Approach to child with joint pain

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Case 1

- 5 year old boy with swelling of Rt knee for 3 months
History

• Morning stiffness
• Preceding viral illness or gastroenteritis
• Exposure to TB/family history of TB
• Difficulty chewing food
• Any other joint symptoms
Presenting features in the toddler

- Refusing to weight bear
- Walking with a limp
- Delayed motor milestones
# Growing pains

<table>
<thead>
<tr>
<th>Growing Pains</th>
<th>Serious Cause of leg pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well child, 4-8 yrs</td>
<td>Fever, wt. loss, any age</td>
</tr>
<tr>
<td>Either leg</td>
<td>One leg regularly</td>
</tr>
<tr>
<td>Pain located between joints</td>
<td>Pain in the joint</td>
</tr>
<tr>
<td>Occurs at night</td>
<td>Day or night</td>
</tr>
<tr>
<td>Subsides within 10-20 mins</td>
<td>Persistent, prolonged or chronic</td>
</tr>
<tr>
<td>Walks normally</td>
<td>Limps or refuses to walk</td>
</tr>
<tr>
<td>No Physical signs</td>
<td>Redness, swelling or reduced ROM</td>
</tr>
</tbody>
</table>
Initial Investigations

- Full blood count including differential
- ESR and CRP
- Urea, electrolytes, liver function test
- Urine dipstick
- ANA, RF
- X ray
Investigations in our patient

- FBC, U&E, LFTs and renal function – normal
- ANA positive – 1/160
Diagnosis of JIA

• Purely clinical
• Autoantibodies only of prognostic significance
• At least 6 weeks of symptoms/signs
Classification of juvenile arthritis

• JRA or JCA?
• ILAR consensus - JIA!
• Need for classifying
  - to facilitate communication
  - foster research
  - not “diagnostic criteria”
Condition which present as/with arthritis

- Malignancy
- Storage disorders
- Connective tissue diseases (lupus, JDM etc.)
- Syndromic non-inflammatory arthropathy
Pitfalls in the Diagnosis of JIA

• Narrow history taking
• Failure to examine the child’s musculoskeletal system
• Referred pain eg hip to knee, costovertebral to sternm
• Uveitis with silent arthritis
• Earache with TMJ joint arthritis
• Infections
• Malignancy mimicking JIA
• Discitis
• Inflammatory bowel disease
Management of JIA

- NSAID
  - Ibuprofen (30-40mg/kg/day)
  - Naproxen (20mg/kg/day)
- Arthritis pain is not usually severe/nocturnal
- No need for opiates
- COX-2 – no evidence, not advisable
• Treatment for our patient?
• Ophthalmology referral for slit lamp examination
• Never forget this!
Risk factors for Uveitis in JIA

- Age < 7 years
- Female gender
- Oligoarticular subtype
- ANA positivity
JIA Uveitis - Course

- visual loss in 50%
- legal blindness 15-40%
Case 2 – 7 year old boy with multiple joint swellings
History

- Duration of symptoms
- Morning stiffness
- Activity in school and at home
- Difficulty writing at school
Examination

- Gait
- Peripheral joint examination
- pGALS
Management

- Methotrexate
- Short course of oral or IV steroids
Management of JIA - paradigm shift

- Pharmacological
  - Methotrexate
  - TNF agents (etanercept)
- Parent and patient education
- Physiotherapy
Methotrexate

- First choice second line agent
- 25 years of data on safety profile
- Well tolerated by children
- Cheap
- 10-15mg/m$^2$/week
- Need to monitor LFT’s every month
Polyarticular JIA – management of patients refractory to MTX

- Intermittent joint injections
- Biological therapies – etanercept, infliximab, adalimumab, Tocilizumab and abatacept
Windows of opportunity
Intervention with early diagnosis

