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Case report

Severe CIDP-MGUS responsive to Rituximab

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ABSTRACT

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a relatively rare disease with progressive limb weakness and sensory loss. A few patients show a severely progressing course without major response to intravenous immunoglobulin or plasma exchange therapy. CIDP-MGUS (monoclonal gammopathy of undetermined significance) is a seldom CIDP variant that has been rarely addressed in therapeutic studies. In the presented CIDP-MGUS case, B cell depletion with rituximab had a favourable effect on the disease course, clinically and in nerve conduction studies.

1. Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a relatively rare disease with a prevalence around 2.8 per 100,000 [1]. In most instances, CIDP leads to progressive limb weakness associated with sensory loss. An autoimmune pathogenesis has been proposed and anti-gangliosid autoantibodies may be detected [2]. The spectrum of disease dynamics varies widely. The majority of patients responds to glucocorticosteroids [3] or to intravenous immunoglobulin (IVIG) interval therapy [4]. Few patients show a severely progressing course without major response to IVIG or plasma exchange therapy [5]. Such a severe CIDP case is described here.

2. Case report

At first admission, the 69 year old caucasian male reported a gait disturbance since 5 months. He suffered from premature exhaustion and complained of tingling sensations in his feet at rest. During walking he reported about pain in the soles. Gabapentin had been of no benefit. On clinical examination, he displayed gait ataxia, absence of all tendon reflexes, and bilateral 4/5 paresis of foot flexors and foot extensors (according to Medical Research Council; MRC). Vibration sensation (128 Hz vibration Rydel-Seiffer fork) was absent at the medial and lateral malleolus on either side. An inflammatory neuropathy cause and treatment (INCAT) disability score of 1 point was assigned due to walking difficulties. Cerebrospinal fluid (CSF) total protein was 964 mg/l. Immune electrophoresis revealed a paraproteinemia type IgG lambda (monoclonal gammopathy of undetermined significance - MGUS). Urinary Bence Jones protein was negative. Bone marrow cytology was normal and did neither reveal hints for the presence of myeloma nor for AL amyloidosis. Serologic testing was negative for Borrelia IgG and IgM, Hepatitis A, B, C, D and E, and HIV. CSF/serum antibody indices for HSV and VZV did not show an intrathecal antibody production. C-reactive protein was mildly elevated to 11 mg/l (limit of normal below 5). Blood sugar tests, HbA1c, Vitamin B12, thiamine, folic acid, homocysteine and creatine kinase values were within normal limits. On electrocardiogram, a tachyarrhythmia absoluta was present. The patient had suffered cardiac ischemia twice in previous years. Nerve conduction studies (NCS) showed signs of demyelination in sensory and motor nerves (Figure 1, Table 1) predominantly in his legs. NCS results were compatible with a CIDP diagnosis. Organomegaly or endocrinopathy such as in POEMS (polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes) syndrome were not present. After a 14 day treatment course with 100 mg/d prednisolone there was no subjective or objective improvement of symptoms or signs. The neurological status of the patient deteriorated progressively over the next 15 months when different

