Case report

Multiple sclerosis after hepatitis B vaccination in a 16-year-old patient

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Since the first description of multiple sclerosis (MS), it has been known that relapse of the disease may be triggered by febrile infections. [1] Although the prevention of febrile illness is therefore clearly advantageous for those with MS, there is considerable controversy as to whether vaccine should be administered to such individuals. A further subject of debate is the possibility that vaccination (against influenza, or hepatitis B) leads to the development of MS. The coincidence observed between the administration of hepatitis B vaccine and the onset or relapse of MS and other demyelinating diseases [2-5] has stimulated a number of studies of the possibility of their association. [6-12]

Previous case reports found controversial relationship between hepatitis B vaccination and MS. In the case presented here, the close temporal association suggested a possible casual link between the encephalomyelitis episode and hepatitis B vaccination.

CASE REPORT

A 16-year-old female patient was vaccinated against hepatitis B in May 1999. Neurological symptoms were observed 10 weeks later. There was an insidious development of weakness in the left arm [4/5 Medical Research Council (MRC) scale] and later in the right hand (4/5 MRC scale), and the neurological examination revealed bilateral proximal weakness in the lower legs (3/5 MRC scale). The deep tendon reflexes were brisk in all four limbs, the plantar responses were up-going and abdominal reflexes were absent on both sides. Sensory loss was noted distally from the Th6 level.

The cerebrospinal fluid (CSF) examination revealed an elevated IgG level (all other CSF results were normal). Enzyme linked immunosorbent assay (ELISA) for Borellia (from the serum and CSF) was negative. The brain MRI demonstrated an inhomogeneous lesion with a hyperintense signal on T2-weighted images in the lower brainstem (Fig. 1A), and numerous T2 hyperintense lesions measuring 10-20 mm that enhanced gadolinium in the cervical and thoracic spinal cord (Fig. 1). The diagnostic possibilities considered acute disseminated encephalomyelitis, collagenosis, sarcoidosis and a first attack of MS. [13]

The patient was treated with intravenous methylprednisolone for 6 days (100 mg/d) and then with intravenous immunoglobulin for 5 days (1 g/kg per day). Within a few weeks after the therapy, her condition showed a marked improvement, the remission being almost complete.

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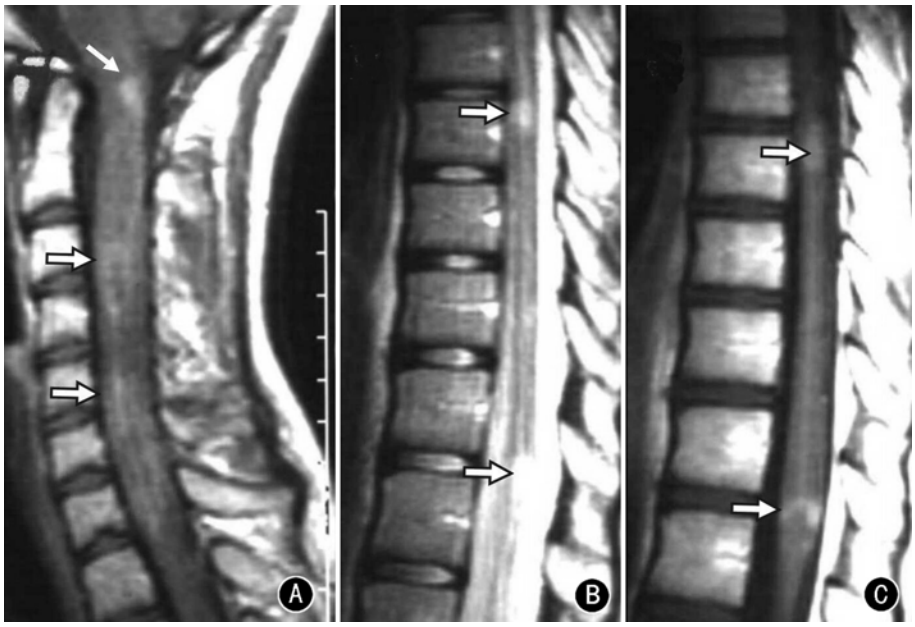

Fig. 1. There are inhomogeneous contrast-enhancing lesions (arrows) in the lower brainstem, and the cervical (**A**) and thoracic spinal cord (**C**) that show inhomogeneous high signal intensity on T2-weighted images (**B**).

