REACTIVE ARTHRITIS

Background
1. Definition: aseptic inflammatory arthritis occurring 1 to 4 weeks after an enteric or urogenital 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 predisposing factor) in two-thirds of cases.\(^4\)
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
   - Rare: aortic root involvement and 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
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1. Clinical Presentation

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

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

Prognosis
1. Signs and symptoms usually remit within 6 months
   o 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
   o Heel pain
   o Sacroiliitis
   o 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

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