UCSF Fresno Medical Education Program
School of Medicine

Atypical Presentation of IPEX Syndrome

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IPEX Syndrome

- Immune Dysregulation
- Polyendocrinopathy
- Enteropathy
- X-linked inheritance

Clinical Features

- Classic triad:
  - Watery diarrhea
  - Endocrinopathy
  - Eczematous dermatitis
- Can include additional autoimmune manifestations
- Usually presents within 1st year of life
- Treatment: HSCT and immunosuppression

Pathogenesis

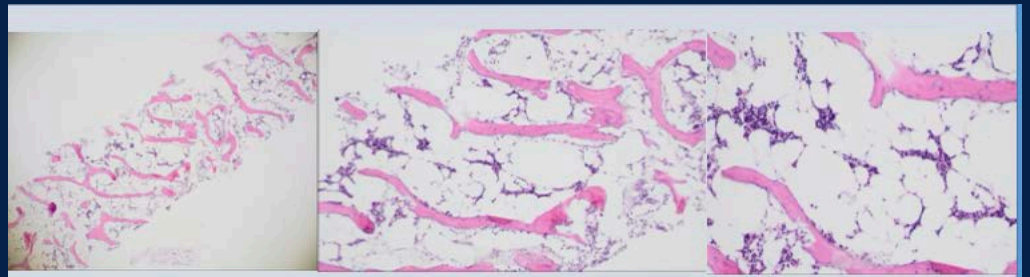
- FOXP3 gene mutation
- Impaired regulatory T-cell function, specifically regulatory T cells
- Failure of immune tolerance → uncontrolled proliferation of effector T cells and alterations in signaling responses of T-cell receptors

Case Presentation

- 13 year old male presenting to ED with worsening periorbital edema and development of anasarca
  - Nephrotic syndrome diagnosed at 9 years of age
- Initial pertinent labs
  - Anemia (Hgb 8.5 gm/dl)
  - Thrombocytopenia (23 x 10^3)
  - Hyponatremia
  - Elevated Cr
  - Hypoalbunemia
  - Proteinuria and hematuria

Initial management

- Methylprednisolone, albumin, and furosemide
- Admission to ICU given severity of presentation
  - Acute renal failure
  - Respiratory distress with findings of pulmonary edema and bilateral pleural effusions
- Renal biopsy
  - Acute tubular necrosis and focal segmental glomerulosclerosis → initiation of tacrolimus
- Bone marrow biopsy: Hypocellular marrow (<10% cellularity) for age



Figures 1-3: Bone marrow biopsy specimens showing markedly hypocellular marrow (<5% cellularity) with minimal hematopoiesis, consistent with aplastic anemia

Investigations

Hemoglobin	6.7 g/dL
Platelet count	19.0 10^3/mcL
Reticulocyte count	0.034 10^6 mg/dL
Creatinine	1.38 mg/dL
Fanconi anemia panel	Negative
FISH & cytogenetics testing	Negative
Platelet antibodies pane, indirect	Negative
Bone marrow failure panel	Negative
PNH study	Negative

ANCA (MPO/PR3) antibodies	Negative
ADAMTS-13 activity	Negative
T-cell interleukin proliferation panel	Negative
T-cell spectratyping	Normal CD3+ total, CD4+ T cell and CD8+ T cell counts
FOXP3 protein expression	Not detectable
PID Invitae panel	VUS ZAP70, CF3R, MAP3K14,
GAD antibody	5.3 IU/mL
IA-2 antibody	>120.0 U/mL

Management

- Significant clinical response to tacrolimus and prednisone
- Resolution of anemia, thrombocytopenia, FSGS, and proteinuria
- Referral for HSCT to prevent disease progression

Discussion

- Unusual case of IPEX syndrome
  - Late onset of age
  - Uncommon organ involvement
- Significant clinical improvement with tacrolimus and steroids
  - Both his aplastic anemia and nephrotic syndrome in remission
  - Sirolimus initially considered, but avoided due to potential renal podocyte toxicity

Discussion

- Reasons for consideration of stem cell transplantation
  - Reduce risk of developing type 1 diabetes
  - Longer interval of free disease
  - Indication given SAA with known HLA compatible donor
- Rarity of such cases makes treatment challenging, and requires careful consideration of both HSCT and immunosuppressive therapy.

References

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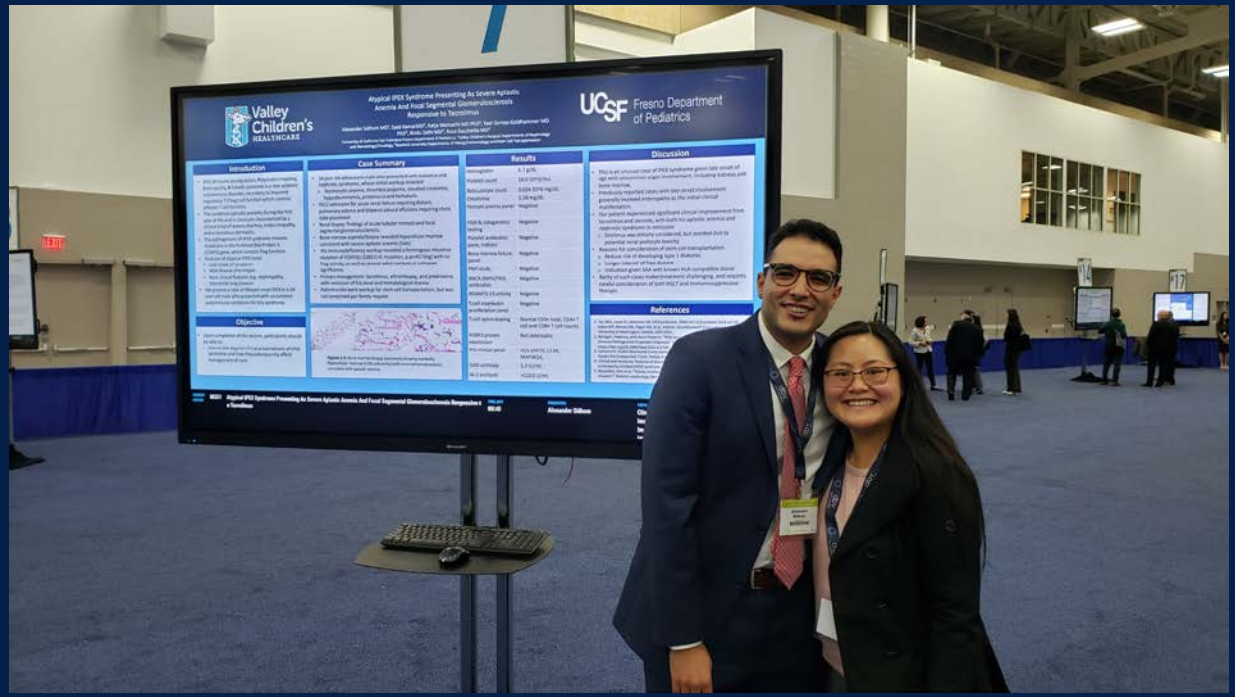
Thank you! Any Questions?



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