EARLY DETECTION = TIMELY TREATMENT

Relevant time points

DISEASE ACTIVITY >

Damage

Symptomatic

Asymptomatic

Occult disease

Phenotypic / prognostic

Active disease

Start therapy

TIMELINE >

Windows of opportunity
Prevent progressive damage and aim for quiescence

RAPID INTERVENTION = PREVENTION OF IRREVERSIBLE DAMAGE

Case 3

• 15 year old boy with low back pain
• Stiff back in mornings and long car journeys
Back Pain in Children

• Common
• Mechanical back pain common in teenagers
• Tight hamstrings or weak abdominal muscles
• Physiotherapy and general fitness
• School bag position
Back Pain in Children

• Uncommon under the age of 10, rare under the age of 5
• Fever, weight loss, bowel or bladder dysfunction
• Pain at night
• Weakness, numbness and radiating pain
Hip pain in a child – age under 5

- Transient synovitis – most likely
- Exclude Hx of trauma
- Exclude sepsis in all
- Plain X ray
- FBC, CRP
- USS for persistent symptoms
Hip pain – 5 to 10 years of age

- Perthes most likely
- Exclude sepsis

- Plain X ray, frog leg lateral view
- Consider referral to orthopaedics
- Early Perthe’s X ray normal
Hip pain – children more than 10 years

• SUFE most likely
• Exclude sepsis

• AP and frog lateral x-rays
• X-ray can be hard to interpret
• Urgent referral
• MRI
Back pain in Children

- Mechanical
- Sacroilitis – juvenile spondyloarthropathy
- Kyphoscoliosis
- Spondylosis (stress fracture)
- Spondylolisthesis (slipped vertebrae)
- Discitis
- Tumour
Kawasaki syndrome - Update
Kawasaki Disease – diagnostic criteria

• Fever >5 days, plus 4 of below 5
  • Non-purulent conjunctivitis
  • Polymorphic rash
  • Cervical lymphadenopathy
  • Oro-mucosal changes
  • Extremity changes
Clinical Presentation

• Typical Kawasaki
  – ≥ 5 days of fever +4/5 KD features

• Atypical Kawasaki
  – absence of clinical criteria, but presence of coronary artery lesions CAL

• Incomplete Kawasaki
  – clinical features of Kawasaki but not complete set of features and no CAL
Tropospheric winds from northeastern China carry the etiologic agent of Kawasaki disease from its source to Japan

Xavier Rodó\textsuperscript{a,b,1}, Roger Curcoll\textsuperscript{b}, Marguerite Robinson\textsuperscript{b}, Joan Ballester\textsuperscript{b,c}, Jane C. Burns\textsuperscript{d}, Daniel R. Cayan\textsuperscript{e,f}, W. Ian Lipkin\textsuperscript{g}, Brent L. Williams\textsuperscript{g}, Mara Couto-Rodriguez\textsuperscript{g}, Yosikazu Nakamura\textsuperscript{h}, Ritei Uehara\textsuperscript{h}, Hiroshi Tanimoto\textsuperscript{i}, and Josep-Anton Morgui\textsuperscript{b}
Differences in the mycobiome distribution from tropospheric and surface-level aerosols.

Xavier Rodó et al. PNAS 2014;111:7952-7957
Inflixiimab in KD

- Phase 3 RCT
- Lancet 2014
- IVIG + infliximab vs. IVIG + placebo
Infliximab in KD - RCT

Tremoulet AH et al. Infliximab for intensification of primary therapy for Kawasaki disease: a phase 3 randomised, double-blind, placebo-controlled trial, Published online February 24, 2014 http://dx.doi.org/10.1016/S0140-6736(13)62298-9
Infliximab in KD – RCT
Treatment resistance, IVIG infusion reactions, duration of hospital stay and days of fever in the study population by treatment group

