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Letter to Editor

Mycoplasma and other Intracellular Bacterial Infections in Rheumatic Diseases: Comorbid Condition or Cause?

Letter to Editor

Although the causes of rheumatic diseases have remained relatively unknown, systemic intracellular bacterial infections are commonly found in rheumatic disease patients [1-4]. Because of this, certain infections have been confused with comorbid conditions.

Often patients with rheumatic diseases have co-morbidities, and some authors have concluded that this can include chronic infections. "Infections continue to be a significant cause of morbidity and mortality in patients with rheumatic diseases, and, consequently, early diagnosis and treatment of infection is critical to the successful medical management of these patients" [5].

A link between certain types of infections and rheumatic diseases has been seen by a number of authors. For example, infections with *Mycoplasma* species, *Borrelia* species and other intracellular bacteria have been linked to various forms of rheumatic disease [1-4, 6-13]. In addition, animal models of rheumatic disease have been established by infection with *Mycoplasma* species [13-15]. In one of these contributions experimental arthritis was induced by a clinical isolate from *M. fermentans* injected into the joints of rabbits [15]. Outbreaks of rheumatic disease, such as polyarthritis, have been traced to infections by *Mycoplasma* species [16]. Arthritis in animals caused by *Mycoplasma* species infections closely resemble the signs and symptoms found in patients with rheumatoid arthritis [17]. In addition, reactive arthritis following *M. pneumoniae* infection has been seen in patients [18]. *Mycoplasma* infections have also been found in the joints of patients with rheumatic disease [19-21].

In a case-control study the presence of antibodies against *Mycoplasma pneumoniae* have been statistically correlated to the clinical features of rheumatoid arthritis ($p < 0.001$)

[21]. Furthermore, genetic analyses and transmission in animals indicate that arthritis is not directly linked to genetic abnormalities [22]. The pathogenesis of rheumatoid arthritis appears to be linked to immunological features of infection(s) involving host recognition of foreign antigens that mimic host antigens or host antigens that are incorporated into microorganism structures and the presence of localized immune complexes and the influences of environmental conditions [22].

Standard treatments of chronic infections like mycoplasma often employ long-term antibiotics, such as but not limited to tetracyclines and other antibiotics [23-26]. The U.S. National Institutes of Health sponsored a double-blind, placebo-controlled, long-term clinical trial that showed that the antibiotic minocycline was safe and effective for the treatment of rheumatoid arthritis. The antibiotic-treated patients showed greater improvements in joint swelling and tenderness ($p < 0.02$), and the treatment group also had better improvements in hematocrit, SED rate, platelet counts and rheumatoid factor with no serious toxicity [27, 28]. A 4-year follow-up indicated that the minocycline-treated patients had fewer relapses and less frequent need for immune-suppressive drugs to control their RA ($p < 0.02$) [29]. Although treatment of arthritis with antibiotics was effective and safe, treatment failures can, just as in any treatment for arthritis, be due to therapeutic failures, resistance and/or mutation of the microorganism [30].

Part of the reason that most rheumatic disease patients do not receive antibiotic treatment may have more to do with the enormous pressure from the marketing and sales of various drugs that do little to address the underlying causes of rheumatic diseases than the effectiveness of various treatments.

In summary, intracellular bacteria are commonly linked to rheumatic diseases, especially rheumatoid arthritis and similar conditions, and these infections can be successfully treated with antibiotics. Treatment often but not always resulted in significant reductions in rheumatic signs and symptoms. Thus chronic infections, such as intracellular bacterial infections,

do not appear to be simply co-morbid conditions in rheumatic disease patients. Although there is circumstantial evidence, such as the animal transmission experiments discussed above, that infections like *Mycoplasma* species may be the cause of rheumatic diseases like rheumatoid arthritis, this has still not been conclusively proven in clinical cases

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