IMMUNE DYSREGULATION IN A PEDIATRIC PATIENT

Kristin Ammon
Fellow, Pediatric Hematology-Oncology
University of California, San Francisco
INITIAL PRESENTATION

- Term infant, no significant infections during infancy
- 9 months of age: minimal change disease
  - Initially responsive to steroid treatment
- Relapsed after several months with concomitant onset of bullous pemphigoid
  - Initial treatment with cellcept and IVIg

WORSENING COURSE AND COMPLICATIONS

- 2 years: acquired hemophilia due to high-titer Factor VIII inhibitor
  - Life-threatening GI bleed, requiring continuous Novo-7 infusion
- Recurrent S. aureus osteomyelitis and bacteremia
- 4 years: inflammatory bowel disease
  - Treated with remicade, methotrexate, steroids
FAMILY HISTORY

- No immunodeficiency, autoimmune disease, or malignancy
- No consanguinity

PHYSICAL EXAM, AGE 5

- Weight 50\textsuperscript{th} %ile, height <5\textsuperscript{th} %ile
- No oral lesions
- Skin: diffusely thickened and dry, excoriated, significant peeling. Chronic changes of thumbnails and toenails. Normal hair.
- No hepatosplenomegaly or lymphadenopathy
LABORATORY EVALUATION

- Normal lymphocyte subsets when off Cytoxan
- T cell proliferation
  - “Non-reactive” to candida & tetanus toxoid stimulation
  - “Markedly diminished” to PHA, PWM, & ConA stimulation
- Immunophenotyping:
  - CD4+CD25+ cells 14%
  - CD45RA 16%, CD45RO 27%
- Abnormal humoral immunity (pre-IVIg)
  - IgG 276 (L)
  - IgG1 148 (L)
  - IgG2 65
  - IgG3 8 (L)
  - IgG4 2.8
  - IgM 25 (L)
  - IgA 37
  - IgE 91 (H)
- Anti-tetanus titers 1.64
- Isoagglutinin titer 1:2
DISCUSSION: DIFFERENTIAL DIAGNOSIS

- Autoimmune disease
- Primary immunodeficiency with autoimmune manifestations
  - DiGeorge Syndrome
    - No evidence of 22q11 deletion by FISH
  - X-linked lympoproliferative disease
    - SH2D1A gene sequencing negative
  - IPEX
  - Common variable immunodeficiency
- Immune dysregulation with secondary immunodeficiency due to therapy
DISCUSSION: TREATMENT

- PTLD-like regimen: 6 cycles of cytoxan, prednisone, and rituximab
  - Goal to “reset” immune system

- Allogeneic stem cell transplant
  - Matched unrelated donor transplant
  - Conditioned with busulfan, fludarabine, campath
  - Resolution of FVIII inhibitor and bullous pemphigoid
  - Mixed chimera: 90% donor overall, 93% CD3 cells
  - Regained T-cell function; remains IVIg-dependent
  - 9 months post-transplant: hemolytic anemia

- Difficult decision to transplant given lack of definitive diagnosis
  - Role of stem cell transplant in autoimmune syndromes