<table>
<thead>
<tr>
<th></th>
<th>Infliximab</th>
<th>Placebo</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment resistance</td>
<td>11 (11.2%)</td>
<td>11 (11.3%)</td>
<td>0.81</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVIG infusion reaction</td>
<td>0</td>
<td>13 (13.4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Days of hospital stay</td>
<td>3 (3-4); range: 2-7</td>
<td>3 (3-4); range: 1-8</td>
<td>0.65</td>
</tr>
<tr>
<td>Days of fever</td>
<td>1 (1-2); range: 0-4</td>
<td>2 (1-2); range: 0-6</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Infliximab in KD – RCT
Change from baseline in coronary artery outcomes at weeks 2 and 5 and \( Z_{\text{max}} \) for the study population by treatment group

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<th>p value</th>
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<tr>
<td><strong>Proximal left anterior descending artery Z score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change at week 2</td>
<td>-0.61 (-0.81 to 0.40)</td>
<td>-0.31 (-0.51 to 0.11)</td>
<td>0.045</td>
</tr>
<tr>
<td>Change at week 5</td>
<td>-0.8 (-1.03 to -0.57)</td>
<td>-0.51 (-0.73 to -0.28)</td>
<td>0.074</td>
</tr>
<tr>
<td><strong>Proximal right coronary artery Z score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change at week 2</td>
<td>-0.29 (-0.49 to 0.09)</td>
<td>-0.22 (-0.41 to 0.02)</td>
<td>0.59</td>
</tr>
<tr>
<td>Change at week 5</td>
<td>-0.53 (-0.77 to -0.30)</td>
<td>-0.29 (-0.52 to -0.05)</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Zmax</strong></td>
<td>1.8 (1.5 to 2.0)</td>
<td>1.8 (1.5 to 2.1)</td>
<td>0.87</td>
</tr>
</tbody>
</table>
Infliximab in KD

- No significant difference
- Trends towards early improvement
RAISE study – steroids in severe KD

- RCT
- Lancet 2012
- IVIG + Pred (2mg/kg – 15 days) vs. IVIG
RAISE study – steroids in severe KD

• Coronoary outcomes better with steroids
• 3 % vs 23%
• Steroid course in severe KD
### IVIG + Pred vs IVIG as Retreatment

**Comparison of clinical and coronary outcomes between treatment groups**

<table>
<thead>
<tr>
<th></th>
<th>IVIG (n = 136)</th>
<th>PSL (n = 72)</th>
<th>IVIG+PSL (n = 151)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fail to respond to first-line rescue therapy, n(%)</td>
<td>51 (37.5%)</td>
<td>23 (31.9%)</td>
<td>18 (11.9%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CAAs until 1 mo, n(%)</td>
<td>39 (28.7%)</td>
<td>22 (30.6%)</td>
<td>24 (15.9%)</td>
<td>0.010</td>
</tr>
<tr>
<td>CAAs at 1 mo, n (%)</td>
<td>21 (15.4%)</td>
<td>12 (16.7%)</td>
<td>10 (6.6%)</td>
<td>0.023</td>
</tr>
</tbody>
</table>

### Scoring systems for predicting IVIG resistance

<table>
<thead>
<tr>
<th></th>
<th>EGAMI</th>
<th>KOBAYASHI</th>
<th>SANO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Na ≤133 (2 points)</td>
<td>Total bilirubin ≥0.9 mg/dl (1 point)</td>
<td></td>
</tr>
<tr>
<td>≤4 days of illness (1 point)</td>
<td>≤4 days of illness (2 points)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT &gt;100 U/L (1 point)</td>
<td>ALT ≥ 100 U/L (1 point)</td>
<td>AST ≥200 U/L (1 point)</td>
<td></td>
</tr>
<tr>
<td>≤300 × [10⁹/L platelets (1 point)]</td>
<td>≤300 × 10⁹ /L platelets (1 point)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP ≥8 mg/dL (1 point)</td>
<td>CRP ≥10 mg/dL (1 point)</td>
<td>CRP ≥7 mg/dL (1 point)</td>
<td></td>
</tr>
<tr>
<td>Age ≤6 months (2 points)</td>
<td>Age ≤12 months (1 point)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥80% neutrophils (2 points)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>High risk</strong></td>
<td><strong>≥3 points</strong></td>
<td><strong>≥5 points</strong></td>
<td><strong>≥2 points</strong></td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; IVIG, intravenous immunoglobulin.
Evaluation of suspected incomplete Kawasaki disease.

