Pediatric Rheumatology: A Case-based Approach to the Basics

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Disclosures

- I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity.
- I am not discussing any off-label uses of medications.
- Duty hours (if they applied to me) were violated in the making of this presentation.
Objectives

- Identify signs and symptoms of common rheumatologic disorders
- Understand appropriate laboratory testing in each disorder
- Understand disease course and therapy for common rheumatologic disorders
The “Five” Pediatric Rheumatology Disorders

- Juvenile Arthritis
- Systemic Lupus Erythematosus
- Juvenile Dermatomyositis
- Scleroderma (localized and systemic)
- Vasculitis
Case One

- A two-year-old female is brought to your office by her mother who reports that the patient was running in the front yard and fell and the mother, upon picking her up, noticed that the right knee was swollen and is worried that “something is broken”
- Exam reveals a large effusion, widening of the surrounding bones, and you are unable to fully extend the knee on range of motion
Juvenile Idiopathic Arthritis (JIA)
(FKA Juvenile Rheumatoid Arthritis)

- Most common childhood arthritis**
- Occurs in 1:1000 children
- Affects children of all ages, but two peaks, at age 1-2 and age 8-12**
Basic Questions to Ask

- Acute or Chronic?
- Localized to joints or more systemic features?
- Fever or not?
- Actual arthritis or arthalgias? (ie., evidence of inflammation?)
- Complaints proportionate to physical findings or not?
JIA: Diagnosis

Evidence of joints inflammation
- redness
- swelling
- limitation of range of motion
- pain

Duration of Arthritis > 6 weeks
Age at onset < 16 years
JIA: Evidence of Chronicity

- Synovial thickening
- Bony proliferation
- Contracture
- Limb length discrepancy
Classification of JIA

- Oligoarticular JIA
  - involvement of <5 joints

- Polyarticular JIA
  - involvement of ≥ 5 joints
  - RF positive vs. RF negative

- Systemic JIA
  - presence of systemic inflammation

- Juvenile Spondyloarthopathies
  - Juvenile ankylosing spondylitis
  - Inflammatory bowel disease-related arthritis
  - Juvenile psoriatic arthritis
  - Reactive Arthritis (FKA Reiter’s syndrome)
Oligoarticular JIA: Clinical Features

- Less than 5 joints
- Typically affects medium to large joints
- Asymmetric
Polyarticular JIA: Clinical Features

- 5 or more joints affected
- Typically affects small to medium joints, but can include large joints
- Symmetric
- Other less common joints
Polyarticular JIA: Other Features

Temporomandibular Joint

Cervical Spine Involvement
Systemic JIA (aka Still’s Disease)

- Think of it as a systemic inflammation that precedes the onset of arthritis
  - typical fever curve**
    - daily or diurnal temperature spike over 39°C
    - returns quickly to below baseline
    - child feels well between temperature spikes
Systemic JIA (aka Still’s Disease)

- Characteristic rash**
  - occurs frequently at peak of fever
  - erythematous macules on trunk and proximal extremities
  - migratory and evanescent
Still’s rash
Koebner’s Phenomenon (dermatographia)

- Isomorphic reaction in which skin lesions appear at the site of trauma
Systemic JIA (Cont’d)

- Signs of visceral involvement**
  - hepatomegaly
  - splenomegaly
  - lymphadenopathy
  - serositis
    - pleuritis
    - pericarditis, including pericardial effusions
    - peritonitis
- No peak age of onset
- No gender predilection
Laboratory Testing in JIA

- Evidence of systemic inflammation**
  - white blood cell count
  - red blood cell count
  - platelet count
  - erythrocyte sedimentation rate
  - C reactive protein
  - serum proteins
- Antinuclear antibodies
- Rheumatoid factors
Rheumatoid Factors

- Antibodies directed against the Fc portion of another antibody
- Rheumatoid factors are negative in children with JIA**
- Rheumatoid factors are positive in adolescents and adults with rheumatoid arthritis
- Most common reason for child to make a RF is infection.
ANAs in JIA

- Frequency varies from 24-66% overall
- Highest frequency in patients with young (<7yrs), female
- Highest prevalence in patients with oligoarticular JIA and uveitis 

