Myths and Misconceptions in Pediatric Rheumatology

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Disclosures

• None
Case 1:

From Epic inbox: “Hi, Johanna. I have a 2 yo patient whose parents have noted that she has been limping for the past few weeks. Her right knee is a little swollen but it doesn’t seem to bother her. I was thinking of sending her to orthopedics but was wondering if you might want to see her also. If so, what labs would you want? Thanks, _____”
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Juvenile Idiopathic Arthritis (JIA)

- Defined as arthritis in a child < 16 yrs of age with a duration of disease of 6 weeks or longer with exclusion of other forms of juvenile arthritis
- Arthritis is defined as
  - Swelling/effusion OR
  - Painful limitation of range of motion (Wallace et al., 2004)
- Incidence of JIA in the US may be as high as 1/1000 (Peterson et al., 1996)
- Estimated 1.7-8.4 million children in the world with juvenile arthritis (Petty and Cassidy, 2011)
ILAR classification of JIA (Petty et al, 2004)

• Most recent classification system in which JIA is divided into 7 subtypes

1. **Oligoarticular**: 1-4 joints during first 6 months of disease
   a. Persistent: <=4 joints
   b. Extended: >4 joints after first 6 months
2. **RF neg polyarticular**: >4 joints in first 6 months of disease AND RF neg
3. **RF pos polyarticular**: >4 joints in first 6 months of disease AND RF pos x 2
4. **Psoriatic**
   • Arthritis and psoriasis OR
   • Arthritis and 2 of the following: dactylitis, nail pitting/oncholysis, psoriasis in 1st degree family member
5. **Systemic**: Arthritis and preceding or concurrent fever x 2 weeks with at least 3 consecutive days of quotidian fever plus 1 of the following: red, evanescent rash, generalized lymphadenopathy, hepatomegaly, serositis

6. **Enthesitis-related**
   - Arthritis and enthesitis OR
   - Arthritis or enthesitis plus 2 of the following: presence or history of SI tenderness, HLA-B27+, onset in male >6 yrs, acute anterior arthritis, history of AS, ERA, sacroiliitis with IBD, Reiters, or uveitis in a 1st-degree relative

7. **Undifferentiated**: Does not fit any of the above categories or fits in 2 or more of the above categories
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Question 1
Based on the description of the child in Case 1, this patient most likely has

A. Systemic JIA
B. Oligoarticular JIA
C. Polyarticular JIA
D. Undifferentiated JIA
Question 1

Based on the description of the child in Case 1, this patient most likely has

A. Systemic JIA
B. Oligoarticular JIA
C. Polyarticular JIA
D. Undifferentiated JIA
Oligoarticular JIA

• This is the MOST COMMON type of JIA
  • 50-80% of all chronic arthritis (Petty and Cassidy, 2011)
  • 20% of all peds rheum referrals to the US (Bowyer et al., 1996)
• Peak incidence 1-2 years of age
• Female to male 3:1
• Ddx of monoarthritis
  • Infectious arthritis
  • Malignancy
  • Hemophilia
  • Trauma
  • PVNS, pseudoarthritis
Oligoarticular JIA

- Clinically, affected joint is swollen and may be warm but IS USUALLY NOT VERY PAINFUL OR TENDER
- No red joints

**MYTH #1: ARTHRITIS IS ALWAYS PAINFUL**
Work-up and management

- **NO LABS TO START**
  - Usually normal ESR and CRP
  - However, if needing lab draw for some other reason or for suspicion of other causes of arthritis, I would recommend CBCD, CMP, ESR, CRP, UA, (ANA, RF, CCP)
- **Xray of affected joint to document baseline**
  - Usually with normal radiograph
  - May show soft tissue swelling
  - With poly JIA or long-standing arthritis may show osteopenia or joint space narrowing
Xray findings in JIA