Children with fever ≥5 days and 2 or 3 compatible clinical criteria OR Infants with fever for ≥7 days without other explanation

Assess Laboratory Tests

CRP<3.0 mg/dL and ESR<40 mm/hr

Serial clinical and laboratory re-evaluation if fevers persist
Echocardiogram if typical peeling develops

CRP≥3.0 mg/dL and/or ESR≥40 mm/hr

3 or more Laboratory Findings:
1) Anemia for age
2) Platelet count of ≥450,000 after the 7th day of fever
3) Albumin ≤3.0 g/dL
4) Elevated ALT level
5) WBC count of ≥15,000/mm³
6) Urine ≥10 WBC/hpf

Positive echocardiogram

Treat


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Establish Diagnosis of Kawasaki Disease

**High Risk Factors**

- 1. Already failed IVIG?
- 2. Severe disease: the very young (<12mo); those with markers of severe inflammation
- 3. Features of HLH or shock
- 4. Coronary and/or peripheral aneurysms with on-going inflammation
- 5. Kobayashi risk score >5
- 6. IF IN DOUBT SEEK ADVICE

**Seek expert advice to consider:**

- IVIG 2g/kg; Aspirin (as per non-high risk group); **AND**
  - Prednisolone 2mg/kg/day PO and wean over next 2-3 weeks
  - Methylprednisolone 10-30mg/kg IV once a day for 3 days, followed by Prednisolone 2mg/kg/day PO until day 7 OR until CRP normalises; the wean over next 2-3 weeks
  - Perform echocardiography and ECG as soon as possible but do not delay therapy prior to obtaining echo

- **Or seek expert advice to consider:**
  - Corticosteroids as above if not already received
  - Second dose of IVIG at 2g/kg over 12 hours
  - Infliximab (6mg/kg) IV 1-2 doses (2 weeks apart if doses)
  - Other immunomodulators

**Yes**

- IVIG 2g/kg as a single infusion over 12 hours
- Aspirin 30-50mg/kg/day in four divided doses
- Perform echocardiography and ECG

**No Disease deffervescence within 48 hours or disease recrudescence**

- Repeat Echocardiography at 2 weeks and 6 weeks

**CAA>8mm; or for infants Z Score >7; and/or stenosis**

- Lifelong aspirin 2-5mg/kg/day
- Warfarin (with initial full heparinisation to prevent paradoxical thrombosis)
- Consider coronary angiography (catheter, MR or CT; if catheter will wait at least 6 months from disease onset), and exercises stress testing
- Repeat echocardiography and ECG at 6 monthly intervals
- Lifelong follow up and advice on reduction of cardiovascular risk factors

**CAA<8mm, no stenosis**

- Continue Aspirin until aneurysms resolve
- Repeat echocardiography and ECG at 6 monthly intervals
- Consider stopping Aspirin in aneurysms resolve
- Consider exercise stress test
- Lifelong follow up and advice on reduction of cardiovascular risk factors
- Consider Imaging by MR or CT angiogram

**No CAA**

- Stop Aspirin at 6 weeks
- Follow up for 12 months and d/c if well after that

Adapted from Elftheriou et al, ADC 2014
Passive autoimmunity with anti-Ro (SSA) antibodies
External hydrocephalus and subdural bleeding in infancy associated with transplacental anti-Ro antibodies
R J Edwards, T D Allport, N G Stoodley, F O’Callaghan, R J Lock, M R Carter, A V Ramanan
Archives of Diseases in Childhood, 2012 April; 97(4): 316-9
Questions?