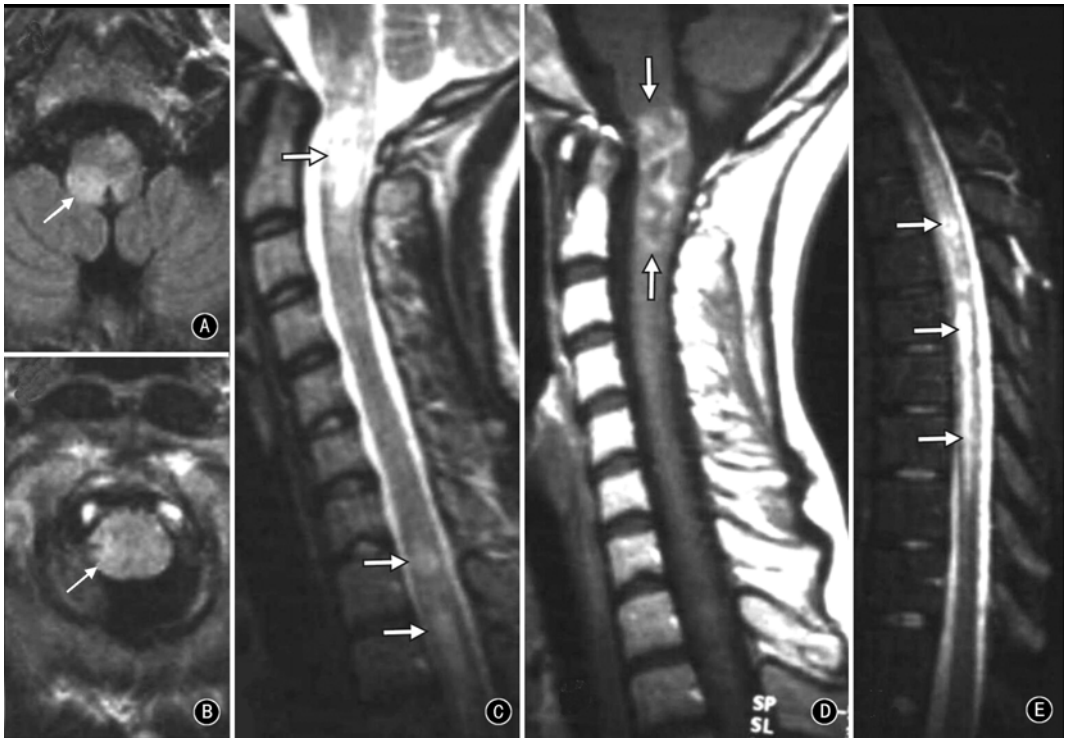

Fig. 2. Four years later, there are inhomogeneous lesions (arrows) in the lower brainstem, and the cervical and thoracic spinal cord that furnish a high signal on FLAIR (**A, B**) and T2-weighted images (**C, E**), and inhomogeneous contrast enhancement (**D**).

Four years later the patient experienced gait abnormalities. The neurological examination revealed paraparesis (3/5 MRC scale) with a bilateral Babinski response. Sensory loss was again noted distally from the Th6 level. The brain MRI demonstrated an inhomogeneous lesion in the lower brainstem, in the same localization as previously, with acute hyperintense intramedullary lesions enhancing gadolinium in segments CVII and ThIV-V in positions different from those observed in the previous examination (Fig. 2). The CSF examination revealed an elevated Link-index and oligoclonal bands, but no other abnormalities. Intravenous methylpre-

dnisolone therapy for 4 days (100 mg/d) was tried again, but the patient's condition worsened. Flaccid tetraparesis, burning and painful paraesthesia were present on both sides. However, treatment with immunoglobulin for 10 times (1 g/kg per day), was followed by a marked improvement, the remission being almost complete (Fig. 3).

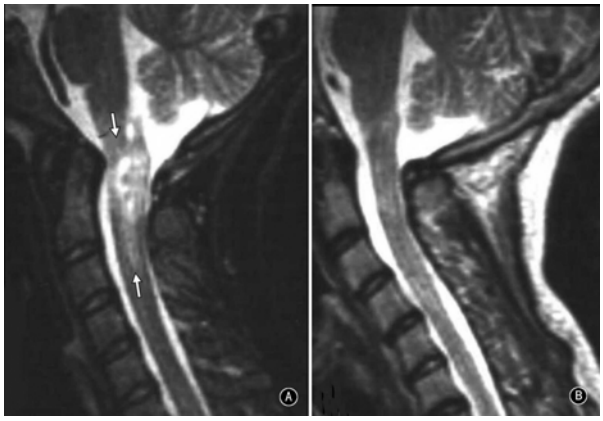

Fig. 3. The brainstem and upper cervical cord lesions (arrows) are very inhomogeneous and space-occupying after 2 weeks (**A**), but have disappeared almost completely after 1 month (**B**).

DISCUSSION

Multiple sclerosis is an immune-mediated chronic disorder of the central nervous system (CNS), characterized by spatial and temporal dissemination of the pathological process. The pathogenesis is thought to involve an autoimmune process that occurs in genetically susceptible individuals, triggered by an exogenous agent.

Since autoimmunity is recognized as being an important factor in MS, it appears theoretically possible that immunization might play a role in its pathogenesis. However, a number of large-scale studies have failed to establish a conclusive relationship between hepatitis B vaccination and MS. [1, 6-9] Although the most recently published findings demonstrated a statistically significant elevated risk. [11, 12]

In the case presented here, a direct casual link between the encephalomyelitis episode and the hepatitis B vaccination is suggested by the close temporal association. The controversy between the studies suggests the need of further investigations of the causality between hepatitis B vaccination and development of MS.

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