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Chronic Inflammatory Demyelinating Polyneuropathy in a diabetic patient : deterioration after intravenous immunoglobulins treatment and favorable response to steroid treatment

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Abstract

The authors report the case of a 54-year old type-2 diabetic female patient with a Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). She progressively developed distal hypoesthesia and tetraparesis. She deteriorated after two courses of intravenous immunoglobulins (IVIG) administration and became rapidly wheelchair bound. After one month of steroid treatment, the patient was walking alone. This case raises the question whether IVIG is to be considered as first line treatment for diabetes associated CIDP.

Key words : Chronic Inflammatory Demyelinating Polyneuropathy ; diabetes ; steroids ; intravenous immunoglobulins.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is an immune mediated inflammatory disorder of the peripheral nervous system.

CIDP may be isolated (I-CIDP) or associated with systemic diseases (2) including diabetes. The relationship with diabetes is not completely understood but the odds ratio of the occurrence of CIDP was reported to be 11 times higher in diabetic than in nondiabetic subjects. CIDP associated with diabetes (DM-CIDP) and I-CIDP patients present similar clinical and electrophysiological features and response rate to treatment (2, 3). The recognized treatments of CIDP include plasma exchange, steroid and Intravenous Immunoglobulin (IVIg) (5). The efficacy of all treatments in I-CIDP seems to be equivalent (5).

Some studies suggest to consider IVIg as first line treatment for DM-CIDP patients (1, 7). We report the case of a patient whose condition deteriorated after IVIg treatment. In contrast clinical response to steroids was surprisingly favourable.

Case report

A 54-year-old type-2 diabetic woman developed progressively in April 2002 distal paresthesias and hypoesthesia of the four limbs. Progressively tetraparesis with walking difficulties occurred. In June 2002 a diagnosis of CIDP was made in another hospital. The patient received an initial course of IVIg (0.4 gr/kg/d over 5 days). After a moderate positive response during 3 days she rapidly deteriorated and became wheelchair bound despite a second course of IVIg given 15 days after the first one.

Neurological examination on admission in October 2002 revealed tetraparesis (Table 1). She was unable to walk. Generalized areflexia and diminished perception of touch, pain, vibration and position sense in the four limbs were demonstrated. Babinski signs were absent.

Laboratory data showed a glycosylated hemoglobin of 5.5%, erythrocyte sedimentation rate of 36 mm/h, normal C-reactive protein level, negative anti-GM1 and antinuclear antibodies, absence of cryoglobulin, negative serology for HCV, HBV, EBV and HIV. Electrophysiological examination (Table 1) revealed conduction blocks (Fig. 1), severely decreased conduction velocities, absent F waves, relatively preserved sensory nerve conduction velocities. EMG in the right tibialis anterior and left first dorsal interosseous muscle revealed fibrillations and polyphasic motor unit potentials. CSF analysis showed a mild hyperproteinorachia (62 mg/dl) and 3 cells/mm^3.

In October 2002 methylprednisolone treatment (0.5 mg/kg/ orally) was initiated. After one month, the patient was able to walk alone. Her strength was improved (Table 1). Azathioprine was added to the treatment. In April 2003, the patient had normal sensations in the upper limbs. She could walk 400 meters without help. Ankle, biceps and supinator reflexes were present. Vibration was perceived at the ankles. Electrophysiological evaluation showed improvement (Table 1). After two years, treatment consisted in methylprednisolone 32 mg every two days and 150 mg/d of azathioprine. Neurological examination showed only weakness of the right interosseous scored 4/5, weak right ankle jerk and diminished perception of vibration at the toes.

