

Intravenous immunoglobulin therapy in sensory neuropathy associated with Sjögren's syndrome

Subacute sensory neuropathy has been recognised as a neurological complication of Sjögren's syndrome,^{1,3} but its treatment is not well established. Therapeutic trials with corticosteroids, immunosuppressive agents, or plasmapheresis have been unsuccessful.² We report a patient who improved with intravenous immunoglobulin treatment, which has not been used previously.⁴

A 60 year old man developed mild paresthesiae and numbness in the feet four years ago. In August 1993, these symptoms began to progress, ascending up to the thighs; the patient developed a progressive loss of dexterity in both hands—being unable to write, to button his shirt, or to use cutlery—and was unable to walk without a cane. The patient was first evaluated in February 1994. There was a mild decrease of sensation in the distribution of both trigeminal nerves. There was profound loss of both positional and vibratory sensation in all limbs and pain and temperature sensation were mildly impaired in the lower limbs. Distal involvement was greater than proximal. Muscle strength was well preserved. Deep tendon reflexes were absent, with flexor plantar responses present bilaterally. His gait was ataxic and Romberg's sign was present. The patient noticed a slight sensation of dryness in his eyes, but not in his mouth.

Cranial CT was normal. Spinal MRI showed a mild C6-C7 disc herniation. Serum electrophoresis and immunoelectrophoresis did not show oligoclonal bands but there was a polyclonal increase of gammaglobulin bands. Serum concentrations of folic acid, vitamin B12, vitamin E, and thyroid hormones were normal. Anti-Ro(SS-A) was positive and anti-La(SS-B) negative. Erythrocyte sedimentation rate was 7 mm/hour; rheumatoid factor was negative; antinuclear antibodies were positive at a titre of 1/40; extractable nuclear antigens and anti-DNA and anti-Hu antibodies⁵ were negative. Shirmer's test and rose bengal staining were positive. A lip biopsy was examined and scored by the criteria of Greenspan *et al*, showing grade 3—that is, the presence of a moderate infiltrate or less than one aggregate of 50 or more lymphocytes, histiocytes, and plasma cells per 4 mm².⁶ Analysis of CSF showed no cells, glucose 60 mg/dl (glycaemia 99 mg/dl), protein 30 mg/dl, and a normal IgG index. All CSF cultures were negative. Right and left median, ulnar, and sural nerve sensory action potentials were absent. Motor nerve conduction studies in the right and left median, ulnar, tibial, and peroneal nerves were normal. A needle EMG study performed in right biceps brachii, right abductor pollicis brevis, right first dorsal interosseus, right extensor digitorum brevis, left vastus medialis, left anterior tibial, and left gastrocnemius muscles did not show abnormalities. Bilateral median and tibial nerve somatosensory evoked responses showed absent cervical and lumbar potentials and slowing of cortical potentials. A sural nerve biopsy showed loss of large myelinated fibres with Wallerian-like degeneration. There were no inflammatory cells around epineural blood vessels and no necrotising angitis. Immunofluorescence did not show deposition of IgG, IgM, IgA, IgE, complement, or fibrinogen.

The patient was treated with 0.4 g/kg

intravenous immunoglobulin for five days. One week later, he showed good clinical improvement, up to the point that he was able to button his shirt, use cutlery, and walk without a cane, although he was not able to write. The treatment with immunoglobulins was repeated three weeks later, adding prednisone (90 mg/day), and the patient was discharged from hospital. Three to four weeks later, there was a relapse. He returned to the clinical state before the start of the immunoglobulins, despite continuing prednisone at the same dose. He was readmitted to hospital in June 94. After receiving a further dose of immunoglobulins, he again showed considerable improvement. Since then, prednisone has been gradually withdrawn and a dose of 0.4 g/kg immunoglobulin is given every three weeks. The clinical improvement is maintained at present. A repeat electrophysiological study was unchanged.

Our patient had a sensory neuropathy associated with Sjögren's syndrome.¹ This is related to a dorsal root ganglionitis.² The clinical course is strikingly variable and occasional patients may stabilise or improve.^{1,3} Our patient had had a progressive deterioration of his functional abilities in the past months, so the improvement could be related to the treatment with intravenous immunoglobulin. This hypothesis is supported by the clinical worsening after the initial withdrawal of immunoglobulin, the improvement after reintroduction, and the maintenance of this improvement with repeated doses every three weeks, despite withdrawal of prednisone.

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Diagnostic usefulness of apolipoprotein E ε4 in the diagnosis of the dementias

Recently, papers have been published suggesting that apolipoprotein E (apoE) genotyping might be useful in the differential diagnosis of the dementias.^{1,3} It has been claimed that an apoE ε4/ε4 genotype in a demented patient might suggest a diagnosis of Alzheimer's disease with about 95% probability.¹

However, the specificity of the increased prevalence of the ε4 allele to Alzheimer's disease is the key factor for such a conclusion. A demented patient who is ε4/ε4 has a 95% likelihood of having Alzheimer's disease only if it is assumed that the prevalence of ε4 in non-Alzheimer's disease dementias is similar to controls.³ However, we and

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others¹⁻⁶ have found that the frequency of ε4 in the most prevalent non-Alzheimer's dementia—vascular dementia—is similar to that found in probable Alzheimer's disease. Whereas the drawbacks of the clinical diagnosis of vascular dementia are well known and have already been discussed,⁷ increased prevalence of ε4 in vascular dementia is biologically plausible for the increased risk of vascular diseases associated with ε4.⁸ The table shows the probability of having Alzheimer's disease for a demented patient with a given apoE genotype, as computed from other authors' data¹ and from our own data.⁹ The assumption is made that two thirds of all demented patients have Alzheimer's disease—that is, that any demented patient has a probability of having Alzheimer's disease of 66% before any other

Likelihood for Alzheimer's disease in apoE genotypes according to Roses' and as computed from our sample of 99 sporadic late onset (> 60 years) patients with Alzheimer's disease, 34 patients with vascular dementia, and 70 elderly controls

ApoE genotype	Probability for AD (%) according to						
	AD	Vdem	Controls	Prior probability for AD (%)	Roses'	Our data without correction for Vdem	Our data with correction for Vdem
2/2	0/99	0/34	2/70	66	—	—	—
2/3	3/99	1/34	6/70	66	38	41	51
2/4	2/99	0/34	0/70	66	51	—	—
3/3	46/99	16/34	53/70	66	54	55	60
3/4	23/99	6/34	6/70	66	81	84	78
4/4	25/99	11/34	3/70	66	94	92	73

AD = Alzheimer's Disease; Vdem = vascular dementia. It is assumed that prior probability of AD is 66%,¹ and that 50% of non-AD dementias are Vdem and 50% are other forms which have apoE allele frequency similar to controls. Data on the largest proportion of our patients and all controls have been published.⁹

information is collected. The table shows that if the prevalence of $\epsilon 4$ in non-Alzheimer's disease dementias is similar to controls, the prior probability of 66% would increase to 92% or 94% in the case of an $\epsilon 4/\epsilon 4$ and decrease to 41% or 38% in the case of an $\epsilon 2/\epsilon 3$ patient if our own⁹ or other data¹ are used, respectively. However, if the increased frequency of $\epsilon 4$ in vascular dementia is taken into account, these figures draw closer to the prior probability, of 73% and 51% in $\epsilon 4/\epsilon 4$ and $\epsilon 2/\epsilon 3$, respectively.

This scenario will need to be verified in clinicopathological studies considering the association of $\epsilon 4$ with non-Alzheimer's dementias, but, if confirmed, the diagnostic gain of apoE genotyping might be poor.

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