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CASE REPORT

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Hyperpyrexia-triggered relapses in an unusual case of ataxic chronic inflammatory demyelinating polyradiculoneuropathy

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Abstract The ataxic form of chronic inflammatory demyelinating polyradiculoneuropathy (ataxic-CIDP) has been recently described as a subtype of chronic ataxic neuropathy, distinguished by steroid responsiveness and relative preservation of myelinated fibres at sural nerve biopsy. We report on a case of progressive, predominantly sensory, steroid-responsive neuropathy with clinical, laboratory, electrophysiological and pathological features of this uncommon form of CIDP. Moreover, the present case displays peculiar hyperpyrexia-triggered relapses leading to transitory severe tetraparesis, bilateral facial drooping, dysphonia, dysphagia and dyspnoea, which leave clinicians with some unresolved questions.

Key words Ataxic neuropathy • Chronic inflammatory demyelinating polyradiculoneuropathy • Hyperpyrexia

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Introduction

Ataxic neuropathies are characterised by predominant involvement of proprioceptive sensation with sensory ataxia and clinical preservation of muscular strength [1, 2], usually in association with cancer [3], toxicity [4], vasculitis [5] or as a residual deficit after Guillan-Barré syndrome. The idiopathic form, "chronic idiopathic ataxic neuropathy" (CIAN), has also been described as a clinical entity, possibly with a specific immunological marker, antidisialosyl antibodies [6]. Recently, a neglected subtype of ataxic neuropathies has been described, ataxic chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) [1]. The 5 cases of ataxic-CIDP reported by Ohkoshi et al. [1] were distinguished from other forms of chronic ataxic neuropathies because of steroid responsiveness and relative preservation of myelinated fibres at sural nerve biopsy. We report on a peculiar case displaying features of ataxic-CIDP, which leaves unresolved diagnostic and pathophysiologic questions.

Case report

A 56-year-old male had an 8-year-standing history of mild gait disturbances and slight difficulties in fine motility of hands. These were slightly worsened by minor body temperature increases, but had not prevented him from working as a teacher, jogging for 30 min daily and trekking every summer. Within this near-normal life, he experienced the first of two dramatic episodes leading to hospital admission because of sub-acute (2-day onset) occurrence of severe tetraparesis, dysphonia, dyspnoea, dysphagia and bilateral facial drooping. Both episodes had been triggered by hyperpyrexia due to a flu-like affection and were characterised by a surprisingly rapid resolution, beginning spontaneously after fever remission without

any specific treatment, and bringing the patient to his previous basal condition in a few days. This was characterised by moderate sensory ataxia with Romberg's sign, mild reduction of fine motility and strength of hands, apallesthesia up to the hip; absent position sense in the toes, with normal pinprick and touch sense; absent deep tendon reflexes; flexor plantar response and normal cranial nerves.

During the first hospitalisation, neurophysiological investigation disclosed widespread signs of chronic sensory-motor neurogenic alterations at both upper and lower limbs with conduction blocks (motor potential amplitude reduction more than 50% at right median nerve and both ulnar nerves), markedly delayed F-wave in right median, ulnar, tibial and peroneal nerves and absent sensory median and ulnar potentials (Table 1, lines A). Lumbar puncture disclosed a cerebrospinal fluid (CSF) protein level of 0.59 g/l with 2 cells/mm^3. General, immunological, infectious and metabolic work-up was unremarkable. In particular there was no monoclonal gammopathy and anti-GM1, GD1a, asialo-GM1, GD1b, antibodies and GQ1b IgG were negative. There was no detectable serum electrolyte derangement in either the acute phase or the chronic phase of relapses. Primary and secondary periodic paralyses were excluded on a clinical and laboratory basis. Cerebral and spinal MRI were compatible with small vessel disease, without any other pathological sign.

Sural nerve biopsy (Fig. 1) disclosed a loss of large fibres, clusters of regeneration and formation of small onion bulbs composed of a single turn of Schwann cell processes. In paraffin section, no inflammatory cell infiltration was observed. Direct immunofluorescence ruled out the presence of immunoglobulin and complement C3d fraction deposition.

The second acute severe episode occurred five years later, with the same characteristics as the first one.

Subsequent follow-up examinations in the inter-critical period, 9 months later, did not disclose substantial changes in the electrophysiological picture when compared to the acute phase of the first episode (Table 1, lines C). Conduction blocks registered in the acute phase were still evident, motor conduction velocities were comparable and sensory potentials were absent.

Nevertheless, since the second relapse and after a 13-year history, the patient started to feel a gradual deterioration, mainly due to gait imbalance.

Steroid therapy was started with prednisone 1 mg/kg for ten days, followed by a progressive attempt to switch to an alternate daily schedule. This brought about a sensible improvement in the patient's everyday life. Unfortunately, a satisfactory alternate daily therapy could not be achieved, and four months later the patient was started on a 5-day infusion of immunoglobulin (IVIG) 0.4 mg/kg/day. IVIG efficacy was dramatically evident; a personalised schedule with the minimal required dosages (0.4 mg/kg for two days every 40 days) and yearly anti-influenza vaccine have been administered thereafter. Today, nearly two years later, the patient is dependent on monthly 0.4 mg/kg IVIG for two days. Under the effect of IVIG the patient displays a slightly ataxic gate, but is able to walk unassisted for up to 3 km. Up to now, he has not had either further hyperpyrexia episodes or new relapses.

