REACTIVE ARTHRITIS

Background

1. Definition: aseptic inflammatory arthritis occurring 1 to 4 weeks after an enteric or urogential infection[1,2]
2. General Information:
    - Formerly known as Reiter's Syndrome – classic triad of arthritis, urethritis and conjunctivitis (only seen in approximately one-third of Reactive Arthritis cases[7]).
    - Member of the spondyloarthritis family of disorders

Pathophysiology

1. Pathology of Disease
    - Triggered after enteric (dysentery) or urogenital infection (urethritis, cervicitis or proctitis)- unclear exact mechanism[1]
    - Common pathogens: *Chlamydia trachomatis (40%), Neisseria gonorrhea, Shigella, Salmonella, Yersinia, Campylobacter and Clostridium difficile*[2,3]
    - Association with HLA-B27 (presumed to be a genetic predisoposing factor) in two-thirds of cases[7]
2. Incidence, Prevalence
    - Not well defined but thought to be uncommon, 10-19 cases per 100,000[1,6]
    - Male-to-female ratio in post venereal infections: 10:1; post enteric: 1:1[2,4]
    - Peak onset 15-35 yo[2]
    - May be more common than Rheumatoid Arthritis[1]
3. Risk Factors
    - HLA-B27
    - History of enteric infection as stated above (longer episodes of diarrhea associated more closely with reactive arthritis) or urogenital infection (40% associated with antecedent Chlamydia infection, which may be asymptomatic) within 3 months of onset of arthritis
    - HIV/AIDS- tends to portend a more virulent course of arthritis [3]
4. Morbidity / Mortality[1-7]
    - Course is typically variable but most patients have arthritis symptoms lasting weeks to 6 mo but synovitis may be present for over a year
    - Recurrent bouts of arthritis are common (25-50% of patients)
    - Chronic arthritis (symptoms persisting 6 mo to 5 years or more) or sacroiliitis [occurs in 20-30% of patients; more closely associated with HLA- B27 gene
    - Chronic uveitis may rarely lead to visual impairment or blindness
    - Rareaortic root involvementand heart block

Diagnostics

1. History[1-4]
    - Genitourinary (may be asymptomatic) or enteric infectious process precedes arthritis by 1-4wks
    - Conjunctivitis – often mild and transient but 20% with acute anterior uveitis (iritis) which may be severe

- Asymmetric mild to moderate joint stiffness (knees, ankles, or feet)
- Low back pain with radiation to buttock
- Enthesitis – inflammation at bony insertion site of tendons and ligaments
- Fatigue, malaise, fever, weight loss (minority of patients, approximately 10%)

2. Physical Examination
   - Asymmetric oligoarthritis, particularly of the lower extremity (rare to have isolated upper extremity involvement)[1]
   - Enthesitis in 40% classically at Achilles and plantar fascia areas[4] and Dactylitis(sausage shaped fingers),
   - Asymmetric sacroilitis (low back and buttock pain) in 10-50%[1]
   -
   - Skin manifestations:
     - Balanitis circinata: shallow painless ulcers on meatus and glans penis (20% of men)[5]
     - Keratoderma blennorhagica: (12% of patients[4]) hyperkeratotic skin found on feet, toes, palms, scrotum, trunk, and scalp- similar to pustular psoriasis lesions
     - Nail thickening and superficial oral ulcers which may be painless[1]
   - Conjunctivitis with mucopurulent discharges (30-50% of patients- usually mild) or Uveitis (requires slit lamp exam for diagnosis) in up to 20% during course of disease[4]
   - Aortic valvular insufficiency and conduction abnormalities (infrequent and often asymptomatic)[3]

3. Diagnostic Testing
   - Diagnostic "Criteria" – not well established, more a diagnosis of exclusion based on clinical scenario and findings on exam[2]
   - Laboratory evaluation – if chronology of arthritis symptoms consistent with possible preceding infection; but no specific diagnostic test exists for Reactive Arthritis[2]
     - Cervical or urethral swab or urine specimen for *Chlamydia* via culture, DFA, NAAT or EIA (may also consider throat or rectal swab as applicable)
     - Consider stool cultures (usually negative at time of arthritis symptoms)
     - Arthrocentesis and fluid analysis (cell count, gram stain, culture, crystal analysis) to rule out other causes of arthritis -especially in cases of single joint involvement

     Other tests to consider but none are specifically diagnostic[2,3,4]:
     - CBC (leukocytosis/anemia/thrombocytosis)
     - ESR/CRP (acutely elevated)
     - RF/ANA (negative)
     - HLA-B27 (positive; little diagnostic value but may be helpful in atypical cases)
     - HIV (in patients found to have other STDs)
   - Imaging: X-rays of affected joint(s)- not needed for diagnosis but may help to rule out other types of arthritis[2]

