A novel hyper-IgE syndrome with enhanced $T_H^{17}$, autoimmunity, and neurocognitive disease

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A young boy with ‘hyper-IgE’ syndrome

- 12 year old Egyptian male
  - Elevated IgE and atopy
    - atopic dermatitis, food allergy, asthma, allergic rhinitis
  - Recurrent bacterial infections
    - recurrent staphylococcal skin infections/abscesses
    - recurrent pneumonia
    - chronic otitis externa
  - Leukopenia
Additional Birth & Childhood History

• Egyptian Coptic Christian parents
  – first cousins
• Uncomplicated birth; full term via C-section
  – no delayed separation of umbilical cord
  – no perinatal or early childhood illnesses
• Received IVIG in Egypt
  – no significant benefit noted
• No history of scoliosis, fractures, newborn rash, or retained primary teeth
• Known to have missed immunizations
  – unknown how many/which
Neurocognitive impairment

• Developmental delay
  – neurocognitive evaluation at age 11yo c/w 6yo
  – impaired fluid reasoning; difficulty with visual-spatial problems

• Ataxia and discoordination
  – impaired fine motor control and visual tracking

• Speech abnormalities/dyspraxia
  – misarticulation, discoordination, slow processing

• History of febrile seizures
Pertinent Physical Exam

• Dysmorphic
• EACs with erythema, crusting and purulent drainage
• Mucopurulent nasal secretions
• High arched palate
• Multiple axillary abscesses with associated LAD
• Eczematous skin with excoriation; silvery plaque over extensor elbow
• Ataxic, with impaired coordination, pressured/dyspraxic speech; 1+ DTRs
Laboratory Abnormalities

- **ESR 16, CRP 0.4**
- **WBC 2.4**
  - ANC 329, ALC 987
  - Low naïve CD3+, low CD8+
  - Low CD27+ Bcells
- **IgG 1,690, IgA 497, IgM 147, IgE 30,786**
  - Protective titers
- **Bone marrow biopsy**
  - Normocellular; trilineage hematopoiesis; abundant maturing myeloid forms
- **DHR wnl**
Family History

• 10yo brother
  – atopy, staph, neurocognitive impairment, hemolytic anemia
  – **IgE 11,405**, IgG 2,060, IgA 600
  – ANC 1,000, ALC 1,000, CD4/8 ~3:1

• 9mo M cousin
  – moderate AD, staph, unable to sit unassisted
  – neutropenia
The clinical phenotype

• Allergy
  – high IgE; atopic dermatitis; asthma; food and environmental allergies; IV contrast sensitivity

• Infection
  – chronic otitis externa
  – recurrent staph and URI/pneumonia
  – lung, cutaneous, parotid, periodontal abscesses

• Autoimmunity
  – increased $T_H17$; elevated IgG; psoriatic lesions
  – ?hemolytic anemia, ?neutropenia

• Neurocognitive impairment
  – developmental delay, ataxia, discoordination and speech abnormalities/dyspraxia
  – febrile seizures