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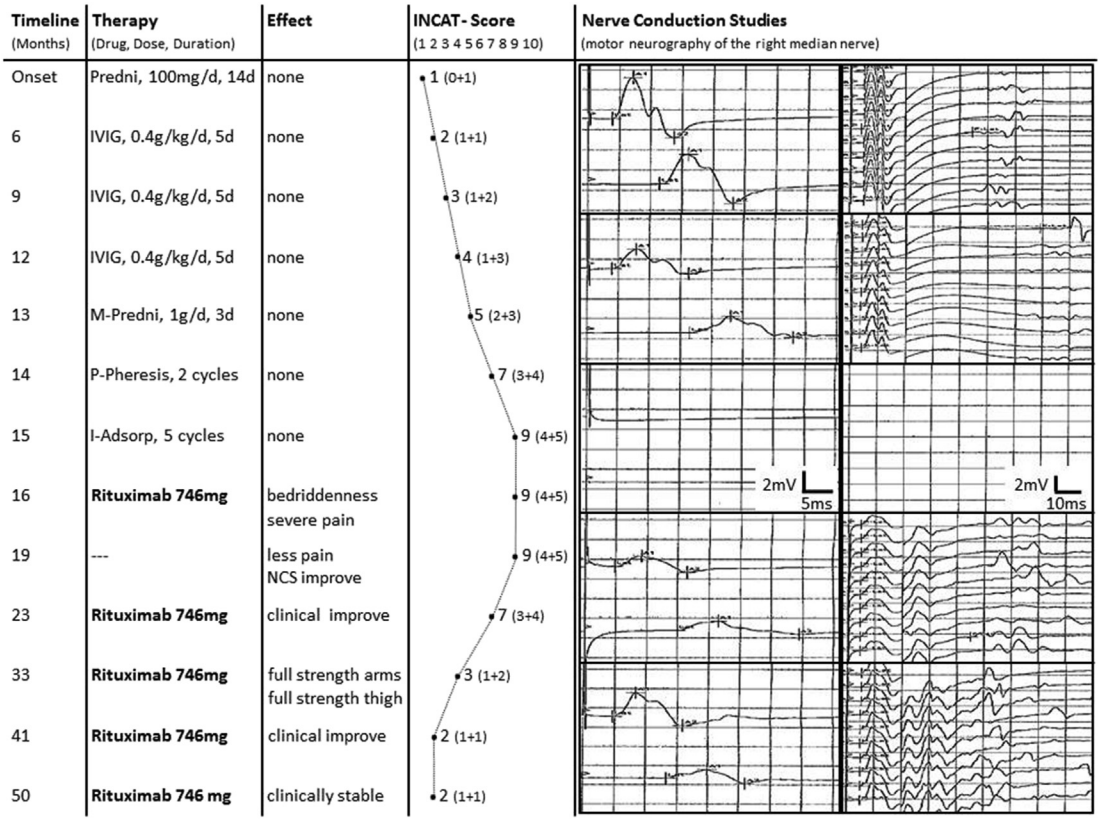

Figure 1. Timeline of therapy, clinical effect, INCAT-score and nerve conduction studies; d, day; g, gram; I-Adsorp, immunadsorption; INCAT-Score, inflammatory neuropathy cause and treatment disability score, IVIG, intravenous immunoglobulin; kg, kilogram; M-Predni, methylprednisolone; mg, milligram; ms, milliseconds; mV, millivolt; NCS, nerve conduction studie; P-Pheresis, plasmapheresis; Predni, prednisolone.

therapy cycles were given in relatively rapid sequence, including IVIG, i.v.-Methylprednisolone, plasmapheresis and immune adsorption (Figure 1). The INCAT score finally was 9, and the patient was bedridden and completely dependent. NCS showed absent sensory and motor nerve responses in his feet and hands and also highly diminished responses at more proximal sites. Sixteen months after first admission, he received 746 mg i.v. rituximab. This rituximab dosage has been adopted from what had revealed good clinical results in our department in a MuSK positive myasthenia gravis patient before [6]. The patient has agreed to treatment with rituximab. Afterwards, he soon reported of slackening pain. Over the next months, his status improved progressively in his arms and legs. With time, he was able to feed himself, to walk and to climb stairs.

Table 1. Nerve conduction studies.