**BUT…up to 20% false positive rate, especially with Hep-2 substrate**
Laboratory Studies for Critical Exclusions

- Joint fluid analysis
  - if acute presentation, must exclude septic arthritis

- Complete blood count
  - try to exclude hematologic malignancy

- Serologic testing for Lyme

- Radiography
  - may show peri-articular osteopenia
  - may demonstrate other abnormalities, including osteomyelitis or bone cancer
Goals of therapy for JIA**

- Control of pain and inflammation
- Preservation and improvement of function
- Prevention of disability and chronic deformity
Pharmacologic Therapy for JIA**

Anti-inflammatory agents
- NSAIDs
- ASA
- [corticosteroids]

Disease-modifying agents
- hydroxychloroquine
- methotrexate
- sulfasalazine
- biologic agents (etanercept, infliximab, adalimumab, etc)
- anakinra
Complications of JIA: Uveitis

- Inflammation of the iris, ciliary body, and choroid
- Tends to be asymptomatic in children
- Screening in required for all children with chronic arthritis
- Number One treatable cause of blindness in children
Complications of JIA**

- Musculoskeletal Deformity
  - Regular stretching program
  - Splinting or bracing
  - Regular physical exercise
- Constitutional Growth Delay
- Macrophage Activation Syndrome (HLH)
Outcome in JIA

- Remission rates 70-85% within 2-5 years**
  - oligoarticular  >90%
  - polyarticular  ~50%
  - systemic      <50%

- After disease, all that’s left is chronic deformities and visual disturbance previously untreated
Case Two

- A 14-year-old male presents to the local ER in September with complaints of headache for one week. He also notes some weight loss, rash on his face, and diffuse joint pain.
- Exam reveals a tired-appearing male with a pulse of 122, blood pressure 186/96, resp rate 16, temp 36.7
Case Two (continued)

- Facial rash
- Diffuse joint swelling
- UA reveals blood, protein, and red cell casts
Systemic Lupus Erythematosus

- Incidence/Prevalence
  - 0.53-0.6 per 100,000 incidence
  - approx 5-10,000 cases in US

- Approximately 15% present before age 16
  - rare < 5 years, ↑ in freq through adolescence

- Gender
  - 0-9 years, 4:3 F:M
  - 10-14 yrs, 4:1
  - 15-19 yrs, 5:1
Clinical Manifestations of SLE**

Mucous Membranes

- Frequency 12%
- Mouth ulcers
- Nasal ulcers
Clinical Manifestation of SLE

- **Musculoskeletal (72%)**
  - arthralgias/arthritis
  - myalgias/myositis

- **Serositis (30-40%)**
  - pericarditis
  - pleuritis
  - peritonitis

- **Cardiovascular (15%)**
  - raynaud’s phenomenon
  - myocarditis/endocarditis
Clinical Manifestations of SLE**

- Renal (82%)
  - proteinuria
  - casts

- Neurologic (44%)
  - seizures
  - psychosis
  - Depression

- Hematologic (50%)
  - Bleeding/bruising
  - Petechiae
Clinical Manifestations of SLE**

- Non-specific (100%)
  - malaise
  - fever
  - weight loss

- Cutaneous (80-95%)
  - malar rash
  - discoid LE
  - subacute cutaneous LE
  - photosensitivity
Laboratory Testing in SLE**

- **Cytopenias**
  - hemolytic anemia
  - leukopenia/lymphopenia
  - thrombocytopenia
- **Antinuclear antibodies**
- **Anti-DNA antibodies**
- **Extractable Nuclear Antibodies (Ro, La, Sm, RNP)**
- **Complement**
Criteria to Diagnose SLE

- 2012 SLICC Criteria versus 1997 ACR criteria
- Require presence of both clinical and immunologic abnormalities
- Both require at least 4 criteria**
  - SLICC includes at least 1 clinical and 1 immunologic
- SLICC includes renal-isolated lupus and more neuro features
ACR Criteria for SLE 1997: Clinical

- Malar rash
- Discoid rash
- Photosensitivity
- Oral ulceration
- Arthritis
- Serositis
- Renal
- Neurologic (seizures or psychosis)
- Hematologic (hemolytic anemia, leukopenia, lymphopenia, thrombocytopenia)
ACR Criteria 1997: Laboratory

