THE MANAGEMENT OF JUVENILE IDIOPATHIC ARTHRITIS

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JIA

Chronic Arthritis

>6wks

<16yr

No other cause
JRA vs JCA
JIA adopted by ILAR in 1997
JIA ‘subtypes’

- Oligoarticular <4 joints
- ANA
- Uveitis
- Enthesitis Related hlab27
- Psoriatic
- Polyarthritis RF negative
- Polyarthritis RF positive
- Extended > 5 6 months

Systemic JIA
Oligoarticular

- < 4 joints
- ANA positive in 85%
- Chronic Uveitis is a major problem
- Need regular Eye screening, up to 4 times a year in the first year after diagnosis

- If more than 5 joints after 6 months, then known as Extended oligoarticular arthritis
Polyarticular

- > 5 joints
- RF positive < RF negative
- RF negative can also have ANA positive
- Uveitis in 5%

- RF positive = highest risk of persistent destructive illness
Enthesitis Related Arthritis

• ‘Juvenile Ankylosing Spondylitis’- Arthritis and enthesitis

• Arthritis and two of following:
  • Sacro-iliac joint tenderness
  • Spinal pain
  • HLAB27 +
  • Family history +
  • Anterior uveitis

• Usually large joints of the lower limbs

• Usually older children, esp boys over 6yrs
- Periosteal new bone formation
- Subchondral bone inflammation and resorption


Image 1: Radiographic findings of the spine.

Image 2: Radiographic findings of the pelvis with arrows pointing to specific areas of interest.

Image 3: Radiographic findings of the vertebrae with an arrow indicating a specific area.

Image 4: Radiographic findings of the spine, with arrows indicating specific areas of interest.
Psoriatic

- Arthritis and psoriasis
  - Arthritis and 1st degree relative
    - Psoriasis
    - Dactylitis
    - Nail abnormalities
Systemic JIA

- Arthritis and Fever:
  - Associated with Rash ‘salmon patches’, also maculo-papular or urticarial.
  - Serositis - pericardial or pleural
  - Hepato-splenomegaly and lymphadenopathy

NEED TO RULE OUT OTHER CASES FOR JOINT PAIN AND FEVER
13. A typical swinging fever chart.
QUOTIDIAN FEVER
Presenting Features

Figure 2. Documented presenting musculoskeletal features in incident cases of patients with juvenile idiopathic arthritis.
Arthritis

- Hot, swollen joint, fever, irritability – MSK sepsis
- Bruising, pallor, night sweats - **malignancy**
- Preceding URTI / gastroenteritis - reactive
- Toddler limping + sitting with spine in extended position - discitis
- Stiffness worsened by immobility / early AM, ‘gelling’, pain, loss of function - inflammatory
- Night pain / waking – **red flag**
- History incompatible with signs, bruising, multiple fracture episodes - NAI
- FTT
- TB contact
- TB

? Inflammatory?

? malignancy
Onset Pain:
- Sudden (injury, Septic) vs indolent (JIA)

Timing Pain:
- EMS
- Nocturnal Pain
- Bone Pain

Intensity Pain:
- JIA not severe
- Enthesitis can be
- Severe septic, malignancy or amplified pain

Disability:
- Severe not common in early JIA

Response to Meds:
- JIA, reactive and Osteoid Osteoma
- Malignancy and septic not

Family:
- Psoriasis, Ank spond, crohns, Lupus?

Social, infectious contacts, immunisations, Growth etc
<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FBC</strong></td>
<td>Differentiate as inflammatory vs non-inflammatory disease Thrombocytopenia and peripheral blood smear: haematological malignancies.</td>
</tr>
<tr>
<td><strong>ESR/CRP</strong></td>
<td>Non-specific inflammatory marker, more useful in monitoring</td>
</tr>
<tr>
<td><strong>Anti-Nuclear Antibodies(ANA)/Anti-Nuclear Factor(ANF)</strong></td>
<td>high titres are associated with autoimmune conditions. Some subtypes of JIA are associated with positive tests for ANA.</td>
</tr>
<tr>
<td><strong>Rheumatoid Factor(RF) and Anti-Cyclic Citrullinated Peptide Antibodies(anti-CCP):</strong></td>
<td>small subgroup of children with RF positive poly-articular disease will have a positive Rheumatoid Factor</td>
</tr>
<tr>
<td><strong>HLA B27</strong></td>
<td>associated with Enthesitis Related Arthritis</td>
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</tbody>
</table>
Pannus invading Bone: Ultrasound
Aims of management

