LETTERS TO THE EDITOR

A single focus of multiple sclerosis in the cervical spinal cord mimicking a radiculopathy

A 46 year old man was first examined in January 1996 for an impairment in the fine movements of his right hand. His history showed an optic retrobulbar neuritis, four years before, with a residual decrease of visual acuity to 6/10 and a pale disc on the left. Neurological examination disclosed only a disturbed stereognosis on his right hand. Visual evoked potentials (EPs) were very abnormal in the left, normal in the right eye. Brainstem auditory EPs and somatosensory EPs were normal. Both MRI of the brain and of the cervical spinal cord failed to show any aspect suggesting plaques. Cervical MRI showed extreme degenerative changes at the C5-C6 and C6-C7 level with a C6-C7 bulging disc. A cross section at the C5-C6 level showed a posterior osteophyte impressing the subarachnoid space but no areas of abnormal signal intensity within the spinal cord. Analysis of CSF showed a protein concentration of 310 mg/l with gammaglobulins at 21% and oligoclonal banding. Investigation of blood and CSF for infectious and immunological diseases was negative. The diagnosis at discharge was cervical discopathy and possible multiple sclerosis. Two months later the patient complained of a sharp throbbing, burning pain in the first and second finger of his left hand and on the outer side of his left arm, with an intense itching character. At examination scratch lesions drawn on the skin showed the C6 dermatome in its full extension. The bicipital reflex was reduced on the left. Sensory disturbance was limited to hyperalgesia in the C6 dermatome without a clear deficit of specific sensory modalities. Spinal MRI cross section at the C5-C6 level showed in T2 weighted images an area of abnormally high signal intensity within the cord, localised in the left posterolateral and posterior sections and extending to the central region (figure). The spondylosis was unchanged and there was no evidence of spinal or radicular compression.

A left pseudoradicular C6 syndrome, secondary to a fresh plaque of multiple sclerosis in the dorsal root entry zone and posterior horn was diagnosed. Treatment with 1000 mg methylprednisolone/day for three days led to partial improvement. Repetition of the treatment 20 days later led to remission of symptoms.

Pain in multiple sclerosis has been known since 1872, when Charcot referred to shoulder and pelvic girdle pain as symptoms of the disease.¹ However, its incidence is variously quoted in the literature, from "uncommon" to 82%.² Acute pain syndromes include trigeminal neuralgia, paroxysmal burning extremities, painful tonic seizures; chronic pain syndromes include dysaesthetic extremity pain, back pain, and painful leg spasms.³ To our knowledge only two reports are expressly dedicated to radicular pain in multiple sclerosis. Ramirez-Lassepas *et al.*⁴ during a 15 year span, found 11 patients (3% of the newly diagnosed cases of multiple sclerosis in

MRI examination. The T2 weighted axial slice at the C5-C6 level shows an area of increased signal intensity in the spinal cord, mainly affecting the left posterolateral and posterior quadrants.

patients admitted to hospital) who presented with radicular pain and in whom radicular compression was ruled out by imaging techniques; eventually, multiple sclerosis was diagnosed when new neurological symptoms occurred, and was judged to be responsible for the acute radicular pain. In two cases demyelinating plaques within the spinal cord at MRI were thought to be in the appropriate location to explain the radicular (or more properly, pseudoradicular) symptoms. Uldry and Regli⁵ reported four patients with a formerly diagnosed multiple sclerosis who complained of a radicular limb pain and in whom a relation between the location of one of the plaques shown at MRI and limb pain was postulated. In the present case the relation is unquestionable; in a patient with a possible multiple sclerosis but with previously non-contributory imaging, a single demyelinating plaque appeared within the spinal cord, in the appropriate location to explain the concomitant pain syndrome.

A further note of interest in this case concerns the physiopathology of the pain. The distribution of pain was strictly dermatomeric; however, intense itching, unusual in radicular pain syndromes, suggested a peculiar mechanism. Indeed, a plaque in the dorsal column may generate ectopic bidirectional sensory discharges with abnormal central and antidromic conduction to peripheral endings.⁶ There is evidence that antidromic impulses cause the release of substance P at the peripheral terminals of primary afferents; substance P in turn has been shown to cause release of histamine from mast cells.⁷ Antidromic conduction and release of histamine could explain the uncommon feature of pain in this case.

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Production of endogenous interferon- α and β in patients with multiple sclerosis

Multiple sclerosis is considered to be an autoimmune disorder affecting the CNS, and several lines of evidence have supported the role of immunological mechanisms in its pathogenesis.^{1,2} The clinical finding that viral infections are often associated with or followed by acute multiple sclerosis relapses also suggests that an activation of the peripheral immune compartment may contribute to an acceleration of disease progression. Interferons (IFNs)—known as cytokines with antiviral, antiproliferative and immunomodulatory properties—have become part of the treatment of the disease as IFN β -1b has been shown to alter the natural course of relapsing-remitting multiple sclerosis.³ The interferon system forms an integral part of the defence system against infections. In response to viral stimulation, whole blood leucocytes of healthy people mainly produce IFN- α and a small proportion of IFN- β . IFN- α and β are

structurally and functionally related and classified as type I interferons.⁴ However, studies on the role of endogenous type I interferons in the disease process of multiple sclerosis are rare and the results have been largely inconclusive, so that the exact mechanisms by which IFN β -1b lessens the frequency of attacks of multiple sclerosis still remain open to speculation.⁵

