Who brought the eos?

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Clinical History - 1

- 30-year-old African American female
- Presented to outside facility with rash over entire body including palms and soles
- Found to have “hypereosinophilia” at that time
Clinical History - 2

- Treated with a trial of immunosuppressants without a response, including:
  - Steroids
  - CellCept
  - Cyclosporin
  - Imuran

- Subsequently presented to Cedars-Sinai Medical Center 2 years after initial presentation with fever, rash and eosinophilia

- Pertinent negatives:
  - No travel history
  - No other medications except those above
  - No history of allergies or asthma
Various consults were requested, including:
- Rheumatology
- Infectious disease
- Hematology/oncology
- Pathologic evaluation: Peripheral blood, flow cytometry and bone marrow biopsy
Initial Labs

- WBC: 9.6 with **39%** eosinophils
  - **Abs eos:** **3.9** (nl <0.4 x10^3/ul)
- Stool ova and parasite: Negative
- Blood cultures: Negative
- Urine eosinophils: None seen
- C-reactive protein: 2.77 (nl: 0.8 mg/dl)
- Anti-nuclear antibody: 80 = Moderate positive with a speckled pattern (nl: < 40)
- Double stranded-DNA, SCL 70, RNP, smooth muscle, SS-A, SS-B and myeloperoxidase antibodies negative
- Thyroid peroxidase antibody negative
- IgE >**3000** (nl <160 IU/ml)
Additional Pending Labs

- Cocci serologies
- Galatcomannan
- Aspergillus serologies
- Serum Tryptase
- RAST antibody panel
- Complement C1q levels
- Serum cortisol
Imaging

- CT Chest: Diffuse bilateral infiltrates
- CT abdomen: No evidence of lymphadenopathy or hepatosplenomegaly
Flow cytometry on peripheral blood and bone marrow aspirate
Eosinophils
T-cells - 1
T-cells - 2
Bone marrow findings - 1

- Normocellular marrow with trilineage hematopoiesis and prominent eosinophilia
- No increase in blasts
- No morphologic abnormalities suggestive of a myeloproliferative process
Bone marrow findings - 2

- Flow cytometry with the same abnormal T-cell population
  - CD4 positive, CD3 negative with bright CD5 expression and loss of CD7 antigen expression
- Karyotype pending
- Molecular studies pending
Summary of findings

- Chronic eosinophilia (2 years)
- Rash
- Bilateral pulmonary infiltrates
- Moderate positive ANA titer
- Abnormal T-cell population identified in blood and bone marrow by flow cytometry
What is your differential and how would you pursue work-up?
Differential diagnosis of eosinophilia

- Neoplasm
- Allergy
- Asthma
- Collagen vascular disease (auto-immune)
- Parasite
Follow-up consult results - 1

- Rheumatology
  - Did not favor an auto-immune mediated process
  - Skin biopsy showed non-specific findings
    - Immunofluorescence was negative
- Infectious disease
  - All infectious disease related tests were negative (fungal, parasite and blood cultures)
  - The lung biopsy showed eosinophilic pneumonia without the presence of organisms
Follow-up consents results - 2

- Hematology
  - Molecular studies
    - Positive
      - T-cell gene rearrangements
    - Negative
      - BCR-ABL rearrangement and JAK2 and MPL mutation
      - CHIC-2 (4q12) deletion
      - KIT D816V mutation
  - Cytogenetic studies
    - Normal karyotype
      - Negative for FGFR-1 and PDGFRB abnormalities
    - No lymphadenopathy or hepatosplenomegaly
Diagnosis

Everything was excluded...

- Neoplasm
- Allergy
- Asthma
- Collagen vascular disease (autoimmune)
- Parasite

Diagnosis: Hypereosinophilic syndrome, lymphocytic variant
Eosinophilia

Secondary causes
(i.e. reactive secondary to cytokine secretion)

- Allergic
  - Asthma, Atopic eczema, allergic rhinitis
  - Urticaria
  - Allergic bronchopulmonary aspergillosis
  - Drug rxn
- Skin Disease
  - Pemphigus vulgaris
  - Bullous pemphigoid
  - Dermatitis herpetiformis
- Parasitic infection
- Fungal infection
- Vasculitis (e.g. Churg-Strauss)
- Neoplasia
  - Hodgkin lymphoma
  - T-cell lymphoma
  - Systemic mastocytosis*
  - Other: carcinoma, sarcoma, ALL
- Endocrine: Addisons, Hypopituitarism

Primary causes
(Declon Neoplastic eosinophils)

- AML
  - t(8;21)
  - Inv(16)
- Lymphoid and Myeloid Neoplasms with PDGFRα rearrangements
- Myeloid Neoplasms with PDGFRB rearrangements
- Lymphoid and Myeloid Neoplasms with FGFR1 rearrangements
- Systemic Mastocytosis*
- Chronic eosinophilic leukemia
- Eosinophilic transformation of MPN (CML, PMF)

Unknown causes
(diagnosis of exclusion)

- Idiopathic Hypereosinophilic syndrome
- Lymphocytic variant of Hypereosinophilic syndrome
  - Clonal T-cell population
  - CD4+CD3- T-cell population
Lymphocytic variant of HES

- Diagnosis of exclusion
- Elevated IL-5 and IgE
- Abnormal T-cell population:
  - CD4+CD3-
  - Can show clonal T-cell gene rearrangements
  - Can subsequently develop into a T-cell lymphoma
- Treatment with anti-IL-5 agents (Mepolizumab)
  +/- immunomodulatory agents
References


Thank You!