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Infections and arthritis

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A B S T R A C T

Bacteria, viruses, fungi, and parasites can all cause arthritis of either acute or chronic nature, which can be divided into infective/septic, reactive, or inflammatory. Considerable advances have occurred in diagnostic techniques in the recent decades resulting in better treatment outcomes in patients with infective arthritis. Detection of emerging arthritogenic viruses has changed the epidemiology of infection-related arthritis. The role of viruses in the pathogenesis of chronic inflammatory arthritides such as rheumatoid arthritis is increasingly being recognized. We discuss the various causative agents of infective arthritis and emphasize on the approach to each type of arthritis, highlighting the diagnostic tests, along with their statistical accuracy. Various investigations including newer methods such as nucleic acid amplification using polymerase chain reaction are discussed along with the pitfalls in interpreting the tests.

Introduction

The colonization of the human body by an enormous load of microbes has been the focus of several research initiatives over the past decade, with a steady influx of new insights into their association with autoimmunity [1,2]. The possible role of external microorganisms – viruses, bacteria, fungi, and parasites – both in causation and in the triggering of inflammatory arthritis is complex, but it has been appreciated since the time of Hippocrates [3]. The World Health Organization, in association with the

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Arthritis and Rheumatism Research Council, analyzed the connection between joints and infection critically in 1974, and they classified the relationship into the following four groups [4]:

Group I: This group includes septic or infectious arthritis with the causative organism being identified in joints secondary to an infection elsewhere in the body.
Group II: This group comprises post-infectious arthritis with bacterial antigens being detected in the joint.
Group III: This group includes reactive arthritis (ReA) with the infection originating in the uro-genital or gastrointestinal system causing inflammatory joint disease, but the microbe not being detected in the joint.
Group IV: This group consists of inflammatory arthritis triggered by microbes, where neither the organism nor its product or antigen is established in the joint.

The type of arthritis is generally determined by both microbial and host factors alike. Age, genetic susceptibility, gender of the individual, presence of comorbidities, and status of the joints are some of the critical host factors. Important microbial factors include virulence of the organism, ability of the organism to produce toxic substances, degradability of microbial products, and tissue tropism [5]. Pyogenic bacteria and viruses are generally the perpetrators of acute infectious arthritis, while chronic arthritis is usually caused by mycobacteria and fungus. With new viruses emerging as etiologic agents in acute inflammatory arthritis, swiftly changing its epidemiology, and with advances in the field of molecular biology, genetics (whole exome sequencing), and immunological investigations, it is important to understand the relationship between microorganisms and joints.

This review focuses on the role of various etiological agents causing primary infective arthritis, their myriad clinical presentations, laboratory tests aiding in diagnosis, and the common pitfalls to be considered while interpreting the tests.

Determinants and mechanism of infection-related arthritis

Microbial factors

Staphylococcus aureus and *Neisseria gonorrhoeae* are bacteria with a strong predilection for joint cavities, adhering to the synovial tissue and producing toxins which promote colonization during the bacteremia phase [6,7]. *S. aureus* has multiple receptors, termed as microbial surface components recognizing adhesive matrix molecules, which aid in adherence to joint extracellular matrix or implanted devices [8,9]. Certain strains of *S. aureus* that are positive for cytotoxin virulence (Panton–Valentine leukocidin, PVL) survive in neutrophils, and they are associated with fulminant joint infections in healthy individuals [10]. *N. gonorrhoeae* strains possess many cell surface structures that are responsible for their virulence. They express specific cell surface and extracellular proteins, which make them resistant to killing by factors in the serum [11]. Microbes responsible for causing ReA are generally facultative or obligate intracellular pathogens in the gastrointestinal or genitourinary tract, capable of infecting stable mucosa.

Host factors

Systemic, local, and social host risk factors play a vital role in infectious arthritis. Normal joints, as compared with diseased or prosthetic joints, are resistant to infections. Certain factors in hosts increase the risk of bacteremia and weaken inherent defensive mechanisms. Age and gender of the patient are two important factors which determine the type of organism. Staphylococci are the most common agents of septic arthritis in adults [12,13]. In children younger than 2 years, *Haemophilus influenzae*, *S. aureus* and group A streptococci are the common organisms [14]. Of late, arthritis caused by *Kingella kingae* is on the rise in children [15]. Women in their first week of menstrual cycle, pregnancy, puerperium and those with complement deficiencies (C5–C8) have a greater incidence of gonococcal arthritis [16,5]. Genes, especially human leukocyte antigen (HLA) alleles, play a cardinal role in diseases