Intra-articular co-infection by _Borrelia burgdorferi_ and _Chlamydia trachomatis_

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Abstract

Objective—_Chlamydia trachomatis_ and _Borrelia burgdorferi_ infections are frequently the cause of unexplained oligoarthritis, as shown by identification of bacteria specific DNA in joint material from patients with reactive arthritis, Lyme arthritis, and undifferentiated oligoarthritis. The aim of this study was to determine whether the two organisms occur simultaneously in joint material from patients with arthritis.

Methods—Seventy six patients with unexplained arthritis were prospectively studied. Synovial fluid was obtained from all patients and examined for DNA from _C trachomatis_ and _B burgdorferi_ using specific polymerase chain reaction (PCR) protocols. Data concerning prior genitourinary infection or a history of tick bite were recorded and serum antibodies to _C trachomatis_ and _B burgdorferi_ were determined.

Results—Six patients (8%) had DNA from both _C trachomatis_ and _B burgdorferi_ in the same synovial fluid specimen (mean leucocyte count 11.925/mm³, 65% granulocytes). These patients (four men, two women; mean age 33.7 years) all had oligoarthritis of the knee, ankle, or both (mean disease duration 11.3 months). From the history and serological examination, four patients had some evidence of actual or previous infection with one or other of the bacteria, while the other two patients had a positive serological test for _Chlamydia_ only.

Conclusions—DNA from two different microorganisms which are known to be triggering agents for arthritis may be present simultaneously in joint material from patients with unexplained oligoarthritis. This finding raises the question as to whether, in such cases, one or both bacteria contribute to the pathogenesis of the disease or whether they are only innocent bystanders.

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_Chlamydia trachomatis_ and _Borrelia burgdorferi_ are thought to cause arthritis by persisting intra-articularly in a metabolically active though usually a non-culturable state.\(^1\)

Polymerase chain reaction (PCR) is the method of choice for detecting persisting bacteria in joints.\(^1\) Recently, universal PCRs have been developed for use in the diagnosis of undifferentiated arthritis. However, their sensitivity is lower than species specific PCRs and, to date, the universal PCR has not detected _B burgdorferi_ in cases of undifferentiated arthritis.\(^2\)\(^,\)\(^3\) Nevertheless, universal PCR has detected several organisms simultaneously in one inflamed joint which have not been related to arthritis.\(^2\)\(^,\)\(^3\)

This study was undertaken to determine whether _C trachomatis_ and _B burgdorferi_, the two most important arthritis triggering organisms in western countries,\(^1\)\(^,\)\(^4\) can be simultaneously detected by species specific PCR in unexplained oligoarthritis, or whether the detection of one of these bacteria excludes the presence of the other.

Methods

As part of a comprehensive study on early arthritis we prospectively studied 76 patients with unexplained oligoarthritis visiting a tertiary care outpatient clinic for the first time. The results of an extended rheumatological diagnostic programme in patients who fulfilled the criteria for unclassified arthritis will be published elsewhere. In this study patients with unexplained oligoarthritis are analysed.

Synovial fluid was obtained from all patients and examined for DNA from _C trachomatis_ and _B burgdorferi_ using species specific PCR protocols: _C trachomatis_ nested PCR was used to target _C trachomatis_ major outer membrane protein (MOMP) with 152 base pairs using the primer CT05/CT06/CT03/CT04\(^6\) and _Borreliaburgdorferiensenslato_ nested PCR was used to target _B burgdorferi_ outer surface protein A (OspA) with 146 base pairs using the primer BBSL1/BBSL2/MRL7/MRL11a.\(^7\)\(^,\)\(^8\) Both tests were able to detect the specific bacteria with a sensitivity of one organism/ml synovial fluid. Numerous negative controls were included; PCRs were defined as positive only when the results were reproducible twice and when all negative controls remained negative. The correct identity of the PCR products was confirmed by restriction analysis or by direct sequencing of the PCR product.\(^3\)

Data concerning prior infection of the genitourinary tract and a history of tick bite were recorded and serum antibodies for _C trachomatis_ IgA/IgG (ELISA test; Medac, Wedel, www.annrheumdis.com
that monocytes that have phagocytosed bacteria elsewhere in the body may have been disseminated into the inflamed joint. Therefore, because of its extreme sensitivity, a positive PCR result may reveal a previously unexpected degree of intrinsic microbial presence at many anatomical sites. Recently, Schumacher et al reported the detection of C trachomatis in healthy joints and in the joints of patients with diseases not related to C trachomatis such as osteoarthritis, which suggests that the presence of C trachomatis in joints does not necessarily indicate that C trachomatis is the causative factor. Furthermore, they noted several patients with different forms of arthritis in whom DNA from C trachomatis as well as from C pneumoniae was found in the synovial tissue of the same individual.

The detection of two known arthritis causing microorganisms in one inflamed joint sets the scene for several possible pathogenetic models. Either both organisms are causing inflammation, or one organism is triggering the disease and the second is an innocent bystander disseminated into the inflamed joint by increased vascularisation, or none of them is responsible for the disease. The finding of two pathogenic organisms at the disease site does not primarily indicate that they are both innocent bystanders; numerous examples of co-infection, either bacterial or viral, are known in medicine.

In four of the six patients reported here, additional evidence such as coincidental history, serological tests, and urogenital smears for C trachomatis indicated co-infection by both B burgdorferi and C trachomatis. Some patients were seronegative for B burgdorferi or C trachomatis, or both. This may be because C trachomatis is an intracellular agent or because of the relatively low sensitivity of the serological tests used for B burgdorferi. Furthermore, most patients (nos 1, 2, 3, and 6) had already been treated with steroids before serological testing.

To examine the pathogenesis and define the precise causative role of these organisms, further analysis of the host-bacteria interaction such as specific T cell responses, gene induction, and cytokine profiles need to be studied.

Antibiotic treatment should be reserved for patients with chlamydial infections of the urogenital tract, those with arthritis in whom B burgdorferi DNA is detected in the inflamed joint, or those with unambiguously positive B burgdorferi serological tests. No benefit of antibiotic treatment has so far been reported for patients in whom C trachomatis DNA has been detected in the joints.

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