Association of Reactive Arthritis with Enteric Pathogens

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ABSTRACT

Reactive arthritis (ReA) also known as post infectious arthritis, affects 1-4% of people days to weeks after being infected by an enteric, urogenital or upper respiratory infection. The most common enteric bacterial pathogens that have been associated with ReA include Salmonella, Shigella, Campylobacter, enterotoxigenic *Escherichia coli* and Yersinia. It is quite necessary to determine the burden of ReA due to enteric infections using standard criteria. The clinician should investigate for the evidence of previous bacterial infections. In addition, it is very important to carry follow-up studies of patients with enteric infection so as to clarify the association of ReA with enteric pathogens. No curative treatment for reactive arthritis (ReA) exists. Instead, treatment aims at relieving symptoms and is based on symptom severity. Prevention of enteric and genitourinary bacterial infections is the best option.

Reactive arthritis (ReA), formerly termed Reiter syndrome(RS), also known as post infectious arthritis, is a spondylo arthropathic disorder characterized by inflammation of the joints and tissues that develops following a bacterial infection of gastrointestinal or genitourinary tract.[1,2] The classic triad of ReA consists of post-infectious arthritis, nongonococcal urethritis and conjunctivitis.

It is relatively an uncommon disease, affecting 1-4% of people days to weeks after being infected by an enteric, urogenital or upper respiratory infection. The most common enteric bacterial pathogens that have been associated with ReA include Salmonella, Shigella and Campylobacter.[3] It was also found to be associated with asymptomatic enteric infections, enterotoxigenic Escherichia coli and Yersinia.[4-6]

Reactive arthritis occurs because of a cellular immune response involving CD8 T-cells. Reactive arthritis is seen more in immunocompromised patients than immunocompetent patients, specifically in those with low CD4 T-cells counts.[7]

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Reactive arthritis usually begins after an infection involving the gastrointestinal or genitourinary tracts. Initial symptoms include malaise, fatigue, stiffness, pain and arthralgia in the joints of the lower extremities. The onset of this joint pain can occur suddenly and can be accompanied by a fever of over 102°F, weight loss and inflammatory back pain. Arthritis can occur in association with bacterial infections or can occur few days to weeks after the infection has cleared. Thus, blood, urine and stool cultures should be collected from these patients who present with a suspected gastrointestinal or urogenital bacterial infection to confirm the causative organism. The arthritis often occurs within 2 weeks after the onset of gastroenteritis but the onset can range from 4 to 35 days. Reactive arthritis has been reported as a complication of Salmonella infection in 0.2-7.3% of cases.[8] Reactive joint complications triggered by Salmonella are increasingly reported but the outcome and long term prognosis of the patients is incompletely known.

Due to scarcity of Shigella in developed countries, it is the least common of the gastroenteritis inducing organisms which are associated with ReA. A survey of Shigella infected subjects describes an annual incidence of Shigella induced ReA of only 1.3 per million.[9] It has also been stated that susceptibility of ReA is strongly associated with HLA-B27.[10] Some studies showed lack of association with HLA-B27 but a Salmonella outbreak investigation in Australia showed only 2 of 19 subjects with ReA had HLA-B27.[11] However, there was a

List of organisms associated with Reactive Arthritis:-

Bacterial agents	
Salmonella Typhi	*Campylobacter jejuni*
Salmonella Enteritidis	*Campylobactercoli*
Salmonella Typhimurium	*Yersinia enterocolitica*
Shigella flexneri	*Clostridium difficile*
Shigella sonnei	*Borrelia*
Escherichia coli O157	*Chlamydia trachomatis*
Enterotoxigenic E coli (ETEC)	*Hafnia alvei*
Parasitic agents	
Cryptosporidium	*Strongyloides stercoralis*
Giardia lamblia	*Schistosoma mansoni*

study which was conducted to look for the presence and role of any common bacterial antigen among the pathogens isolated from ReA patients. They found a common 30kDa antigen specifically present among seven arthritogenic enteric bacterial strains belonging to three genera Salmonella, Shigella and Hafnia. Post-dysenteric ReA patients' sera showed higher levels of immunoglobulin G, immunoglobulin M and immunoglobulin A antibodies against this antigen as compared to the controls. 30kDa antigen may be a common arthritogenic factor associated with post dysenteric ReA/RS. The association of Hafnia alvei with post-dysenteric ReA was described for the first time. Four cases of mycobacterial ReA had an association with this antigen, suggesting that the arthritogenic antigen of mycobacteria and enteric bacteria may be of a similar nature.[12]

The diagnosis for ReA is based entirely on clinical presentation and physical examination as there is no “gold standard” diagnostic test or imaging finding is available for ReA. Also the patients present with wide range of symptoms, some of which resemble other spondyloarthropathic disorders which leads to difficulty in making diagnosis.[1,13] Therefore, it is quite necessary to determine the burden of ReA due to enteric infections using standard criteria. The clinician should investigate for the evidence of previous bacterial infections. Even if the gastrointestinal symptoms are not present, the health provider should recommend the stool culture for these patients. Serologic testing for Yersinia, Salmonella and Campylobacter are relatively easy to perform and inexpensive. The use of imaging studies, including magnetic resonance imaging (MRI) is quite helpful to diagnose enteritis that is not clinically obvious. Although ReA can be self-limiting, resolving within 6 months, it has been estimated that up to 63% of affected patients will develop a chronic form of ReA.[14]

The treatment of ReA is still under investigation. Treatment aims at relieving symptoms and is based on symptom severity. Around two thirds of patients have a self-limited course and about 30% develop chronic symptoms leading to a therapeutic challenge. Non-steroidal anti-inflammatory drugs (NSAIDs) are currently the mainstay of treatment. Sometimes, joint injections with glucocorticoids and disease modifying antirheumatic drugs (DMARDs) may be beneficial.[13] The best way is the prevention of enteric and genitourinary bacterial infections including sexually transmitted diseases. Patients presenting with recent onset of arthritic complaints should be enquired about recent diarrheal illness. It is very important to carry follow up studies of patients with enteric infection so as to clarify the association of ReA with enteric pathogens. For the optimal treatment of ReA triggered by enteric pathogens, we have to wait for the results of the ongoing placebo controlled studies.

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