We investigated the ability of whole-blood leucocytes of 15 patients with multiple sclerosis to produce endogenous IFN- α and β in response to stimulation with Newcastle disease virus. The whole-blood assay is an effective method for analysing the production of interferons and provides an appropriate model of the *in vivo* situation.⁶ Briefly, 100 μ l heparinised blood were mixed with culture medium at a ratio of 1:10 and stimulated with Newcastle disease virus in a final concentration of 0.8 haemagglutinating units/ml. Unstimulated assays served as controls. Concentrations of IFN- α and β in the supernatants of cell cultures were determined after 48 hours of stimulation by means of quantitative enzyme linked immunosorbent assay (ELISA). All patients had clinically definite multiple sclerosis of the relapsing-remitting subtype and had been in remission for at least three months. None of the patients had received immunosuppressive treatment or steroids during the three months before blood sampling and plasma concentrations of C reactive protein were normal in all patients. As a control group, we examined 20 age matched, healthy blood donors.

We found that patients with multiple sclerosis produced significantly lower amounts of IFN- α and β than the control group (figure). There was no spontaneous release of IFNs in either group. Previous studies on cytokine production in patients with multiple sclerosis have mainly focused on alterations during acute attacks and disclosed an upregulation of proinflammatory cytokines—for example, TNF- α —and an impaired production of immunosuppressive cytokines—for example, TGF- β —in active disease.^{2,7} Our findings imply a deficit in the ability to produce type I interferons in patients with stable multiple sclerosis, which may be a predisposing factor for susceptibility to disease. The finding seems to be specific to multiple sclerosis, as type I interferon responsiveness has been shown to be normal in patients with idiopathic Parkinson's disease

and in schizophrenic patients by our laboratory recently.^{8,9} The mechanisms by which treatment with IFN β -1b exerts its positive effects on the disease process might be explained by substitution of type-I interferon in patients with multiple sclerosis. Certainly, many different explanations may also be found.

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Secretion of endogenous IFN- α and β in response to viral stimulation in patients with multiple sclerosis and controls. Each open figure represents the average of duplicate determination of IFN in the supernatants of cell cultures from (A) patients with multiple sclerosis and (B) controls. The horizontal bars represent mean IFN concentrations in each group. Values are given in Units/ml. * $p < 0.001$; ** $p < 0.0001$ (Mann-Whitney U test). Interferon production was stimulated by Newcastle disease virus (Kumarov strain, inactivated by UV irradiation at 366 nm for 90 minutes) in a final concentration of 0.8 haemagglutinating units/ml. Cell cultures consisted of heparinised blood mixed at a ratio of 1:10 with RPMI 1640 culture medium supplemented with 100 U penicillin and 100 μ l streptomycin/ml.

Repeated syncope and extended paediatric hydrosyringomyelia/Chiari I malformation: relation or coincidence?

Syringomyelia is defined as a condition of tubular cavitations within the spinal cord, lined by glial tissue. In theory it differs from hydromyelia, a dilatation of the central canal of the spinal cord, which is lined with ependyma. However, in practice the distinction between the conditions is often difficult to make; thus the term hydrosyringomyelia for all intraspinal cavities of a non-tumorous nature has been proposed. Hydrosyringomyelia is often associated with anomalies of the posterior fossa, the most common of which is Chiari type I malformation. In a few cases, an association of hydrosyringomyelia with isolated syncopal events has been described. These syncope occurred especially in adult patients with associated Chiari type I malformation and were typically, but not in all cases, preceded by an increase in intrathoracic pressure caused by coughing, sneezing, or other exertion such as a Valsalva manoeuvre.^{1–3} Here, we report the case of a child with repeated syncope, associated with hydrosyringomyelia/Chiari I malformation.

This 10 year old boy from Zaire was admitted for evaluation of syncope. This was the first episode; the syncope occurred while at rest at school. About one minute before the syncope, the patient experienced numbness of the left arm, occipital headache, and double vision, but no coughing, straining, or sneezing. Pallor of mucous membranes accompanying the syncope was not seen. Loss of consciousness lasted about five seconds, after which numbness of the arm as well as the double vision had disappeared. Except for the occipital headache, the patient then felt well.

Thus far psychomotoric development had been normal with excellent school performance in primary school. Family history showed no cases of epilepsy or other neurological affections.

On examination the child was alert and oriented and had fluent speech and intact comprehension. General physical examination was unremarkable with normal findings especially for the cardiovascular system. On neurological examination his mental as well as cranial nerve status was normal. Muscle tendon reflexes, muscle tone, and strength were normal. Testing of the sensory system disclosed no abnormalities; thermal, vibratory, and pinprick sensations were symmetric. Fine and gross motor proficiency were normal. No pyramidal signs, spasticity, or rigidity were evident.

During the follow up of 24 months, four further syncope occurred with the same symptomatology as described for the first episode, but without the preceding numbness of the left arm or headache. Again there was no preceding coughing or sneezing. Three of these five syncopal events were preceded by movements and mild changes of body position such as bending to his schoolbag. Subsequent to all these syncopal events the patient's neurological status was normal.

The patient's cardiological investigation, including repeated Schellong tests, Valsalva manoeuvres, ECG, echocardiographies and 24 hour ECGs, was normal. Under clinical observation changes of body position imitating everyday movements (such as bending to the floor) were repeatedly performed, but did not lead to syncope. Several resting EEG records with photostimulation/hyperventila-