X-linked agammaglobulinemia

Versailles, France
October 22, 2004
INGID
Primary Immunodeficiency Clinic

- Wiskott-Aldrich Syndrome (WAS)
- Severe Combined Immunodeficiency (SCID)
- X-linked Agammaglobulinemia (XLA)
- Hyper IgM Syndrome (CD40 ligand deficiency)
- Common Variable Immunodeficiency (CVID)
- Chronic Granulomatous Disease (CGD)
- Complement Deficiency (C6 deficient)
X-linked agammaglobulinemia

“XLA”
X-linked agammaglobulinemia

- 1952 Colonel Ogden Bruton (Pediatrics, 1952)
- 8 yr old male with recurrent pneumococcal sepsis
- 19 episodes of sepsis (Pneumococcal sepsis X10)
- Treated with SQ gamma globulin q month and improved
- First description of an immune deficiency which improved with treatment
Laboratory Hallmarks

- < 1% CD19+B cells in peripheral blood
- Low serum IgG, IgA, IgM

  - Other:
  - Mutation in Btk (Bruton’s Tyrosine Kinase) gene
XLA

• Clinical presentation
  – Research study
• Medical regimen
  – At St. Jude
• Social issues
• Adults with XLA
  – Research Study
“Typical” Clinical presentation

• Males usually with recurrent infections in the first few years of life
• Diagnosed by about 2 years of age
• Recurrent otitis and sinusitis (pneumococcus and H. influenzae)
• Well until 6 months of age
Clinical Presentation of XLA


- 82 patients with proven mutations in Btk
  - 60 with sporadic disease
  - 22 with family history of XLA
Clinical findings (cont)

Mean age at diagnosis: 35 months for sporadic disease in this study

12 patients dx’d < 12 months of age
29 patients dx’d 13-40 months of age
19 patients dx’d >40 months of age
60 patients
Infants < 12 months
n=12

- All hospitalized at diagnosis
- History of recurrent otitis
- Hospitalized for similar findings of:
  - Pyoderma gangrenosum, perirectal abscess, cellulitis assoc with:
  - Pseudomonas sepsis
  - Staph sepsis
  - Neutropenia
Toddlers 13-40 months (n =29)

- 26/29 patients had been hospitalized at least once before diagnosis
- History of recurrent otitis
- 14/29 hospitalized at least once for pneumonia
Older Children
> 40 months of age (n=19)

- 4 patients were ≥7 years of age (84 months) at time of diagnosis
- 18/19 hospitalized at least once for infection
- 1 patient hospitalized for infection 6 times for infection before diagnosis
- One patient (not hospitalized) tx for pneumonia as outpatient X2
- All with history of recurrent otitis
Summary Findings

• Otitis was the most common first clinical symptom in all of the age groups.
• URI, fever and skin infections common among all groups
• 93% hospitalized at least once for infection
Summary findings (cont)

- Most patients not recognized to have immunodeficiency until hospitalized for infection.
- History of recurrent otitis and sinusitis
- Some with >20 episodes of otitis
Summary findings (cont)

- Familial disease - a diverse group
  - 22 patients
  - 3 hospitalized for infections < 6 months of age
  - 53 yr old man diagnosed with XLA
  - 23 yr old man diagnosed with XLA
  - 3 boys diagnosed due to brothers having XLA but without symptoms
Findings (cont)

• Chronic otitis and sinusitis is common….

• Education for health care providers:
  • ≥ 3 episodes of sinusitis or otitis
  • Marked paucity of cervical lymph nodes and tonsillar tissue could heighten awareness.
  • Low Serum Immunoglobulins
    – (IgG, IgA, IgM)
• St Jude regimen for XLA
Medical Regimen

• Twice yearly visits to Immunology clinic
• IVIG every 21-28 days (400-500mg/kg)
• Chronic prophylactic antibiotics
  – Bactrim (Septra)
  – Augmentin
  – Clarithromycin XL
Medical Regimen (cont)

• Lab evaluation once per year unless “sick”
  – CBC with diff, chemistry, lgs
• Stool testing for Ova and parasites
• Xrays of chest/sinuses once per year
• CT scan of chest every other year?
Social Regimen

• Must attend school unless very ill
• Minimize absences due to medical care
  – IVIG at home
  – Summer clinics are larger
  – Teach mom to give IVIG at home
Social Regimen (cont)

- Encourage sports (team)
- Make child responsible for Medication
- Pills vs. Liquid—when to transition
- Minimize the IVIG treatments
- Treat them as normal children
  - no special privileges for IVIG infusions
- May go out in crowds or be around “sick” people
- Educate regarding genetics of disease
Social regimen (cont)

- Introduce families to each other who have a child with XLA
- Benefits parents as well as child
Adults with XLA
Adults with XLA (non-published data)

• Interested in older men with disease
  – How XLA affected them
  – Socially
  – Medically
  – Financially
  – Survey format
  – Personal invitation to participate by phone
Characteristics of Adults

- Median age: 32 years old
- Range: 21 years to 63 years
- N=41 Alive and well
Characteristics of Adults

- Employed for wages 29/41 (71%)
- Students 7/41
- Not working 5/41
Characteristics of Adults

• Educational level
  – College graduates or higher 21/41
  – Some College 10/41
  – High school graduates 7/41

• Married 20/41
Characteristics of adults

• Age at diagnosis

  – Under 6 months  6/41
  – 6-12 months 3/41
  – 12-24 months 6/41
  – >24 months  26/41
Characteristics of Adults

• Family history
  – 31 had family member diagnosed with XLA
  – 10 had no family history of XLA
Characteristics of Adults

• Pneumonia *before* diagnosis of XLA
  – 59% (24/41)

• Hospitalized since diagnosis *for infection*
  59% (24/41)
Minor medical problems

- Sinusitis/Sinus symptoms  32% (13/41)
- Conjunctivitis
- Cough
- Asthma/ allergies
- Nasal congestion
- Urethritis
- Skin infections
Characteristics of Adults

- On Intravenous gammaglobulin (IVIG)
  - 40/41

- Prophylactic antibiotics
  - 16/41
Limits to XLA

• “How much do you feel that having XLA limits what you can do in each of the following areas? Do you feel your disease limits you……
  – A lot
  – Some
  – Little
  – Not at all
Limits to XLA

Choice of jobs/careers   21/41
Lifestyle               15/41
Sports                  12/41
Travel                  10/41
Social activities       7/41
Sleep                   6/41
Normal physical activity 6/41
(cont) Limits to XLA

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Genetics

“Based on what you know or have heard, if you were to have a (another) DAUGHTER, What are the chances that your

**DAUGHTER WOULD BE A CARRIER?**
Genetics

- Correctly answered by 34%
- Incorrectly answered by 49%
- No idea 12%
- No response 5%
Continuing Adults with XLA

• Quality of Life
  – As measured by the “SF-12”
    • Compare to other adults/individuals
      - with chronic disease
      - normal adult population
Continuing Adults with XLA

- Insurance issues
- Health care costs
- Anxiety regarding traveling abroad
- Other “serious” chronic conditions
  - Cancer
  - GI disease (Crohn’s or other)
  - Chronic Lung disease
Contact Information

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