LETTERS TO THE EDITOR

Chronic progressive motor polyneuropathy after ganglioside treatment

Autoantibodies against ganglioside GM1 are associated with selective motor nerve involvement in motor neuropathy, lower motor neuron syndrome, amyotrophic lateral sclerosis, senso-motor neuropathies, and acute axonal Guillain-Barré syndrome.1-2 On the other hand, gangliosides from bovine brain are used to treat various neurological disorders. Adverse reactions resembling Guillain-Barré syndrome or motoneuron disease with high antibody titres against gangliosides after ganglioside treatment have, however, been reported.1-2 Recently, we found recently ganglioside antibodies were not studied.3 We present a patient who developed a chronic progressive motor polyneuropathy associated with a high titre of serum ganglioside GM1 antibodies after treatment with gangliosides.

A 39-year-old woman with neither family history of neurological disease nor history of drug abuse or exposure to neurotoxins developed progressive pain and weakness of her right thumb and atrophy of thenar muscle over a period of 14 months and was diagnosed as having carpal tunnel syndrome. After operation, weakness of her right hand persisted. She was given bovine brain gangliosides (Cronassial) intramuscularly every other day for three weeks in a total dose of 80 mg. Ganglioside treatment was discontinued when she started to feel ill. During the next six weeks she developed pain, progressive and ascending weakness and muscle cramps in her legs and later in her hands. She lost 6 kg body weight and had outbreaks of sweat and disturbed sleep. Micturition and bowel function were normal.

On admission, there was symmetrical and distal dominant muscular weakness in all four extremities, more pronounced in the legs. Tendon reflexes could not be elicited and the plantar responses were flexor. Sensory nervous function, mental state, speech, pupillary reaction, and cranial nerve functions were intact. There were no fasciculations, and except for right thenar atrophy the bulk of proximal and distal muscles of all four limbs seemed normal. Nerve conduction studies disclosed a decreased compound muscle action potential (CMAP, 2.5 mV) in the right ulnar nerve and a slightly prolonged distal latency (5.0 ms) in the right peroneal nerve, whereas motor nerve conduction along the sciatic-nerve was normal.

Electromyographic examination of upper and lower extremity muscles revealed polyphasic potentials (4-6 mV) of prolonged duration and a reduced recruitment pattern during maximal effort, indicative of a neurogenic lesion. Fibrillations in the tibialis anterior muscle were suggestive of axonal damage. Motor unit action potential was slightly raised (91 IUt). Cerebrospinal fluid protein concentration was increased (134 mg/dl). There were three mononuclear cells/mm3. No oligo-clonal bands were found in CSF or in serum. Common causes for polynuropathy such as metabolic disorders, nutritional deficits, impairment of liver or renal function, collagenosis, neoplasia, paraproteinemia, and infection (for example, Campylobacter jejuni enteritis), and other causes of muscular weakness were ruled out.

The patient was treated with a series of plasma exchanges, leading to a good clinical recovery within one month. During the next two months, however, she again developed symmetrical lower motor neuron disease with mild muscular weakness as well as pronounced atrophy. Nerve conduction studies of the left peroneal nerve revealed a considerably decreased amplitudes (5.15 mV), a prolonged distal latency (6.0 ms), and normal motor nerve conduction velocity; sensory nerve conduction studies gave normal results; the F-wave response in the left median nerve was absent. The patient responded to daily treatment with 40 mg methyldesmolone and 150 mg azathioprine with a significant stabilisation of muscle strength within four weeks and steroids were tapered during the following months.

One year after the last steroid medication there was a significant relapse of neuropathic disease that responded again to steroids.

During the following stable period the patient became included in a screening programme for patients with neuropathy. This involved measurement of serum ganglioside GM1 antibodies by enzyme-linked immunosorbent assay.2 Titres were determined by serial twofold dilution of test serum in triplicate and were expressed as the mean reciprocal value of the highest serum dilution giving a positive, specific (above background without ganglioside GM1) absorbance reading. Twenty eight months after ganglioside treatment had ended very high antisganglioside GM1 IgG (200 000) as well as increased IgA (6400) and IgM (3200) titres were detected in serum from the patient in comparison to mean titres in 26 patients with Guillain-Barré syndrome (IgG, 250; IgA, 140; IgM, 100) and in 20 normal, untreated controls (IgG, 200; IgA, 40; IgM, 120). The patient’s IgG binding to ganglioside GD1b was 2% of that to ganglioside GM1; no binding to ganglioside GT1a was detected. Over the next 15 months ganglioside GM1 antibody titres decreased by 75%. Repeated intravenous immunoglobulin (0.4 g/kg body weight/day for five days) again improved the patient’s strength and steadiness. For the first time in three years she was able to run and to climb stairs without the support of her arms.

In conclusion, after treatment with bovine brain gangliosides, our patient developed a slowly progressive axonal form of pure motor polyneuropathy with massive muscle atrophy and accentuation of symmetrical affecting all four extremities. As the clinical course and symptoms as well as electrodiagnostic results do not support the diagnosis of a Guillain-Barré syndrome or amyotrophic lateral sclerosis-like disease, this neurological disorder seems to differ from those reported after ganglioside treatment.1-2 The immune response in our patient was associated with a significant serum IgM (predominantly IgG) increase without ganglioside treatment; ganglioside GM1 specific antibodies occurred most often in multifocal motor neuropathy and distal dominant lower motor neuron disease.2

Several points argue for the possibility that the ganglioside preparation given may have triggered or contributed to the development of polynuropathy in our patient: (1) the start of ganglioside treatment was followed within weeks firstly by a severe feeling of illness and then by the onset of neuropathy; (2) remarkably high, antiganglioside GM1 (predominantly IgG) titers were seen around two years later strongly suggesting active immunisation; (3) the patient repeatedly responded to immunomodulatory therapies. Therefore, in support of our findings,1-2 we found that in some patients there may be a causal link between parenteral ganglioside administration and neurological disease via immune mechanisms. Thus the possible risk involved in the therapeutic use of gangliosides should be carefully considered.

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Hereditary multiple exostosis with spinal cord compression in a 13-year-old boy

Multiple exostosis is one of the most common bone dysplasias. The disorder is characterised by exostosis arising in the metaphysis of the long bones.1-2 Growth disturbance or malignant transformation to chondrosarcoma are rare but well recognised. Neurological symptoms in our patient, however, are rarely, and usually caused by direct compression of a peripheral nerve, nerve root or, less often, the spinal cord.

This case is that of an otherwise healthy boy (the second of three children) known to have familial (four generations of affected family members) multiple exostosis. He was examined at the age of 13 years, six months, with the onset of a slowly progressive left-sided weakness.


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