

Case report

Lupoid sclerosis: a possible pathogenetic role for antiphospholipid antibodies

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SUMMARY The case of a 45-year-old woman is described who developed transverse myelitis over a one-year period. Serological tests suggested a lupus-like illness. Antibodies to cardiolipin of the IgM class were detected in high titres in her serum. These may have played a part in the pathogenesis of her disease.

Key words: anticardiolipin antibodies, false positive test for syphilis (BFP-STs), transverse myelopathy, systemic lupus erythematosus, cerebral lupus.

Recently we have described a sensitive solid phase radioimmunoassay to detect anticardiolipin antibodies.¹ Cardiolipin is a phospholipid antigen used in standard tests for syphilis.² Of particular interest are two disease entities in which transverse myelopathy is associated with a biological false positive test for syphilis. The first is 'lupoid sclerosis' described by Fulford *et al.*,³ in which six young women were described with transverse myelopathy, resembling multiple sclerosis, a biological false positive test for syphilis (BFP-STs), and a positive test for antinuclear antibody (ANA). The second is Jamaican neuropathy, a common neurological disorder in Jamaica and the Caribbean, features of which include transverse myelopathy, posterior column deficits, and a false positive test for syphilis.⁴ The pathogenesis of these disorders is unknown, but it has been suggested that they may be autoimmune.^{3,5}

A major portion of the dry weight of central nervous tissue is made up of phospholipids.⁶ There is experimental evidence to suggest that antiphospholipid antibodies, primarily raised in animal systems, but also described in a few patients with Waldenström's macroglobulinaemia, show a great deal of cross reactivity with other phospholipids.⁷⁻¹¹ It is conceivable that anticardiolipin antibodies

present in patients with transverse myelopathy may damage neural tissue structures by binding directly to phospholipids in these tissues.

We describe a patient who presented with a transverse myelopathy causing a spastic paraparesis. Serological tests were suggestive of an autoimmune disease, but most striking was the presence of anticardiolipin antibodies of the IgM class.

Case report

The patient was a 45-year-old woman who presented in 1974 with a one-year history of numbness in the saddle region, progressing over the course of several months to numbness and weakness of both legs. Examination revealed spastic paraparesis, absent abdominal reflexes, and impairment of position and vibration sense in both legs. Pain and temperature sensation were absent below the T4-T6 level. Investigations showed an erythrocyte sedimentation rate (ESR) of 28 mm/h, a positive test for ANA (1:80), and a positive Venereal Disease Research Laboratory (VDRL) test (1/4) with negative *Treponema pallidum* haemagglutination (TPHA) test. Cerebrospinal fluid (CSF) was VDRL and TPHA negative. A myelogram was normal. She was given a short course of dexamethasone, with little response, and was referred to the Hammersmith Hospital. Examination was as noted previously. Investigations showed a normal full blood count and normal biochemistry and clotting. The ESR was 35 mm/h.

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The ANA test was positive (1:40) and deoxyribonucleic acid (DNA) binding 34% (normal <30%). A latex fixation test for the rheumatoid factor, auto-antibody screen, and VDRL and TPHA tests were all reported to be negative. Antibodies to extractable nuclear antigens were not detected. CSF examination was unremarkable. Scans by electroencephalography (EEG) and computerised tomography (CT) were normal. In view of the clinical findings and false positive VDRL test, a diagnosis of 'lupoid sclerosis' was made. The patient has remained clinically stable since 1979. Despite a negative VDRL test she was noted to have very high levels of anticardiolipin antibody levels of the IgM class and moderately increased levels of the IgG class. Retrospective examination of her sera over the last three years revealed persistently raised cardiolipin antibody levels of the IgG and IgM classes.

Discussion

The syndrome of transverse myelopathy, a BFP-STs, and positive ANA test was described by Fulford and coauthors.³ Because this syndrome resembled multiple sclerosis clinically, the name 'lupoid sclerosis' was suggested. Wilson and Hughes postulated that lupoid sclerosis resembled Jamaican neuropathy, a common neurological disorder in Jamaica and the Caribbean, in which transverse myelopathy, posterior column deficits, and a BFP-STs occur.⁵ Both groups of authors suggested that these might be autoimmune disorders, but there has been no work to determine the role, if any, of anticardiolipin antibodies in these disorders.

