Journal of the Neurological Sciences 388 (2018) 146–149

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Letter to the Editor

Improvement of distal acquired demyelinating symmetric (DADS) neuropathy after exposure to factor Xa inhibitor

ARTICLE INFO

Keywords:
DADS neuropathy
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
Factor Xa inhibitor
Rivaroxaban
Demyelinating neuropathy

Dear Editor,

Factor Xa, an enzyme in the coagulation cascade, has recently been identified as having a role in inflammation, generating interest in factor Xa inhibitors as anti-inflammatory agents beyond their established use as anticoagulants [1–4]. We report sustained clinical and electrophysiologic improvement of the distal acquired demyelinating symmetric (DADS) neuropathy phenotype, which shares some features with sensory chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), in a patient treated with the factor Xa inhibitor rivaroxaban for deep venous thrombosis (DVT).

1. Case presentation

Over 9 months, an 87-year-old man with no significant past medical history developed progressive tingling in the fingers and feet, decreased manual dexterity, and gait imbalance requiring a cane. Neurologic examination demonstrated normal strength including the intrinsic hand and foot muscles, decreased vibratory sensation in the distal interphalangeal (DIP) joints of the hands and to the level of the knees, pseudoathetosis of the toes, areflexia, a Romberg sign, and a wide based unsteady gait. Serum hemoglobin A1c, vitamin B12, and serum protein electrophoresis (SPEP) and immunofixation (IFE) were normal, and antinuclear, anti-Ro, La and Lyme antibodies were negative. There was no history of alcohol use.

Nerve conduction studies (NCS) revealed absent right median, ulnar, and radial sensory responses, and an absent right median motor response. The right ulnar, left peroneal, and left tibial distal motor latencies were prolonged (7.2, 10.0, and 13.0 ms, respectively), with preserved amplitudes (Fig. 1). Conduction block was not seen. The findings met the European Federation of Neurological Societies/Peripheral Nerve Society diagnostic criteria for atypical CIDP. The distal demyelinating pattern and clinical features including sensory ataxia and distal pattern of sensory deficits suggested DADS neuropathy. Repeat SPEP and IFE were negative. Serum anti-myelin-associated glycoprotein (MAG) antibody testing could not be performed due to financial constraints. The patient declined immunomodulatory treatment.

One month later, the patient developed a spontaneous right lower extremity DVT and was treated with rivaroxaban 20 mg by mouth daily. Over 2 months, the patient had marked improvement of his manual dexterity and gait. Vibratory perception improved to normal in the DIP joints of the hands but remained diminished to the level of the knees. Romberg sign was absent, though there was residual mild pseudoathetosis of the toes. All deep tendon reflexes returned to normal except the left Achilles reflex.

Repeat NCS demonstrated reemergence of the previously absent median and radial sensory responses and median motor response. The right ulnar and left peroneal and tibial motor responses showed improved distal latencies of 6.3, 8.4 and 10.0 ms, respectively, with essentially unchanged amplitudes (Fig. 1).

After 9 months of rivaroxaban treatment, the patient reported continued improvement of his gait such that he no longer required a cane. Rivaroxaban was discontinued, and the patient has had no recurrence of symptoms or change in his neurologic examination after 4 months.

2. Discussion

In addition to its role in the coagulation cascade, factor Xa participates in the inflammatory response through activation of proteinase-activated receptors and thrombin, leukocyte activation, recruitment of mast cells, T cell modulation, and potentiation of mononuclear cell proliferation [1]. Rivaroxaban is a direct factor Xa inhibitor used as an oral anticoagulant. Rivaroxaban's potential anti-inflammatory properties are currently being investigated by evaluating the effects of the medication on inflammatory markers in patients with sickle cell anemia [2], type 2 diabetes mellitus [3], and non-valvular atrial fibrillation [4].

DADS neuropathy shares features with the sensory variant of CIDP and is characterized by primarily distal demyelination. Sensory ataxia is the most common presentation of DADS neuropathy. The DADS-I (idiopathic) subtype is not associated with monoclonal gammopathy, as in this case, and may respond to immune therapy like classical CIDP. Pathological nerve damage in DADS neuropathy may be similar to classical CIDP [5–7]. Proposed mechanisms of nerve damage in CIDP include migration of activated T cells with breakdown of the blood-nerve barrier and defective suppressor regulatory T-cell function. Pro-inflammatory cytokines may mediate demyelination and axon loss [7,8]. Antibody to MAG is present in many DADS cases and may be a

https://doi.org/10.1016/j.jns.2018.03.016
Received 25 January 2018; Received in revised form 25 February 2018; Accepted 7 March 2018
Available online 10 March 2018
0022-510X/

STUDY 1						
Sensory NCS						
Nerves/Sites	*Rec. Site*	*Peak Lat (ms)*	*Amp (μV)*	*Distance (cm)*	*Velocity (m/s)*	*Temp (°C)*
R Median- Dig II						
Wrist	Dig II	NR	NR	13	NR	32.6
R Ulnar- Dig V						
Wrist	Dig V	NR	NR	11	NR	32.6
R Radial - Snuff						
Forearm	Snuff	NR	NR	10	NR	32.2
R Sural – Lat Mall						
Calf	Lat Mall	5.5	5.1	14	31.6	30.6
L Sural – Lat Mall						
Calf	Lat Mall	4.5	9.0	14	37.3	30.7
Motor NCS						
Nerve/Sites	*Distance (cm)*	*Segments*	*Latency (ms)*	*Amp (mV)*	*Velocity (m/s)*	*Temp (°C)*
R Median-APB						
Wrist	7	Wrist-APB	NR	NR	NR	33
R Ulnar-ADM						
Wrist	7	Wrist-ADM	7.2	6.0		31
B.Elbow	21	B.Elbow-Wrist	12.6	5.7	38.8	31.1
A.Elbow	10	A.Elbow-B.Elb	15.1	5.6	40.0	31.3
R Comm Peroneal - EDB						
Ankle	8	Ankle-EDB	11.9	1.6		32.1
Fib Head	30	Fib head-Ankle	20.5	1.2	34.7	32.1
Knee	11.5	Knee-Fib Head	24.5	1.2	28.7	32.1
L Comm Peroneal-EDB						
Ankle	8	Ankle-EDB	10.0	1.6		28.7
Fib Head	29.5	Fib head-Ankle	20.0	1.0	29.5	28.7
Knee	10	Knee-Fib Head	24.0	1.2	29.1	28.8
R Tibial-AH						
Ankle	8	Ankle-AH	11.6	2.2		32
Knee	36	Knee-Ankle	23.1	1.9	31.3	32.4
L Tibial-AH						
Ankle	8	Ankle-AH	13.0	4.0		28.5
Knee	39.5	Knee-Ankle	22.8	3.3	40.6	28.5

Fig. 1. Nerve Conduction Study Results – Before (Study1) & After (Study 2) rivaroxaban initiation.
* = marked swelling present in the distal right > left lower extremity.
NCS = nerve conduction study, Rec. = recording, Amp = amplitude, Temp = temperature, Dig = digit, Lat-lateral, Mall-malleolus, APB = abductor pollicis brevis, ADM = abductor digit minimi, EDB = extensor digitorum brevis, AH = abductor hallucis.