Motor		Onset			15 months later			50 months later		
Nerve	Side	DML (ms)	CMAP (mV)	CV (m/s)	DML (ms)	CMAP (mV)	CV (m/s)	DML (ms)	CMAP (mV)	CV (m/s)
Median	R	3.9	6.0	36.0		0.0		4.7	3.4	30.8
	L	4.4	3.3	43.5	7.0	0.2	11.2	3.8	3.1	33.8
Ulnar	R	3.3	4.0	42.9	8.4	0.2	12.9	3.2	4.8	41.8
	L	3.8	6.8	49.1	5.0	0.3	16.3	3.0	4.8	55.6
Tibial	R	9.6	0.1	23.6		0.0			0.0	
	L		0.0			0.0			0.0	
Peroneal	R	12.1	0.2	22.5		0.0			0.0	
	L		0.0			0.0			0.0	

Sensory		Onset		15 months later		50 months later	
Nerve	Side	SAP (μV)	CV (m/s)	SAP (μV)	CV (m/s)	SAP (μV)	CV (m/s)
Median	R	19.3	48.6	0.0		4.5	51.7
	L	22.2	46.5	0.0		4.6	48.3
Ulnar	R	23.1	41.9	0.0		5.5	40.0
	L	29.2	46.4	2.5	32.4	6.0	50.0
Sural	R	0.0		0.0		0.0	
	L	0.0		0.0		0.0	

DML: distal motor latency; CMAP: compound muscle action potential; CV: conduction velocity; SAP: sensory action potential; R: right; L: left.

3. Discussion

CIDP-MGUS is a CIDP variant that has been rarely addressed in therapeutic studies [7]. Interestingly, among the 13 CIDP patients either refractory to IVIG or not satisfied with this therapy, 7 patients showed a B cell dyscrasia [5]. Severely progressive CIDP cases may be therapeutically challenging. When the disease course is lifethreatening such as in our case, more aggressive therapies may be encountered that may be potentially associated with more severe side effects than the standard therapy. In the presented CIDP-MGUS case, B cell depletion with rituximab had a favourable effect on the disease course, both clinically and in NCS. Obviously, B cell driven humoral factors were of pathogenetic significance and were hit by rituximab. This case may give hope to physicians and their CIDP or CIDP-MGUS patients that even in severely deteriorating cases a turnaround is possible. Nevertheless, while some of the reported cases responded well to B cell depletion, others did not. In the sample of 13 at least partially IVIG refractory CIDP patients reported by Benedetti et al., 2009, 9 responded to rituximab either well (6 patients) or partially (3 patients) [5]. Thus, in IVIG refractoriness, it may be advisable not to wait long for therapy escalation, since it might take several attempts to be successful.

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Author contribution statement

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The authors declare no conflict of interest.

Additional information

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References

[1] M.C. Broers, C. Bunschoten, D. Nieboer, et al., Incidence and prevalence of chronic inflamma-tory demyelinating polyradiculoneuropathy: a systematic review and meta-analysis, Neuroepidemiology 52 (2019) 161–172.
[2] E.K. Mathey, S.B. Park, R.A. Hughes, et al., Chronic inflammatory demyelinating polyradiculo-neuropathy: from pathology to phenotype, JNNP 86 (2015) 973–985.
[3] R.A. Hughes, M.M. Mehndiratta, Y.A. Rajabally, Corticosteroids for chronic inflammatory demyelinating polyradiculoneuropathy, Cochrane Database Syst. Rev. 11 (2017), CD002062.
[4] P.Y. Van den Bergh, R.D. Hadden, P. Bouche, et al., European federation of neurological societies; peripheral nerve society. European federation of neurological societies/peripheral nerve society guideline on management of chronic inflammatory demyelinating polyradi-culoneuropathy: report of a joint task force of the European federation of neurological societies and the peripheral nerve society - first revision, Eur. J. Neurol. 17 (2010) 356–363.
[5] L. Benedetti, C. Briani, D. Franciotta, et al., Rituximab in patients with chronic inflammatory demyelinating polyradiculoneuropathy: a report of 13 cases and review of the literature, JNNP 82 (2011) 306e8.
[6] B. Hain, K. Jordan, M. Deschauer, S. Zierz, Successful treatment of MuSK antibody-positive myasthenia gravis with rituximab, Muscle Nerve 33 (2006) 575–580.
[7] R.A.C. Hughes, Systematic reviews of treatment for inflammatory demyelinating neuropathy, J. Anat. 200 (2002) 331–339.