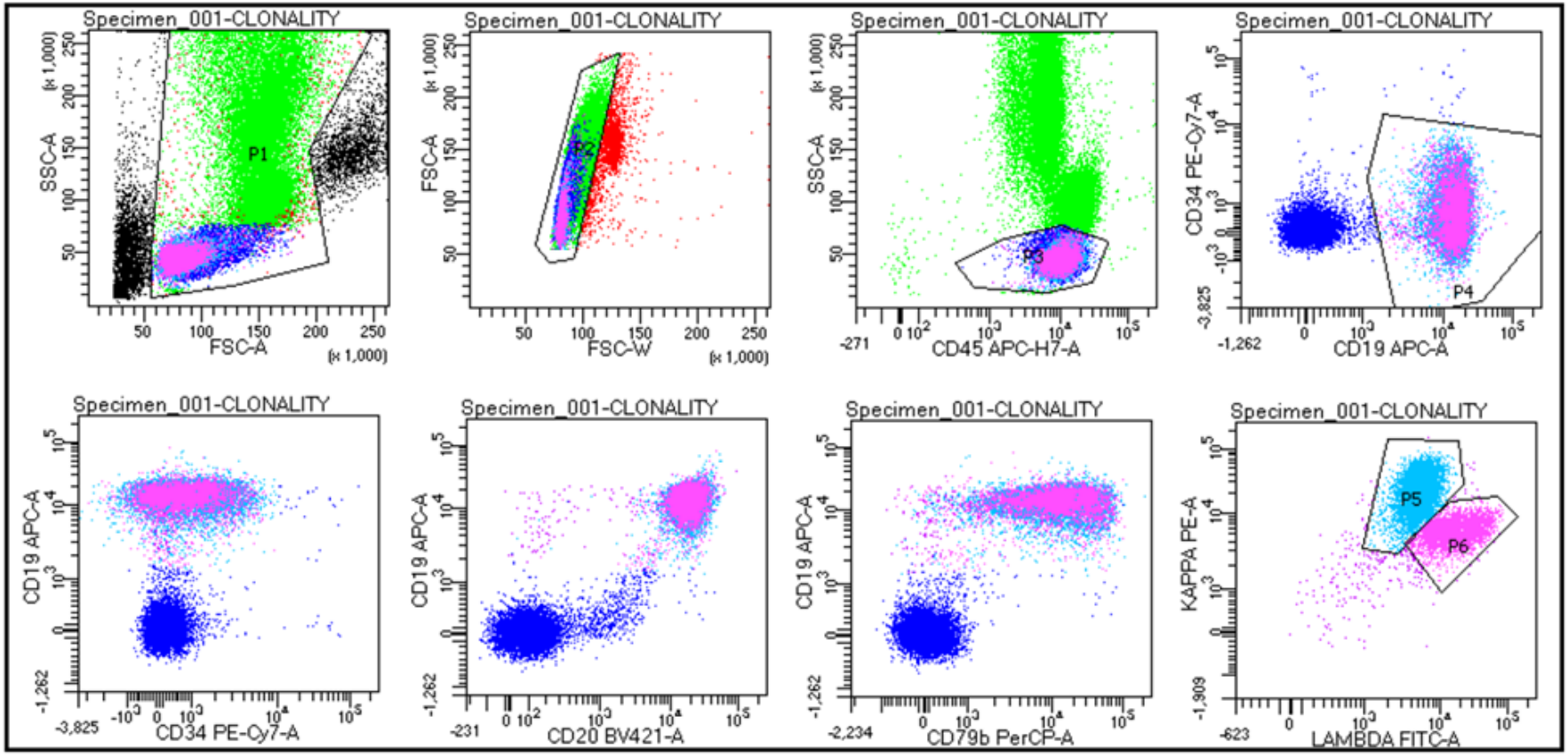


# FLOW CYTOMETRY



# FLOW CYTOMETRY

- Gating Marker: CD19
- Positive markers: CD45, CD19, CD20, CD79b, CD5, CD200, CD23 (Dim), CD10 (Dim), FMC7
- Negative Markers: CD34, T cell markers and NK cells markers
- No double negative T-Cell expansion was seen on T cell analysis
- Light chain restriction: Shows split in kappa and lambda region suggesting polyclonal nature

# INTERPRETATION

- B Cell Hyperplasia
- Multiple Aberrancies
- Still Polyclonal

# **BENTA DISEASE**

# CARD 11 Gene Mutations

- CARD11 gene mutation analysis was sent to NIIH Mumbai
- Most common C49Y, G123S, G123D, E134G, and H234L were negative
- A novel mutation in CARD 11 was found; However still not known whether pathogenic or non pathogenic

# BENTA

- B-Cell Hyperplasia with Elevated NF-kb Activity and T cell Anergy
- Polyclonal B-Cell lymphocytosis that develops in infancy/childhood
- Clinical Presentation
  - Splenomegaly
  - Lymphadenopathy
  - Mild Immunodeficiency symptoms
  - Tendency to develop lymphomas

# BENTA

- Etiology
  - Mutations in CARD11-BCL10-MALT-1 complex gene mutation
  - Most common mutations are in CARD11 gene
- Immunophenotype
  - Polyclonal B cell hyperplasia
  - Positive for many markers associated with naïve phenotype: CD5, CD10 or may be CD23

# Questions Remaining

- Why cytopenias
  - Common with an autoimmune phenomenon or Lymphoma transformation or EBV infection
  - Workup for TORCH and EBC was negative
- Marrow biopsy
  - Replacement of normal structures is not a feature of polyclonal hyperplasia
  - No clonal population identified

# Take Home Message

- High index of suspicion for BENTA should be kept in:
  - Pediatric patients with unexplained lymphocytosis
  - Before giving a diagnosis of small cell NHL in pediatric ages
    - Specifically using IHC as kappa and lambda interpretation is often difficult on sections