Leader

Is there an association between ankylosing spondylitis and multiple sclerosis?

Ankylosing spondylitis (AS) is predominantly a disease of the spine and large joints but may be associated with extra-articular involvement. For example, cardiac, pulmonary and other systemic complications are well recognised.¹ A variety of neurological syndromes have been described, including the cauda equina syndrome^{2,3} and, more recently, an association with multiple sclerosis (MS) has been reported.^{4,5}

Assuming that there is such an association, does it matter? When two chronic diseases are found to be associated more frequently than one would expect by chance the discovery invites a degree of speculation. For example, if MS does occur more frequently than expected in a population of patients with AS (or vice versa) one must ask whether this phenomenon throws light on the pathogenesis of one or both diseases. Does the finding suggest that the two apparently unrelated entities have a common environmental trigger or share a similar genetic background? A confirmed association may provide support for a trial of a therapeutic agent known to work in one of the two disorders but not hitherto tried in the other. These and many other issues could be faced and an opportunity might arise to generate and test useful hypotheses. But first let us look at the claim that AS and MS are associated. Is the claim tenable and can important hypotheses be created and thereafter pursued? Will patients with one or both disorders benefit?

The aetiology of MS remains unknown and although one assumes that the disorder results from the interplay between genetic and environmental factors, virtually nothing is known about its putative infective trigger. By contrast, some information exists pertaining to the genetic background.⁶ Studies of migrant populations have disclosed that factors determining susceptibility to MS are acquired before the age of 15 years. Individuals who migrate before this age assume the risk that is prevalent in their new environment, whereas those moving after the age of 15 carry the risk that is prevalent in their place of origin. The incidence of MS is also greater in urban dwellers. These features suggest an infective

aetiology.⁷ As with AS, however, genetic factors are also implicated in MS. The disease is associated with HLA-Dw2 and the risk of disease is greater when there is a family history of MS and the concordance rate is higher in monozygotic than dizygotic twins.⁶

Whereas AS is predominantly a disease of the entheses and to a lesser extent synovium, MS is a disorder of the myelin sheath. The demyelinating process primarily affects young adults, men and women alike. In the northern United States and Europe the incidence is much greater than in the tropics. For example, the prevalence rises to 1 per 500 in Denmark.⁷ If we consider the prevalence of AS to be in the region of 1 per 200, one would expect some five to 10 individuals in every 1000 randomly selected patients with MS to have AS. But perhaps inevitably in a hospital based rather than population study the apparent co-existence of two chronic diseases in the same individual is a well recognised phenomenon. There are many reasons for this. A referring doctor may feel able to cope with the management of the patient who suffers with one chronic disease but when faced with two such disorders he may wish assistance from hospital colleagues. Secondly, a patient with two disorders may be more likely to seek additional clinical care. Thus patients with two diseases are more likely to come to the attention of a doctor than is an individual with a single disorder.

How supportive are the data relating to the putative AS/MS link? The definitive population study has not been done. The finding of two patients with MS among 196 individuals with AS⁴ and an earlier study⁵ suggesting that patients with AS may have delayed evoked potentials provided support for the earlier suggestion of a link.³ The most recent study assessed the prevalence of HLA-B27 in 420 patients with MS in Edmonton, Canada (10%).⁸ Twenty of the B27 positive individuals were further assessed, five of whom had evidence of AS—a figure that mirrors the oft quoted 20% risk of AS among B27 positive blood donor populations.¹ Although a debate continues as to the true prevalence of AS among random B27 positive populations, the figure

is somewhere between 2 and 15%. Our own population study carried out in conjunction with workers in South West Australia yielded a figure of close to 10%.⁹ Given the above mentioned biases inherent in any hospital based study, one must ask whether this figure is truly greater than one would expect by chance. The Edmonton study⁸ found little evidence of delayed evoked potential in patients with AS, a negative finding that did not support the earlier study.⁵ When information emanating from some 2000 members of the National Ankylosing Spondylitis Society in Britain was reviewed no striking link between MS and AS became apparent. It is possible, however, that individuals with MS would be less likely to join a self help group.¹⁰

It would seem, therefore, that the relation, if any, between AS and MS is a weak one. If the link is real, what hypotheses can be generated? Conceivably individuals with MS and chronic urinary tract infections are more likely to develop AS than is an individual who is generally free of infections. It is possible that the treatment for AS causes MS but there is nothing to support this, apart from the awareness that indomethacin, for example, may be associated with central nervous system toxicity (but not myelin damage). These are all areas which have already been extensively researched, however.

In summary, there are no definitive studies to support an association between MS and AS. Even if data could be produced to substantiate such a link,

there would be no obvious new avenues to explore until more fundamental issues had been defined.

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