Relieve Pain
Preserve/Restore Function
Avoid Disability
Multidisciplinary Team

- paediatric rheumatologist
- ophthalmologist
- paediatrician
- general practitioner
- physiotherapist
- occupational therapist
- orthopaedic surgeon
- dermatologist
- endocrinologist
- rheumatologist
Management

• Non pharmacological management includes
  
  – physiotherapy
  – occupational therapy
  – social support
  – pain management
Counseling

• paramount importance
  – shock, disbelief and fear

• prognosis and implications of the diagnosis
  – goals of therapy
  – side effect of medication.

• well considered, scientifically valid sources of information on JIA
  – avoid bewildering/misleading information and alternative therapies

• counseling and advice regarding sporting activities and schooling
Vaccinations

**EULAR recommendations for vaccination in paediatric patients with rheumatic diseases**

M W Heijstek,¹ L M Ott de Bruin,¹ M Bijl,² R Borrow,³,⁴ F van der Klis,⁵ I Koné-Paut,⁶ A Fasth,⁷ K Minden,⁸ A Ravelli,⁹ M Abinun,¹⁰ G S Pileggi,¹¹ M Borte,¹² N M Wulffraat¹

- Reviewed all the evidence:
- 60 papers on vaccination vs immunosppression
- 147 papers on vaccinations vs rheumatic diseases
- 15 recommendations
Pharmaceutical Treatment of JIA

- NSAIDS
- +/- Intra-articular steroids
- Methotrexate (+/- oral steroids)
- additional DMARD (Chloroquine or Sulphasalazine)
- TNF inhibitor
- other
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Management

• **NSAIDS** (mild disease and symptomatic relief only)
  – Ibuprofen: 10mg/kg/dose (higher than regular)
  – Naproxen/Diclofenac/Indomethacin

• **Corticosteroids**
  – Short term with gentle weaning
  – Not a long term solution
  – Oral or IV initially, depending on Patient condition
  – SIDE EFFECTS - manage them! PPI, Vit. D, Calcium, Diet

• **Intra-articular steroids**
  – Can inject multiple joints at once
  – May need anaesthetic
  – Preferably non-soluble steroids: Triamcinolone Hexacetonide
Early Oligo-arthritis

- NSAID
- IAS
- If no response: Repeat IAS in 3 months.

Or
- short course oral Prednisone®, 1-2mg/kg with rapid reduction over 1 month if IAS is not possible
- Add methotrexate if no response in 6 months (or extended oligoarthritis, or poor prognostic factors).
- Mtx may be added in 3 months for severe or established disease.
- If no remission in 6 months, or more joints involved: treat as for established polyarthritis
Early-Polyarthritis

- NSAID.
- DMARD
  - Methotrexate (Mtx) oral
  - Maximum 25mg/week.
- Salazopyrin (sulfasalazine)
- Chloroquine.
- IAS
- pulse of oral Prednisone®
  - 1mg/kg
  - reduced gradually to 7.5 –5.0 mg daily
Established Oligo/Poly JIA

- S/C Mtx, maximise dose.
- No response within 3 months Add:
  - Salazopyrin
  - Chloroquine
- Try substituting leflunomide for Mtx
- Low dose Prednisone (1mg/kg) should be used at induction for a short period only because of side effects.
- If no response to above steps, or patient is dependent on steroids (at a dose of more than 0.2mg/kg) consider biological therapy.
ERA (enthesitis related arthritis)

- NSAID.
- severe disease: 1-2mg/kg of Prednisone for 2 weeks and taper rapidly.
- Salazopyrin or Mtx. (or added together)
- Early use of Biological therapy, especially with axial disease
Systemic JIA