• Xrays only show soft tissue swelling but do show lack of bony trauma
• Joint space narrowing is present in only 5% early disease (15% 6 yrs after disease)
• Erosions in only 10% early disease (25% 6 yrs later)
• Bone overgrowth in 20% early disease – most commonly at the knees (Oen et al. 2003)
Work-up and management

- No need to refer to orthopedics unless suspected trauma
- **Please refer to ophthalmology!**
  - Presence of uveitis will affect management
  - Subacute chronic uveitis is diagnosed in 50% of JIA patients around time of arthritis diagnosis (Petty and Rosenbaum, 2011); 5% present with uveitis 1st
  - Most common in oligo JIA and RF-negative poly JIA
    - Prevalence 17-26% and 4-25%
    - ANA+, <6 yrs at onset, female sex, and oligo subtype are highest risk factors
Treatment

ACR 2011 Recommendations for treatment of arthritis
Beukelman et al., 2011
Prognosis

- 70-90% without serious disability
- Mortality <0.3%
  - Infection and cardiac dysfunction, secondary amyloidosis (Hull, 1988)
- Risk of decreased growth, leg-length discrepancy, and complications of uveitis
  - 1/3 JIA with complications from chronic uveitis (Saurenmann et al. 2007)
- Systematic review of prognosis in JIA (2014):
  - Poly JIA with worse prognosis
  - Diagnostic delay and systemic JIA highest risk for continued active disease
- May have significant physical/psychosocial impact
  - Peterson et al.: higher disability, more body pain, lower personal health perception, and decreased physical functioning compared to controls.
Prognosis of oligo JIA

- Persistent oligo: 68% clinical remission off medication
- Extended oligo: 31% clinical remission off medication
- High risk of flares: 47% persistent oligo and 67% extended oligo 2 yrs off medication
- Only 6% remain in remission > 5 yrs

Wallace et al., 2005
Case 2:

15 yo female has been complaining of diffuse, intermittent body pains and fatigue. Her thyroid function tests are normal. She has normal cell counts and metabolic panel. Inflammatory markers normal. She has a +ANA. She has a normal physical exam apart from vague complaints of tenderness throughout the exam.
Case 2:

15 yo female has been complaining of diffuse, intermittent body pains and fatigue. Her thyroid function tests are normal. She has normal cell counts and metabolic panel. Inflammatory markers normal. She has a +ANA. She has a normal physical exam apart from vague complaints of tenderness throughout the exam.
The infamous antinuclear antibody (ANA)

- Immunoglobulins directed against structures within the cell (i.e. DNA, ribonuclear proteins, histones, and centromere)
- Immunofluorescent assay incubates patient’s serum with mouse/rat liver nuclear substrate. If ANA is present, they will bind to the nuclear antigens and stain. Titer preformed by serial dilution.
- ELISA method not recommended by ACR
- Pattern of staining = NOT USEFUL.
- Titer of ANA may have some prognostic value.
The infamous antinuclear antibody (ANA)

- Approximately 15% of healthy, asymptomatic population has a positive low titer ANA (<=1:160)
- As one ages, ANA titers increase (40% with low positive ANA by age > 60 yrs)
- Low titers (<= 1:160) found in:
  - Infections
  - Drugs
  - Neoplasias
- High titers (>1:320) found in variety of autoimmune disease
The infamous antinuclear antibody (ANA)

- +ANA is not diagnostic and does not correlate with disease activity
  - Cabral et al., 1992: +ANA in 24/108 kids with musculoskeletal pain but thought unlikely due to autoimmune disease. None developed autoimmune disease over 5 yr follow-up period
  - Deane et al., 1996: +ANA in 113/500 children referred to peds rheum. 31 kids (27%) had no rheum condition at initial visit and followed over 3 years; by end of follow up, 25 patients had resolution of complaints, 5 had significant improvement, 1 autoimmune hepatitis
- Best used as a screening test for suspected lupus and to help evaluate risk of uveitis in patient with JIA
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This patient most likely has:

