Diagnosis and misdiagnosis of IBD in children

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INSERM U989

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Pediatric IBD – is it just a matter of Size
Prevalence of IBD in children <18y in Ontario

YEAR


Prevalent cases (per 100,000 population)

IBD

Crohn’s

UC

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<table>
<thead>
<tr>
<th>AGE</th>
<th>Change in Incidence Rate</th>
<th>95% CI</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>+5.0% / year</td>
<td>0.5% - 10.5%</td>
<td>0.032</td>
</tr>
<tr>
<td>5-9</td>
<td>+7.6% / year</td>
<td>4.4% - 10.8%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>10-14</td>
<td>+0.63% / year</td>
<td>-0.9% – 2%</td>
<td>0.41</td>
</tr>
<tr>
<td>15-17</td>
<td>-0.21% / year</td>
<td>-1.3% – 0.9%</td>
<td>0.72</td>
</tr>
</tbody>
</table>
Pediatric CD has unique characteristics in comparison to adult onset CD

- **Pediatric**
  - Colon involved
    - 80% at 8 yr of age
    - decreases with age
  - Isolated Ileal involvement
    - Rare at <8 yrs of age
  - Positive FH in 30%
  - Structuring in 46%
  - Surgery in 71%

- **Adult**
  - Colon only involved in <20%
  - Ileum involved in 80%
  - Positive FH in 14%
  - Structuring in 29%
  - Surgery in 55%

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Summary of Confirmed CD Loci

~ 10% overall risk

Pediatric Specific Genes?

Kugathasan et al. Nature Genetics 2008 2 loci (DcR3?)
Imielinski et al. Nature Genetics 2009 5 loci (IL27?)

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Differing natural history

Per cent of patients with active disease

Per cent of patients under immunosuppressants

Childhood-onset CD
N= 206

Adult-onset CD
N= 412

Pigneur et al IBD 2009
Evolution of Disease Behaviour

n=404 with follow-up ≥2 years

Years after diagnosis

percentage of cases

- Inflammatory B1
- Stricturing B2
- Penetrating B3

p< 0.0001


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Evolution of Disease Behaviour

n=404 with follow-up ≥2 years

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Pediatric Crohn’s disease
It looks like Crohn’s Disease
– lessons to be learned from Crohn-like diseases?
Neutrophil disorders:

- Defect of the oxidative burst
  - Defective elimination of micro-organisms
  - Dysfunction of macrophages and neutrophils

- Defective superoxide production

NBT test:

- Chemotaxis defects

1) Chronic Granulomatous Disease (CGD)

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Neutrophil disorders:

2) Glykogen Storage Disease 1b

Metabolic Disorder
  Hypoglycemia
Infections (skin)
Oral/perianal Aphtosis
Colonic/SB inflammation
Early-onset pediatric IBD

0-2 years: 31% UC  
33% IC  
34% CD  
44% positive family history  
Up to 70% treatment failures

2-17 years 25% UC  
9% IC  
66% CD  
19% positive family history

Heyman et al Pediatrics 2005
Early-onset pediatric IBD

Genetically determined Diseases?

IL10 signaling defects:
Severe treatment resistant colitis
perianal inflammation

XIAP
Severe treatment resistant colitis (20% of pat)
Hemophagocytic lymphohistiocytosis
EBV-related

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Pitfalls clinical case

A.F., 11.5 years, 20.5 kg, 131 cm

fatigue, asthenic, disturbed eating behaviour with refusal of alimentation « anorexia » weight loss over several months

psychotherapy for anorexia nervosa
Pitfall
Summary

- Pediatric onset of IBD: the earlier the more severe?
- IBD-like disease: CGD, Glykogen Storage Disease 1b
- Very early onset IBD = genetic defects (« disease models »)
- Proof of concept with IL10 signaling deficiency
- Other candidates: IL22, XIAP, TGF, Smad ???

- IL10 signaling defects:
  - Severe treatment resistant colitis
  - Perianal inflammation

- T reg deficiency (FOXP3)
  - Small bowel >> colon
  - Associated autoimmunity

Treatment options
- BMT
Thank you!