



Reactive Arthritis in Children

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Reactive arthritis (ReA) is an autoimmune condition that develops in response to an infection in other part of the body. It is a term reserved for a sterile inflammatory arthritis occurring after an infection in the body. ReA denotes a heterogeneous group of arthritic disorders. Overall it is one of the most common childhood rheumatic diseases. No satisfactory classification and diagnostic criteria are available for (ReA). Clinical and laboratory findings available even are not specific for all the diagnostic category (1). It comprises mainly post streptococcal arthritis, post infectious arthritis, and classical reactive arthritis following genitourinary and gastrointestinal infections.

Post streptococcal Reactive Arthritis (PSReA)

Friedberg first described that a reactive arthritis might occur in response to a streptococcal infection as a separate entity from rheumatic fever in the 1950s. In 1980s, investigators described other cases of reactive arthritis as they were not characteristic of acute rheumatic fever (2). Post streptococcal reactive arthritis (PSReA) encompasses significant heterogeneity and appeared different both from that of acute rheumatic fever (ARF) and from that of HLA B27-associations with HLA class II antigens of PSReA (DRB1*01) and ARF (DRB1*16) were described. But the link between the arthritis and the streptococcal infection is still not proven unanimously (3, 4). Post-streptococcal reactive arthritis differs from acute rheumatic fever by early development of arthritis after pharyngitis and more protracted arthritis or arthralgia with a less dramatic response to aspirin(4). Other factors differentiating from ARF are the age of onset, the non-migratory character, the high incidence of occurrence of erythema nodosum and multiforme, as well as evidence of transient hepatitis and axial arthritis in some cases. Arthritis being the hallmark of this disease, PSReA is probably the proper nomenclature (5). It affects mainly the age group of 5-15 years. It is associated with elevated ASO and anti-DNAse B titre. Involvement of cardiac tissue is seen in approximately

5% of cases in follow-up, which is termed, as silent carditis. Proposed diagnostic criteria in PSReA includes presence of characteristic arthritis with evidence of antecedent group A streptococcal infection without fulfilling the criteria of modified Jones for diagnosis of acute rheumatic fever. NSAIDs as a group of analgesics are the principle drugs used for the treatment without any special advantage of aspirin as that of ARF. Antimicrobials are to be given after initial diagnosis to eradicate streptococcal infection.

All patients with post streptococcal reactive arthritis should receive penicillin prophylaxis. American Heart Association suggests prophylaxis for one year and to be discontinued after that if carditis does not appear by then. But some centers in the West prefers to continue penicillin prophylaxis up to the age of 21 years or minimum of 5 years which ever is earlier. But the proper duration of treatment and appropriate guidelines for patient selection have not been conclusive till now which will only be possible with a collaborative effort made to accurately define this illness, analysis of its etiopathogenesis and natural history. Still then each physician must evaluate the potential risks and benefits of penicillin prophylaxis in view of the risk of rheumatic fever in the individual (6).

Classical Reactive Arthritis (ReA)

This refers to an inflammatory joint disease in the absence of bacteria in the joint, but which is caused by a distant extraarticular infection. They occur as a result of a variety of arthritogenic infections, which are essentially genital or gastro-intestinal in subjects with a particular genetic predisposition characterized by the presence of the HLA-B27 antigen. The most complete clinical expression of classical reactive arthritis is the Fiessinger-Leroy-Reiter syndrome. Reiter syndrome basically had a triad of arthritis, conjunctivitis and urethritis. It is modified with addition of cutaneous changes to form a diagnostic tetrad now (4).

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Many reactive arthritis-evoking agents are known to exist in literature, eg, *Chlamydia traehomatis*, *Ureaplasma urealytium*, pseudotuberculosis, *Shigella flexneri*, salmonella, *Campylobaeter jejuni*, toxocara, yersinia, cryptosporidia, rarely by *Clostridium difficile* and *Giardia lamblia*, etc(3-9). Reactive arthropathies usually show close relationships to each other and to other HLA-B27-associated spondyloarthropathies, ReA may represent an autoimmune response involving T lymphocytes that cross react to antigens in joints (molecular mimicry). A study of synovial fluid from patients with reactive arthritis suggested that T cells may be more engaged in promoting inflammation than in eliminating bacteria through cytotoxic mechanisms. Several viruses (rubella, varicella-zoster, herpes simplex, and CMV) have been isolated from the joint space. Antigens from other viruses (hepatitis B, adenovirus7) have been identified in immune complexes from joint tissue (3, 4, 7, 8). Berlin Third International Workshop on ReA in 1995 formulated a diagnostic criterion as the presence of asymmetric peripheral arthritis with evidence of preceding infection defined spondyloarthropathies.

The exact frequency of occurrence of ReA depends on prevalence of HLAB27 and the community prevalence of infections with arthritogenic bacteria. Reactive arthritis occurs 8-40/100 cases of pediatric rheumatologic disorders, with no sex predilection and more commonly seen in 3-12 year age group.

Frequency of HLA-B27 positivity is tuned to 85% in patients with ReA. Exact role of HLA-B27 in pathogenesis of ReA is still unknown. It probably helps in presenting bacterial antigenic peptides to either CD4 or CD8 cross reactive T cells, which ultimately lead to paramount inflammatory responses characteristics of these conditions. Other association till today noted with TNF c1 allele and TAP2 (Transporter associated with antigen processing) polymorphism.

Diagnostic workup needed for reactive arthritis includes stool and urine culture, serology for arthritogenic bacteria, polymerase chain reaction (PCR) to detect bacterial DNA from synovial material, urethral swab, etc and even lymphocyte stimulation of synovial fluid by suspecting organism. Radiological features are nonspecific with evidence of effusion in joints in some cases on sonography studies. The long-term prognosis varies in children with ReA. Most of them remit after one episode but some cases up to 30% may have recurrent or chronic involvement and even may have identifiable

spondyloarthropathy later. Chronicity is more common with HLA B27 positivity, extra-articular involvement etc.

Treatment modalities include mainly NSAIDs. But in chronic cases intraarticular steroids, systemic steroids or even immunosuppressive agents like methotrexate may require to be used. Uses of antibiotics are controversial requiring more studies till now (3, 4).

Post infectious Arthritis

Apart from the reactive arthritis with a generally accepted etiology, broader definition of ReA includes post streptococcal arthritis, and as well as cases of post infectious arthritis following gonococcal, meningococcal and brucella infections, etc.

Recently there are many case reports of postinfectious arthritis described with meningococcal infection, H influenza B infection, infective endocarditis, infected ventricular shunts, etc in children. In most of these conditions immune complex- mediated pathogenesis is postulated. The patient becomes symptomatic during the recovery phase where immune complexes are demonstrated in the synovium.

It is stressed that ReA should be considered and differentiated in children and it is usually a relatively short lived condition that may last for up to 6 months and in most cases disappear completely leaving no problems in future.

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