- Positive ANA
- Positive immunoserology
  - ds DNA antibodies
  - Sm antibody
  - Antiphospholipid Ab

- 4 of 11 criteria sensitivity of 83%, specificity of 96%
SLICC Criteria for SLE 2012: Clinical

- Acute cutaneous lupus
- Chronic cutaneous lupus
- Oral or nasal ulceration
- Non-scarring alopecia
- Synovitis
- Serositis
- Renal
- Neurologic involvement (seizure, psychosis, mononeuritis multiplex, nyelitis, neuropathy, acute confusional state)
- Hemolytic anemia
- Leukopenia or lymphopenia
- Thrombocytopenia
SLICC Criteria 2012: Laboratory

- Positive ANA
- Anti-ds DNA antibodies
- Anti-Sm antibody
- Antiphospholipid Antibodies (lupus anticoagulant, false-positive RPR, anticardiolipin antibodies, anti-beta 2-glycoprotein I)
- Low complement (low C3, low C4, low CH50)
- Positive direct Coombs’ test without a hemolytic anemia

4 of 11 criteria sensitivity of 97%, specificity of 94%
SLE: Treatment**

- Corticosteroids
  - Oral
  - Intravenous
- Hydroxychloroquine (Plaquenil)
- Methotrexate
- Mycophenolate Mofetil
- Cyclophosphamide
- Other
  - Calcium
  - Vitamin D
Complications of Treatment**

- Growth failure
- Fertility/amenorrhea
- Osteoporosis
- Body image
  - weight gain
  - cushingoid appearance
  - acne
Case Three

- A five-year-old male is brought to your office by his parents for complaints of decreased energy and difficulty performing regular tasks. This has been worsening over the last several weeks. He denies any muscle or joint tenderness. On review of systems, his parents report that he has had eczema on his face for the last several months that has been resistant to any medical therapy.

- Physical exam reveals a cooperative male who is unable to lift his arms above his head or get up from a sitting position. Skin exam reveals a facial rash and red bumps on his fingers.
Juvenile Dermatomyositis (JDM)

- Frequency in population 0.5 per 100,000
- Bimodal peak of age of onset
  - 10-14 years (approx 16-20%)
  - 45-64 years
- Gender predilection: approx 2:1 F:M
Clinical Manifestations of JDM

- **Cutaneous Manifestations**
  - JDM rash
  - heliotrope rash
  - Gottron’s papules
  - periungual erythema
  - ulcerative disease
  - [acanthosis nigricans]

- **Proximal muscle weakness**
  - large muscle groups versus small
  - clues on movement and gait
Clinical Manifestations of JDM

- Evidence of inflammatory myositis**
  - elevated muscle enzymes
  - electromyography
  - muscle biopsy
  - magnetic resonance imaging

- Gastrointestinal
- Respiratory
- Calcinosis
- Lipoatrophy
Laboratory Testing in JDM

- **Muscle enzymes**
  - AST/SGOT
  - ALT/SGPT
  - CPK
  - aldolase
  - LDH

- **Antibodies**
  - Antinuclear antibodies (frequency 10-80%)
  - PM1, Jo1, etc (<20% in children)
JDM: Differential Diagnosis

- Dermatomyositis versus polymyositis
- Muscular dystrophy
- Guillain-Barre disease
- Other inflammatory myopathies
JDM: Treatment

- Immunosuppressive therapy
  - Prednisone
  - Steroid-sparing agents:
    - methotrexate
    - cyclophosphamide
    - cyclosporine
    - azathioprine
  - Intravenous immunoglobulin

- Stretching to maintain range of motion
- Continuation of other regular activities
JDM: Complications**

- Respiratory impairment
- GI vasculitis
- Steroid-related side effects
- Side effects of steroid-sparing agents
- Calcinosis
- Insulin resistance/lipoatrophy
JDM: Long Term Outcomes**

- 70% well and functional
- 20% long term complications
- 10% die
Case Four

- A 13-year-old female presents with persistent and increasing rash on her left lower extremity. It is red, nontender, and nonpruritic, but is interfering with her ability to extend her leg.
- Physical exam reveals a firm, shiny, erythematous strip of skin extending from the left hip, down the lateral side of her leg, across her knee to the dorsal surface of her foot.
Scleroderma and Relatives