Table 1 Neurophysiological data from the acute phase of the first episode, eight days from symptoms onset (A) and from a follow-up examination 5 years later, nine months after the second episode (C)

Nerve	Time	Lat, ms	Amp, mV	CV, m/s	Fw, ms
MR median	A	6.5	3.5	30	60
	C	6.1	3.6	50	63.6
ML median	A	4.5	2.4	45.6	36.2
	C	3.1	5.2	43.3	24.6
MR ulnar	A	3.1	8.0	46.8	66.4
	C	3.2	8.6	54.7	70.7
ML ulnar	A	3.5	7.5	34.8	39.2
	C	3.1	8.1	28.2	50.3
ML peroneus	A	6	3.3	43.4	61.4
	C	4.5	3.4	39.5	80.3
ML tibialis	A				59.2
	C				66
SR median	A	ne	ne	ne	ne
	C	ne	ne	ne	ne
SR ulnar	A	ne	ne	ne	ne
	C	ne	ne	ne	ne

R, right; *L*, left; *A*, acute phase; *C*, chronic phase; *M*, motor; *S*, sensory; *Lat*, latency; *CV*, conduction velocity; *Fw*, F wave; *ne*, not elicited

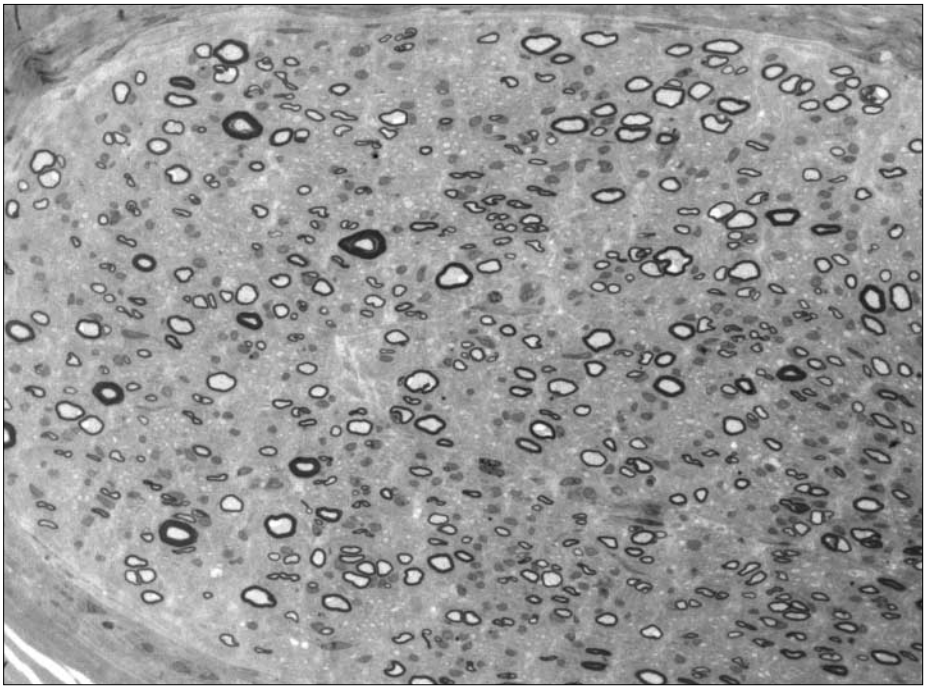

Fig. 1 Sural nerve biopsy showing a nerve fascicle with loss of large myelinated fibres and clusters of regeneration. In some fibres, myelin sheath is abnormally thin compared to axonal diameter. (epoxy section, toluidine blue, 40x original magnification)

Discussion

We report on a case of progressive, predominantly sensory, steroid-responsive neuropathy with clinical, electrophysiological and pathologic features of ataxic-CIDP [1, 7], which is a rare form of ataxic neuropathy. Moreover, our case displayed hyperpyrexia as a trigger factor of severe acute relapses. In the last 8 years, the patient experienced two episodes of fever higher than 39°C, which led him to be nearly tetraplegic, dysphonic, dysphagic and dyspnoeic. Such a severe clinical picture has been almost "switched off" by recovery from the triggering febrile illness. The clinical course of these episodes does recall Uthoff's phenomenon in multiple sclerosis, caused by a worsening of already imbalanced conduction in demyelinated areas following exposure to hot water or fever. Indeed, it has been suggested that temperature could affect peripheral nerve conduction by altering the kinetics of ion channel gating [8].

Another distinguishing feature in the present case is represented by the pathological picture of sural nerve biopsy. At variance with the five cases previously described, in which large and small myelinated fibres were relatively preserved [1], our patient showed a dramatic loss of large myelinated fibres, even though the presence of small onion bulbs suggests a demyelinating component of the pathologic process. The absence of inflammatory infiltration does not exclude the diagnosis of CIDP, as it is found only in 25% of affected patients [9]. Moreover, our patient had a long course of neuropathy compared with the previously reported ones.

In conclusion, the present case fulfils the diagnostic criteria of CIDP [7], with less than 10/mm^3 cell count and elevated protein at CSF examination as laboratory criteria and with neurophysiological features of a demyelinating disease with conduction blocks and proximal conduction alterations. Extensive and persistent involvement of spinal roots, as suggested by electrophysiological examination in the chronic phase, supports the hypothesis that hyperpyrexia could functionally imbalance nerve conduction in already affected areas [8]. From a clinical point of view, this case is a relapsing, predominantly sensory disease, becoming progressive after many years. For these reasons, together with steroid and IVIG responsiveness, it confirms the observation that sensory ataxic neuropathies may represent a distinct subtype of CIDP [10].

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