Our patient developed the symptoms and signs of a transverse myelopathy. The positive ANA test and slightly raised DNA binding were suggestive of a lupus-like illness, though there was insufficient evidence to make a substantive diagnosis of systemic lupus erythematosus (SLE). She fitted well into the category of lupoid sclerosis. We believe that it is of great interest that raised levels of IgM anticardiolipin antibodies were detected in her serum.

There is some experimental evidence that antiphospholipid antibodies may cause neural damage. In experimental animals antispingomyelin and antiphosphatidylinositol antibodies have been raised that bind to phospholipids in neural structures.^{7,8} Antiglycolipid antibodies that bind glycolipids in T cell membrane and brain tissue in patients with central nervous system (CNS) lupus have also been described.¹² It is interesting that, in this patient with evidence of an autoimmune disease, the clinical manifestations of her illness were confined to the central nervous system, while the only major serolo-

gical abnormality was the raised anticardiolipin antibody level. We suggest that these antibodies may have played a part in the pathogenesis of her disease.

It is not clear how antibodies that bind brain tissue might cross the blood-brain barrier. It is currently believed that circulating immune complexes may damage endothelial cells of cerebral vessels resulting in disruption of the blood-brain barrier, so enabling circulating 'antibrain antibodies' to enter neural tissue. We are currently testing an alternative hypothesis suggesting that antiphospholipid antibodies, like circulating immune complexes, may damage the cerebral vascular endothelium by cross reaction with phospholipids in the membrane of endothelial cells.

It is possible that the occurrence of antiphospholipid antibodies may be secondary to neurological damage. However, Fulford and colleagues did not find a BFP-STs in any of 69 patients with multiple sclerosis. We have found slightly raised anticardiolipin antibody levels in only three of 91 multiple sclerosis sera examined. Therefore we believe it unlikely that the occurrence of these antibodies is secondary to neurological damage.

It is also difficult to explain why all patients with raised anticardiolipin antibodies (or the BFP-STs) do not develop neurological disease. Antiphospholipid antibodies may vary in their specificity for various phospholipids.¹⁰ One may postulate therefore that some antiphospholipid antibody groups may be better able to bind neural tissue than others. We are currently testing purified anticardiolipin antibody preparations from different patients to determine whether these antibodies do differ in specificity and whether they can bind brain tissue.

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Metabolic bone disease in rheumatoid arthritis and osteoarthritis

SIR, Revell *et al.*¹ in their paper on the incidence of metabolic bone disease in rheumatoid arthritis and osteoarthritis state that they found evidence of osteoporosis in about a quarter of all patients and that osteoporosis was equally common among patients with osteoarthritis and those with rheumatoid arthritis.

However, in their paper they did not define 'histological osteoporosis', neither did they define the diagnosis of osteoarthritis. From the data mentioned in Table 1, i.e., youngest age in the female and male group of 26 years and three cases of ankle involvement in the osteoarthritis group, one can conclude that their osteoarthritis group is very heterogeneous, mixing secondary and primary osteoarthritis cases.

For establishing the diagnosis of osteoporosis the percentage trabecular bone volume (TBV) is a poor parameter. First of all the variability at the iliac crest is extremely high and may differ by 30% between adjacent samples and between samples taken at the right and left side in one individual.² Furthermore, the percentage total bone volume parameter is influenced by skeletal size: the taller the individual, the lower the percentage TBV. Below an age of 50 men have a lower percentage TBV than women.^{3 4}

Giroux, Courpron, and Meunier⁵ found a significant negative correlation between the width of the iliac crest and percentage TBV in age groups 15-29 and 30-80 years in men.

Since in osteoarthritis the skeletal size is increased, e.g. the periosteal diameter is significantly enlarged, it is not surprising to find a low percentage TBV at the iliac crest in osteoarthritis cases.⁶

Although bone histomorphometry is not good for establishing the diagnosis of osteoporosis, it is very useful for diagnosing osteomalacia and the bone remodelling stage.

We feel that the authors have insufficient evidence and even use anecdotal arguments to conclude that osteoporosis and osteoarthritis are not mutually exclusive. That

osteoarthritis defined as generalised osteoarthritis, and osteoporosis defined as fracture of the femoral neck and/or vertebrae, are separate entities that do not often occur together has recently been substantiated in several papers.⁷⁻⁹

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SIR, Dr Verstraeten and her colleagues draw attention to limitations in the information about osteoporosis provided by our report. The main thrust of our study - as we made clear - was to determine whether there is an excess of osteomalacia or related metabolic bone disorder among