Table 1

Strength evolution and electrophysiological examination

Clinical evaluation						
Treatment with steroids	0		+ 1 month		+ 6 months	
Strength						
	Right	Left	Right	Left	Right	Left
Shoulder abduction	4	3	4	4	5	4
Elbow extension/flexion	4	3	4	4	5	4
Wrist extension	2	1	4	4	5	4
Finger abduction	2	1	4	4	5	4
Hip flexion	4	4	4	4	5	5
Knee extension/flexion	4	4	4	4	5	5
Foot flexion	2	2	4	4	5	5
Foot extension	3	2	4	4	5	4

Electrophysiological examination								
Nerve and site	Latency (ms)		Amplitude (mV)		Conduction velocity (m/s)		F wave (ms)	
	10/2002	07/2003	10/2002	07/2003	10/2002	07/2003	10/2002	07/2003
Peroneal nerve.R								
Ankle	4.4	3.4	1.068	3.38			absent	75.9
Fibular head		15.4	absent	2.445		25		
knee		18.0		1.937		27		
Tibial nerve.R								
Ankle	3.8	3.5	1.888	2.98			absent	63.6
Pop fossa	17.7		0.078	0.117	26	32		
Median nerve.L								
Wrist	3.3	3.3	3.72	4.62			absent	33.4
Elbow	14.3	9.0	0.117	3.74	25	37		
Wrist	3.5	3.0	0.708	5.10			*	33.4
Median nerve.R								
Wrist	4.1	3.6	3.51	5.59			absent	39.8
Elbow	13.1	9.3	1.854	5.604	25	39		
axilla		13.5		2.562		25		
Ulnar nerve.R								
Wrist	3.0	2.9	4.635	5.260			*	36.5
Below elbow	10.3	8.2	0.630	4.698	32	46		
Above elbow	19.4	12.1	0.172	3.958	11	35		

* Not performed.

Discussion

The clinical presentation of our case fulfils the AAN's clinical and electrophysiological criteria for CIDP (1).

Several studies performed in patients with I-CIDP demonstrate the efficacy of PE, IVIg and steroids compared to placebo (5). Response rate is about 65% for each treatment and equivalent to each other.

In DM-CIDP there is no prospective comparative study. In retrospective studies comparing DM-CIDP and I-CIDP response to treatment only a small number of diabetic patients are included and various combinations of treatments are administered, including IVIg, plasma exchange, steroids and cyclosphosphamide (2, 3, 8). There is no statistical difference between I-CIDP and DM-CIDP in the response rate to the different treatments. Some consider IVIg as first line treatment in diabetic patients : IVIg cause less secondary effects than steroids and do not interfere with the glycemic control (1, 7). Sharma reports a significant improvement of the average Neuropathic Impairment Score (7) after IVIg treatment in 80% of 26 diabetic patients. Three patients presented