A. Juvenile arthritis
B. Systemic lupus erythematosus
C. A pain syndrome
D. I don’t know but it’s probably autoimmune since she has a +ANA
Question 2

This patient most likely has
A. Juvenile arthritis
B. Systemic lupus erythematosus
C. A pain syndrome
D. I don’t know but it’s probably autoimmune since she has a +ANA

Myth #2: ANA = rheumatologic illness
Chronic pain syndromes

Can be divided into 2 groups:

1. Mechanical/orthopedic
   - Generalized hypermobility
   - Overuse injuries
   - Osteochondroses
   - Spondylolysis/spondylololithesis
   - Scheurmann disease
   - Growing pains

2. Pain amplification syndromes
   - Aka complex regional pain syndrome, fibromyalgia
Generalized hypermobility

- Beighton scale or Carter-Wilkinson criteria
- Make sure no other findings concerning for syndromes with hypermobility (Marfan, Stickler, etc)
- 20% of the Caucasian population and likely higher in Asians
- Peak ages 3-10; F>M
- Usually FH of “flexibility”
- May have pes planus (mobile flat foot)
- Treatment is supportive
Growing pains

• Aka “benign nocturnal pains of childhood”
• 4-12 yrs, M=F
• Tends to be cramping pain in thigh or calf that occurs later in the day and resolves by morning; responds to massage and mild analgesia
• Normal physical exam
• Treatment is supportive
  • In children with frequent attacks, oral analgesia in the evening may be preventive
  • May benefit from treatment of any underlying mechanical abnormalities

LeBlanc and Houghton, 2011
Pain amplification

• Largely defined as pain out of proportion in the absence of concerning physical exam, labs, or imaging
• Various subsets of chronic pain syndromes
  • CRPS – edema, changes in blood flow in painful area
  • Fibromyalgia – widespread pain for 3 months with pain on digital palpation in 11/18 sites
  • Diffuse idiopathic pain - >=3 sites for >=3 months
  • Localized idiopathic pain – pain in 1 limb
• Up to 10% of new patients presenting to US pediatric rheumatology centers have a chronic pain syndrome

Sherry, 2011
Pain amplification – Work up

- Labs – usually not necessary but would include CMP, CBC/D, CRP, ESR, UA
  - The most common abnormal test is a low +ANA
  - High risk of false positives
- Imaging – again, not usually necessary
  - Some studies suggest that bone scans are most useful study if diagnosis is in doubt (Laxer et al, 1985; Goldsmith et al., 1989)
  - MRI in localized pain amplification can show bone marrow edema
Pain amplification – Treatment

• Goal is restoration of function and relief of pain
• Treatment team is multi-disciplinary and often consists of anesthesiologist or rehab physician, psychologist/psychiatrist, and physical therapist
  • Few pediatric rheumatologists are actively involved in management of chronic pain disorders
• The vast majority of publications focus on PT and OT to reverse immobility and increase function
• Drug treatment (including use of antidepressants and anti-epileptics) is off-label and not well-supported in medical literature as to efficacy
• Psychological support is important
  • Role of guided imagery and muscle relaxation, CBT, traditional psychotherapy
The evolving world of rheumatology

Myth #3: Pediatric rheumatologists treat all autoimmune disease
“So what is it you do again?”

We do it!
Juvenile idiopathic arthritis
Reactive arthritis
Lupus
Juvenile dermatomyositis
Vasculitis
• Leukocytoclastic (refractory HSP)
• Wegeners (shared with pulm and renal)
• MPA (shared with renal)
• PAN
Sjogren’s
Scleroderma (systemic and limited)
Sarcoidosis
Behcet

Not so much (*institution-dependent)
Genetic connective tissues disorders (Ehlers-danlos, Marfan’s)
Immunodeficiency
Urticaria
Abnormal rash
Autoimmune hepatitis
*Kawasaki disease
*Periodic fever syndromes
Thank You!

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