Transverse myelopathy in the antiphospholipid antibody syndrome: pinworm infestation as a trigger?

The antiphospholipid antibody syndrome is a disorder characterised by the production of autoantibodies directed against negatively charged cell membrane phosholipids. Antiphospholipid antibodies have been described in various neurological disorders.

It has been generally accepted that viral, bacterial, and parasitic infections can serve as a trigger factor for autoimmune reactions. Despite the growing knowledge that has accumulated, the relation between parasites and autoimmunity has not been clarified.

Enterobius vermicularis (pinworm) is a nematode rarely found outside the gastrointestinal tract, but allergic reaction due to enterobiasis has been reported.[1] We describe the case of transverse myelopathy preceded by intestinal pinworm infestation in the primary antiphospholipid antibody syndrome. To our knowledge, such an association has not been reported previously. Pinworm therapy was complicated by the Jarisch-Herxheimer reaction manifested by temporary exacerbation of pre-existing neurological symptoms.

In March 1998, a 40 year old woman who complained of perianal itching noticed the presence of worms migrating from the anus. Three days later itching and numbness involved both legs, and the patient had weakness in the legs. These symptoms progressed over the next 3 days to severe paraparesis and urinary urgence. Her medical history was relevant for three unexplained miscarriages which all occurred in midpregnancies. In the local hospital, she underwent brain and lumbar-sacral spine MRI and findings were normal. Cerebrospinal fluid examination disclosed slightly raised proteins of 670 mg/l, 2 lymphocytes/mm^3; oligoclonal immunoglobulin (Ig) G bands were absent. She was treated with methylprednisolone (1 g/day) intravenously for 5 days with subsequent gradual tapering off, which was associated with substantial improvement of motor, sensory, and sphincter disturbances. At the end of April 1998, the patient was transferred to our hospital for further investigation.

Neurological examination showed mild spastic paraparesis, bilateral Babinski's sign, and a Th-12 sensory level.

Erythrocyte sedimentation rate was 34. Complete blood count, tests for hepatic and renal function, angiotensin converting enzyme, concentrations of IgG, IgM, IgA, IgE, and immune complexes, screening for antinuclear (HEp-2 cells), anti-ds DNA, antineutrophil cytoplasmic, antimitochondrial, and antiparietal cell antibodies, rheumatoid factor, and the search for antineurotropic virus and antiBorrelia antibodies were normal or negative. A venereal disease research laboratory flocculation test was negative. A medium positive concentration of IgM anticardiolipin antibody was detected, and lupus anticoagulant was negative. Raised titres of serum IgG and IgM anti-GM1 (1:1600 and 1:3200, respectively) and antisulfatide antibodies (1:6400, for both classes) were also demonstrated. Class II human leucocyte antigen (HLA) typing showed the presence of HLA-DR3, DR4, DR52, DR53, DQ2, and DQ3. Cervical and thoracic spine MRI was normal. Electromyoneurography was normal.

Because the patient complained of reappearence of worms and perianal itching, a cellulose adhesive tape test was performed and diagnosis of enterobiasis was established. Mebendazole was given in a single dose of 100 mg and the next day the Jarish-Herxheimer reaction occurred, with deterioration of leg spasticity, inability to walk, and development of urinary retention. At that time, low positive IgG ACA was detected. The dose of prednisone was raised to 60 mg/day and slowly tapered off within the next 2 months. Sphincter disturbances resolved in 1 day and motor dysfunction gradually improved with only mild spasticity left.

Diagnosis of antiphospholipid antibody syndrome in our patient was based on the presence of reccurrent fetal loss, transverse myelopathy, and raised ACA. The ACA titre was probably lowered by previously administered corticosteroid therapy. There are several reports of transverse myelopathy as a manifestation of antiphospholipid antibody syndrome in the past decade.[2 3] A potential pathogenic role of antiphospholipid antibodies in transverse myelopathy might be based either on vasculopathy or on interaction with spinal cord phospholipids.

Infection by helminths is universally associated with activation of T helper 2 (Th2)-type cells. Regardless of the mechanisms and protective value of antihelminthic Th2 responses, such responses may also be detrimental to the host. The presence of ACA, anti-GM1, and antisulfatide antibodies in our patient suggests a systemic response to *E vermicularis*, as it has been shown that nematodes contain cardiolipin, ganglioside GM1, and sulfatides within their complex lipid composition.[4] When parasites share epitopes with host tissue, such molecular mimicry may exploit host immune tolerance against a self determinant. Autoimmunity may occur if immune tolerance is overriden in genetically susceptible hosts. It has been proposed that the presence of pathogenic cross reactive autoantibodies could be the basis for the relation between nematodes and autoimmunity. It may be also postulated that *E vermicularis* stimulated Th2 response which enhanced polyclonal autoantibody production resulting in the presence of ACA, anti-GM1, and antisulfatide antibodies. The association of transverse myelopathy, ACA, and enterobiasis might be purely coincidental, which we assume to be highly unlikely. The finding of different autoantibodies, as well as the isotype switch of ACA, strongly suggests that pinworm infestation in our patient was the "triggering event" that increased the production of autoantibodies against cardiolipin and led to the development of transverse myelopathy.

The appearance of the spinal cord damage caused by ACA in our patient might have been facilitated by the simultaneous effect of anti-GM1 and antisulfatide antibodies. A significant subset of the human anti-GM1 antibodies that reacted with the Gal(b1–3)GalNAc determinant also bound to oligodendrocyte-myelin glycoprotein which is a constituent of the myelin of the CNS. As for antisulfatide antibodies, their presence has been already shown in some diseases affecting the CNS.

It is clear that parasitic infections can serve as a trigger factor of autoimmune reactivity, but the presence of autoantibodies or self reactive T cells is rarely associated with clinical manifestations. They develop only in patients with adequate immunogenetic and hormonal background for autoimmune diseases. In several studies, increased frequencies of HLA-DR4, DR7, DR53, and DQ7 were found in patients with antiphospholipid antibody syndrome,[5] and in our patient HLA-DR4 and DR53 were present. Additional studies are necessary to further elucidate the complex mechanisms of involvement of intestinal helminths in the processes of autoimmune activity.

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Radiologically selective visual pathway involvement in adult onset cerebral adrenoleukodystrophy

A case of adult onset cerebral adrenoleukodystrophy is presented with serial MRI showing selective involvement of the visual system with spread of disease along the fibre tracts of this system.

Adult onset cerebral adrenoleukodystrophy is the rarest presentation of adrenoleukodystrophy.[1 2] It may present with various symptoms often including visual impairment.[3] Brain MRI may show multiple areas of symmetric high signal intensity within cerebral white matter, usually affecting the occipital lobes.[4–6] We present a case of adrenoleukodystrophy, in whom serial MRI demonstrated selective progression of demyelination through the visual pathways.

A thirty year old man presented in May 1996 with a 7 month history of deteriorating vision, slurred speech, incoordination, poor balance, generalised weakness, sleep disturbance, and headaches. His symptoms were worse on the right. He had no symptoms of postural hypotension.

His mother had been shown to be a carrier of X linked adrenoleukodystrophy (XL-ALD). His two elder brothers had died of XL-ALD at the ages of 6 and 7 years. In 1993 our patient had been shown to have abnormal serum concentrations of very long chain fatty acids (VLCFAs) and to be a carrier of the XL-ALD gene. At that time he was asymptomatic and had no abnormal neurological signs. Crohn's disease had been diagnosed in 1987 after an ileal resection although this had remained in remission.

On examination, visual acuities were 6/12 (right), 6/9 (left). Fields were full to confron-