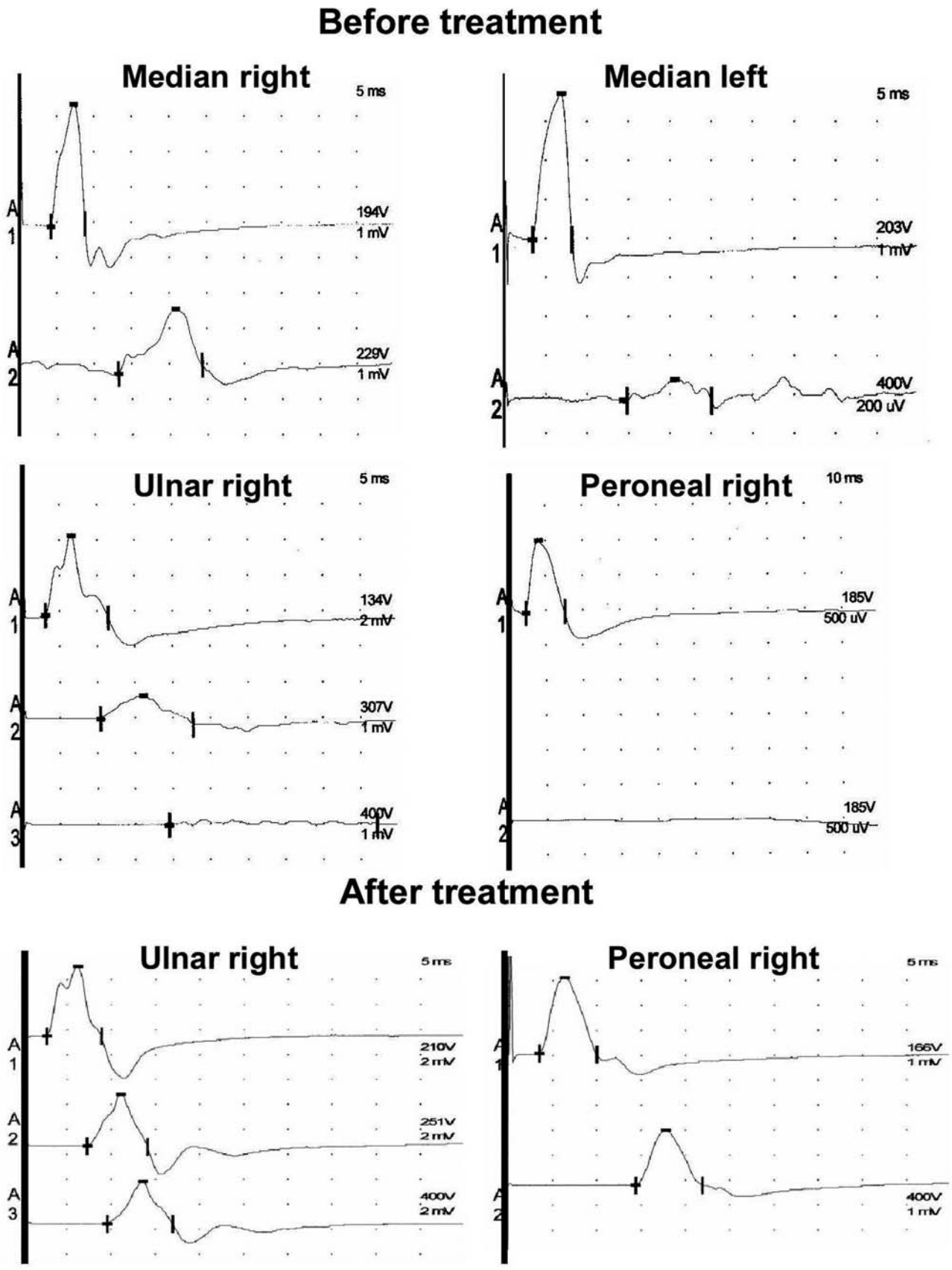

FIG. 1. — Nerve conduction study before treatment illustrating a conduction block on the right ulnar and peroneal nerves and temporal dispersion on the median nerves. After treatment : normalisation of conduction block of the right peroneal and right ulnar nerves.

transient aggravation of abnormal renal function. Cocito reports a moderate effect on the Rankin scale 15 days after first line administration of IVIg in 9 diabetic patients but failed to show a significant effect on the clinical deficit (1).

Some studies identified disease duration less than 1 year, severe weakness, areflexia and conduction blocks as factors predicting a good response to IVIg in I-CIDP (5). Except for a neurological history longer than 1 year our patient meets these criteria. She revealed to be, not only a non-responder but also to deteriorate after IVIg treatment. Clinical deterioration after IVIg treatment in CIDP is seldomly described (4, 7) (3 cases, including one diabetic patient) and is poorly understood.

No prospective study concerning DM-CIDP and steroids exists. Gorson suggest that DM-CIDP has a better response to steroids than to IVIg (2).

Other types of probably immune-mediated neuropathies may complicate diabetes mellitus. Diabetic lumbosacral radiculoplexus neuropathy (DLRPN) is one well recognized entity. Some pathological findings suggest that DLRPN represents a T-cell mediated microvasculitis. This observation prompted the initialization of two double-blind placebo controlled studies : one with IVIG and one with intravenous steroids. At the time of writing the results are not available. Open trials show that IVIG or intravenous steroids may improve recovery and pain control (4).

Conclusion

Our DM-CIDP patient demonstrates clinical deterioration after IVIG treatment but impressive favorable response to steroids.

Predicting criteria to treatment response did not help in this case.

The question of the sequence of the different immunomodulatory treatments recommended for DM-CIDP remains obscure. In every case, each treatment should successively be tried until a favorable clinical response is demonstrated. Our observation suggests that for doubtful cases steroids may be considered as the first line treatment. However, we still need comparative studies of IVIG and steroids treatment efficacy in DM-CIDP.

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