X- linked agammaglobulinemia

Versailles, France
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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

J. Peds (2002) dx between1990-2001

- 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 gangrenosa, 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

- Sex life 4/41
- Friends 4/41

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

- At St. Jude Children's Research Hospital
- Memphis Tennessee, USA

- vanessa.howard@stjude.org