• Systemic JIA is different to other forms of JIA
• More of an auto-inflammatory disease
  – IL-1 and IL-6, rather than TNF play an important role in pathophysiology
  – Traditional DMARDs and TNF inhibitors have limited use
  – NSAIDS and high dose steroids have a place
  – IL-6 antagonists (Tocilizumab) or IL-1 Antagonists (Anakinra) are currently preferred Biologic options
• Can inject multiple joints at once
• May need anaesthetic
Disease Modifying Drugs (DMARDS)

- Methotrexate
  - The first revolution in JIA
  - Massive improvement in outcome
  - Low toxicity
  - Start 0.3-0.5mg/kg once a week
  - Take with Folic Acid
  - Nausea and GIT side effects a problem
  - Monitor FBC and LFT 3 - 6 monthly
  - Can wean after 6 months of inactive disease
  - Cheap

- OTHER AGENTS
  - Sulphasalazine, Chloroquine, Leflunamide, Cyclosporin
Juvenile Idiopathic Arthritis pathogenesis

- **synovium**
- Macrophages
  - TNF-α
    - CTLA-4
    - T lymphocytes
    - IL-6, IL-1
      - IL-6, IL-1
- Fibroblasts
- Adhesion molecules
- Endothelial cells
- Chondrocytes
- Osteoclasts
- cartilage
- bone
TNF-α

- Sinovitis/pannus
  - Osteoclasts
    - Bone resorption
    - Bone erosion
  - Sinoviocytes
    - Articular inflammation
    - Pain, swelling
  - Condrocytes
    - Cartilage degradation
    - Joint space narrowing
Etanercept in polyarticular JIA

Lovell et al, NEJM 2000

Open label: significant clinical improvement 74%
Double blind: disease flare with placebo 81% versus etanercept 28%, median time to flare placebo 28 days versus 116 days
Extension (2 yr): persistence of clinical response 81%, no significant increase of adverse events or infections (4 yr)
TNF antagonism in JIA

Six months before Infliximab therapy

Six months into Infliximab therapy

*Billiau, Wouters, J Rheum 2002*
Anti-TNF therapy and growth in severe JIA

N: 71, 2 yrs pre, 2 yrs post

Tynjala Ann Rheum 2006
Adalimumab with or without Methotrexate in Juvenile Rheumatoid Arthritis

Abatacept in JIA

IL-6 and IL-1

- Tocilizumab: IL-6
- Anakinra: IL-1

Systemic JIA
Aggressive Combination Drug Therapy in Very Early Polyarticular Juvenile Idiopathic Arthritis (ACUTE-JIA): a multicentre randomised open-label clinical trial

Pirjo Tynjälä, Paula Vähäsalo, Maarit Tarkiainen, Liisa Kröger, Kristiina Aalto, Merja Malin, Anne Putto-Laurila, Visa Honkanen, Pekka Lahdenne
Adverse events biologics

- Tuberculosis
- Malignancies
- Autoimmunity
- Anti Drug Antibodies
Tuberculosis

• Cant be too careful!
• Initial Screening:
  – **Latent vs unexposed vs active TB:**
  – Mantoux (5mm or more indicates exposure and latency)
  – CXR (looking for active disease)
  – ?Quantiferon-Gold In-tube/T-Spot (role unclear)
  – Sputum and other as indicated (looking for active)

• Repeat mantoux/CXR every 12 months if initial negative.
• Treatment or INH prophylaxis according to the SARAA guidelines
Side Effects Biologics

- Currently no evidence that biologics increase risk of malignancy
  - Other DMARDS
  - Increased risk in JIA in general
- Other autoimmune diseases
  - Development auto-antibodies and SLE
- Anti drug antibodies can cause hypersensitivity reaction to the drugs (esp infliximab) or lead to dose creep and loss of efficacy
Outcomes

Oen et al, J Rheumatol 200
Conclusion

• JIA is not just one disease
• It is not rare
• Pattern recognition and careful examination are critical
• DMARDs and Biologics are changing outcomes in this condition
• Early identification and management is important
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Thanks for listening!

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