- May be normal in early course of disease
- Up to 20% of chronic cases may show new periosteal bone formation, ossification of entheses, or sacroiliitis [PEPID Internal link] (unilateral)
- Echocardiogram and/or EKG (infrequent aortic root involvement/ aortic regurgitation/ conduction disorder more often found in chronic cases with spondylitis involvement)
- Colonoscopy – if clinically warranted due to overlap with inflammatory bowel disease and associated arthralgias

Differential Diagnosis

1. Key Differential Diagnoses [1-3]
    - Infectious (especially in cases of acute monoarthritis)
        - Disseminated gonococcal infection
        - Septic arthritis
    - Rheumatologic
        - Rheumatoid arthritis (positive rheumatoid factor)
        - Psoriatic arthritis (positive serology)
        - Crystalline arthritis (crystals in joint fluid)
        - Seronegative spondyloarthropathies (ankylosing spondylitis)
    - Inflammatory bowel disease
2. Extensive Differential Diagnoses[1-3]
    - Infectious
        - Lyme disease
        - Rheumatic fever
        - Still's disease

Therapeutics [1-4]

1. Acute Treatment-symptomatic only- no evidence that treatment affects disease course
    - NSAIDs, at anti-inflammatory doses – i.e. naproxen 500mg two times daily or indomethacin at 25-50mg up to four times daily for minimum two week course
        - Proper attention warranted to potential significant NSAID side effects and consideration given to prescribing GI protective medication, i.e. PPI
    - Antibiotics- when chlamydia suspected, treat with Azithromycin or Doxycycline as per current STD treatment guidelines;
    - Role of long term antibiotic therapy is not well established. Unclear if treatment of STD affects course of Reactive Arthritis and probably does not
    - Typically antibiotics are not recommended for uncomplicated infectious diarrhea.
    - If conjunctivitis present, treat with topical erythromycin
    - Rest as needed and Physical Therapy for improved functionality as needed
2. Long-Term Care
    - Consider Sulfasalazine at 2000mg/day if NSAIDs ineffective

- Intra-articular corticosteroid injection (but not as effective as in Rheumatoid Arthritis)
- Methotrexate and/or azathioprine -HIV testing needed at this stage
- Recalcitrant cases may require use of anti-TNf therapies- infliximab or etanercept
- Physical therapy

Follow-Up

1. Return to Office
   - Time frame for return visit- as needed in 2 weeks
2. Refer to Specialist
   - Consultation with **ophthalmologist** for optimal slit lamp evaluation and treatment recommended
   - Aortic valve disease will necessitate cardiology consultation
   - Refer to rheumatologist if diagnosis uncertain
3. Admit to Hospital
   - As needed for pain control or inability to tolerate oral meds
   - Inability to ambulate

Prognosis

1. Signs and symptoms usually remit within 6 months
   - Relapses occur in 25-30% and/or chronic arthritis (10-30% of cases) which may be destructive of affective joints[2]
2. More frequent recurrences and chronic disability associated with
   - Heel pain
   - Sacroiliitis
   - Concomitant HIV disease

Prevention

1. Primary prevention: Avoidance of urogenital and enteric infections [4]
2. Secondary prevention: unclear if early STD treatment affects course of Reactive Arthritis but may prevent it from occurring; treatment of enteric infection usually not indicated and often resolved prior to occurrence of arthritis symptoms. Necessary to perform eye exam and treat uveitis if present to prevent complications.[4]
3. Tertiary prevention: consider EKG and echocardiogram to assess for aortic root involvement as may be entirely asymptomatic[4]

Patient Education

1. American Academy of Family Physicians AFP journal handout: What You Should Know about Reactive Arthritis
2. FamilyDoctor.org handout: Reactive Arthritis

References

1. Klippel JH,Stone JH, Crofford LJ, White PH. Primer on the Rheumatic Diseases, 13th edition, 2008, pp. 217-220.
2. Sigal LH. Update on Reactive Arthritis. Bulletin on the Rheumatic Disease 2001; 50 (4):1-4.

3. Barth WF, Segal K. Reactive Arthritis (Reiter's Syndrome).Am Fam Physician 1999; 60(2):499-503, 507.
4. Clinical Effectiveness Group (CEG). United Kingdom national guideline on the management of sexually acquired reactive arthritis 2008. London (UK): British Association for Sexual Health and HIV (BASHH); 2008. 31 p. [121 references] http://www.guideline.gov/summary/summary.aspx?doc_id=13596&nbr=006959&string=reactive+AND+arthritis
5. Kataria RK, Brent LH. Spondyloarthropathies. Am Fam Physician 2004; 69(12): 2853 Am Fam Physician 2004 Jun 15;69(12):2853
6. . Goldman L, Ausiello D. Cecil Medicine, 23rd edition, 2008, pp.2019-2020.
7. Rakel RE. Textbook of Family medicine, 7th edition, 2007, pp. 936-938.

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