Mycoplasmas and arthritis

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The interest in mycoplasmas as human pathogens has increased again after the discovery of Mycoplasma fermentans strain incognitus in samples from patients with AIDS. The role of mycoplasmas as causative agents in arthritis has been considered since they were found 50 years ago in rats and mice with arthritis.

Their role in human arthritis remains unsolved, however; several workers have been unable to subcultivate primary mycoplasma isolates in cell free media.

Mycoplasmal arthritis in animals

Mycoplasmas are established pathogens in animals and birds. At least 31 mycoplasma species have been implicated. Under field conditions Mycoplasma synoviae is the most common cause of mycoplasma induced joint disease in poultry, resulting in acute or chronic arthritis, tenosynovitis, and lesions in periarticular tissue. In severe cases an erosion of articular cartilage occurs. Systemic changes include anaemia, arthritis, and atrophy of the thymus.

Mycoplasma hyorhinis is one of the aetiological agents of arthritis in pigs. The general pathological changes in mycoplasmal arthritis of pigs are similar to human rheumatoid arthritis. M. agalactiae infection in sheep and goats may be complicated by arthritis as well as M. bovis and M. alabenscens infection in cattle.

In addition to arthritis, Mycoplasma gallisepticum infection of poultry results in disease of many of the arteries in the periarticular soft tissues of the affected joints. These lesions are selective, occurring only in the periarticular tissues and in the neighbourhood of joints with arthritis. Both the arthritis and arteritis can be suppressed by treating the chickens with sodium aurothiomalate.

Experimental Mycoplasma arthritis in mice, rats, and rabbits by Cole and Washburn has been reviewed previously. Deposits containing immunoglobulin and complement were found in joint tissues, suggesting that immune complexes may participate in the chronic phase of mycoplasma induced arthritis in rabbits.

Transmission electron microscopy of articular cartilage in neonatal rats infected with Mycoplasma pulmonis revealed the presence of mycoplasmas within the matrix and lacunae. The mycoplasmas appeared to have a tropism for the chondrocytes and induced lysis of the chondrocytes and the cartilage matrix.

Five different tetracyclines were highly active against Mycoplasma arthritidis and Mycoplasma pulmonis induced arthritis in rodents.

Arthritis associated with mycoplasma infection in humans

Mycoplasma pneumoniae infection may cause arthralgias or less commonly a migratory polyarthritis affecting medium sized joints. This condition may be severe, with joint swelling, morning stiffness, and considerable functional disability. It may be the dominant clinical feature outlasting all other manifestations of the disease, though remission can usually be expected within eight weeks. Rarely, a peripheral symmetrical polyarthritis indistinguishable from rheumatoid arthritis may occur. Isolation of Mycoplasma pneumoniae from joint fluid specimens has been reported in four patients of whom three had hypogammaglobulinemia.

Among 1259 patients with serologically confirmed Mycoplasma pneumoniae infection, 11 (0.9%) had arthritis in one or several large joints, which lasted for one to ten weeks.

Mycoplasma hyorhinis has caused septic arthritis in association with puerperal fever, and non-Hodgkin’s disease as well as traumatic joint infection and prosthetic infections. The arthritic symptoms resolved after prolonged treatment with tetracycline. Mycoplasma salivarium has been described in connection with arthritis of a patient with hypogammaglobulinemia.

Ureaplasma urealyticum has also been recovered from samples of joint fluid, especially in immunocompromised hosts. In one instance both Mycoplasma and Ureaplasma were isolated from a joint.

Fastidious mycoplasmas and human arthritis

The positive findings in this field have been reviewed elsewhere. In Finnish studies mycoplasmas were isolated from several patients with arthritis. Using the same cultivation method Markham recovered mycoplasma-like organisms in nine of 11 patients with rheumatoid arthritis.

In the 1980s we started to use the SP-4 medium developed by Tully et al for spiroplasma work. With this substrate we studied ‘blindly’ 14 joint fluid specimens from patients with arthritis and eight synovial tissue specimens from traumatic joint lesions. Fastidious slow growing mycoplasmas were cultivated
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determine the incidence of To hominis type association growth media the mycoplasmas of and defences.

In studying urethral specimens isolate the resembles membrane we have been unable for a long time. Such a molecules.52 Such a stimulation by an extremely potent protein has been shown to result in extremely potent immune response.53

Two major concepts of mycoplasma induced tissue damage have been presented: a cytotoxic hypersensitivity and an autoimmune reaction.8 Antigen complexed with antibody and deposited in synovial and cartilaginous tissues appears to provide the stimulus for chronic inflammation. Gram positive cocci and mycoplasmas have developed an extremely potent mechanism of T cell stimulation by closely mimicking the recognition of specific antigens. The designation 'superantigens' has been suggested for these molecules.52 Such a superantigen MAM has been isolated from M arthritidis by Cole and Atkin.53 They suggest that MAM not only activates T cells, with a resulting liberation of inflammatory lympohokes, but also suppresses host defences.

As a result of their limited biosynthetic capabilities, mycoplasmas require complex growth media or a close parasitic relation with animal cells.53 They are extremely difficult to isolate from human synovium.54 The surface plasma membrane of mycoplasma closely resembles the biliary of eukaryotic cells. Once attached the mycoplasma may adsorb complement and histocompatibility antigens onto their membranes. This phenomenon could alter the recognition of 'self' antigens by the host, leading to an autoimmune response. The close association of mycoplasmas and host cell membranes may also alter the host's immune response.55

Future prospects

To determine the incidence of mycoplasmas in human arthritis new direct methods such as the polymerase chain reaction and a known human mycoplasma isolate should be used. Cooperation on an international level would be valuable.

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