Types

- Localized scleroderma**
  - morphea
  - linear scleroderma
- Diffuse scleroderma**
  - systemic sclerosis
  - CREST
- Mixed Connective Tissue Disease
- Eosinophilic Fasciitis
Clinical Manifestations of Scleroderma**

- **Cutaneous (skin thickening)**
- **Musculoskeletal**
  - Limitation of range of motion
  - Abnormal limb growth
- **Raynaud’s phenomenon**
- **Gastrointestinal**
- **Pulmonary**
- **Renal**
Laboratory Testing in Scleroderma

- Antinuclear Antibodies
  - SCL-70 (DNA-topoisomerase 1) 26% freq
  - anticentromere (kinetochore) 22% freq
  - anti-RNP (100% freq in MCTD)

- Rheumatoid Factors

- Proteinuria/hematuria

- Hematologic
  - anemia
  - eosinophilia
Scleroderma: Treatment

- Immune modulators/anti-inflammatory therapy
  - Prednisone
  - Methotrexate
  - Cyclophosphamide

- Decrease Collagen cross linking
  - [D-penicillamine]

- Prevention of further organ injury:
  - Ca channel blockers
  - cold precautions

- Preservation of function:
  - intensive PT/OT

- General supportive care
Systemic Vasculitis

- Very rare in children**
- Peak age 9-11 yrs, range 3-16 yrs
- Equal incidence male/female
- Most presentations of systemic vasculitis do not follow specific patterns
- Some more common vasculitic syndromes of childhood present as a constellation of otherwise nonspecific symptoms
- Most common vasculitis of childhood is Kawasaki Disease (discussed elsewhere)
Case Five

- An eight-year-old boy presents to the emergency room with bruising on his lower extremities and abdominal pain.
- Physical exam reveals purpura on both legs, as well as bilateral ankle arthritis. His scrotum is swollen and ecchymotic. Abdominal exam demonstrates normal bowel sounds and no HSM.
Henoch-Schonlein Purpura

- AKA anaphylactoid purpura
- Second most common vasculitis of childhood
- Most common in children 5-15 years of age, rare in adults**
- Male to female 1.5 : 1
- Incidence varies from 0.1 to 13.5 per 100,000
- Seasonal variation: peaks during winter
  - ? Relationship to streptococcus
HSP: Clinical Manifestations

- **Cutaneous Manifestations**
  - Palpable purpura (100%)
    - most prominent in dependent areas, legs, buttocks
    - range from petechiae to ecchymoses
    - can be preceded by urticaria or MP
  - SQ edema of hands and feet, face, scrotum
HSP: Clinical Manifestations

- Arthalgias/Arthritis (65-85%)**
  - usually involves large joints (knees, ankles)
  - periarticular swelling and tenderness, but usually non-erythematous
  - transient, but not migratory
  - lasts few days to a week
HSP: Clinical Manifestations

- Gastrointestinal involvement (60-100%)**
  - Gut vasculitis
  - colicky abdominal pain
  - heme (+) stools
  - intestinal perforation
  - within one wk to one month of rash

- Renal involvement (20-50%)**
  - acute glomerulonephritis
  - hematuria/proteinuria
  - hypertension
  - renal failure
  - within one to three months of rash
HSP: Laboratory Testing

- Pathology: leukocytoclastic vasculitis with IgA deposition
- Must not have thrombocytopenia**
- May have elevated inflammatory parameters
- Normochromic normocytic anemia
- Abnormal urinary sediment
- Normal complements
EULAR Consensus Criteria for HSP

- classical palpable non-thrombocytopenic purpuric rash and any one of the following:
  - Arthritis or arthralgia
  - Abdominal pain and/or GI bleeding
  - Any biopsy with predominant IgA deposition
HSP: Treatment**

- Supportive care
- NSAIDs for arthritis
- Corticosteroids
  - for severe GI disease
  - Active renal disease
  - 1 mg/kg/d divided bid
HSP: Disease Course

- Resolves within one month in 66%
- At least 50% will have recurrence, usually of rash or GI symptoms**
  - usually within first 6 wks, but up to 1-2 years
- Don’t forget intussusception**
- Late renal outcome: less than 5% progress to end stage renal disease
Any additional questions?

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