Clinical/Scientific Notes

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ANTIBIOTIC RESPONSIVE DEMYELINATING NEUROPATHY RELATED TO LYME DISEASE

Neuropathies that occur in the context of Lyme disease are commonly related to axonal degeneration.[1] Acute demyelinating neuropathy has also been described[2] and the possibility of chronic demyelinating neuropathy (CDN) has been raised.[3] We report a patient who developed a demyelinating neuropathy in the context of Lyme disease. Treatment of the infection led to marked clinical and electrophysiologic recovery, suggesting an infectious rather than an immune-mediated pathogenesis.

Case report. A 56-year-old Caucasian man developed numbness and tingling in his feet in August 2002 that within a few days spread symmetrically to the fingertips and hands. He reported weakness with heavy manual labor over the ensuing 8 weeks. He denied ataxia, cranial nerve, respiratory, or autonomic symptoms. There was no history of diabetes, thyroid disease, or renal disease. There was no exposure to toxins, chemicals, or tick bites. Family history was unremarkable and there was no history of tobacco or alcohol abuse. Cranial nerve examination was normal. Motor examination revealed normal strength in shoulder abduction and elbow flexion bilaterally but strength was Medical Research Council (MRC) grade 4 in elbow extension, wrist extension, and finger extension. In the legs, there was weakness only in bilateral hip flexion (MRC 4). He was globally areflexic with downgoing toes. Sensation to temperature, pinprick, and light touch was reduced up to the knees on both sides. Proprioception was normal but vibratory perception was reduced at the toes and ankles. Coordination, gait, and Romberg test were unremarkable.

Complete blood count, serum immunofixation, erythrocyte sedimentation rate, and anti-ENA, GM-1, GD-1b, SGPG, MAG, sulfatide, GALOP, and Hu antibodies were negative. Serum Lyme ELISA, western blot (by Centers for Disease Control and Prevention criteria), and CSF Lyme titer were positive; with ELISA, immunoglobulin G (IgG) titer was 1.2 (positive >1.09), IgM was negative, and with western blot six IgG bands (18, 39, 41, 58, 66, 93) were seen. CSF revealed one erythrocyte, two leukocytes, and protein of 67 mg/dL but IgG index and IgG synthesis rate were normal. No oligoclonal bands were identified. Nerve conduction studies showed conduction slowing and abnormal temporal dispersion consistent with an acquired demyelinating neuropathy (table).

EMG of muscles of the left arm and leg was normal without evidence of denervation.

The patient was treated with ceftriaxone for 4 weeks beginning 8 weeks after the onset of symptoms. After completion of his antibiotic treatment he reported marked improvement in his symptoms over a few days; the extent and severity of numbness had regressed and weakness had resolved. Examination revealed normal strength with hypesthesia to the mid-calf level. Ankle reflexes were absent, knee reflexes were reduced, and reflexes had returned to normal in the arms.

Electrophysiologic studies had also returned to normal apart from persistent prolongation of distal motor latencies; conduction slowing, temporal dispersion, and prolongation of F latencies had resolved (table).

CSF analysis revealed no cells. CSF protein and glucose were both 53 mg/dL. CSF Lyme IgG and IgM titers were negative. The patient remains symptom-free at the current time, more than 5 years since the initial presentation, suggesting that the illness was monophasic.

Discussion. The clinical picture of diffuse areflexia, progressive weakness and numbness, CSF protein elevation, and severe slowing in nerve conduction velocities was diagnostic of a demyelinating neuropathy. Whether the neuropathy was a form of chronic inflammatory demyelinating polyneuropathy (CIDP) or a monophasic acute neuropathy such as Guillain-Barré syndrome (GBS) was not clear. Our impression was that the neuropathy was more consistent with CIDP than with GBS, given that Inflammatory Neuropathy Cause and Treatment (INCAT) criteria for CIDP were met.

Although the possibility of an infection having triggered an immune response cannot be ruled out, the fact that weakness, sensory loss, and electrophysiologic changes reversed with antibiotic treatment alone (without immunosuppression) suggests that

Table Electrophysiology

	Distal latency (msec)	Amplitude (mV)	Conduction velocity (m/s)	F wave latency (msec)
Before treatment				
Motor nerve				
Left median	7.3	2.4 (TD)	39.5	33.8
Left ulnar	4.6	5.04 (TD)	41	38.3
Right median	14.5	1.77 (TD)	41.5	Not done
Right ulnar	5.1	2.93 (TD)	37.5	Not done
Sensory nerve				
Right sural		5.93 μV	36.8	
Left ulnar		No response		
Left median		No response		
After treatment				
Left median	4.6	8.3	53.1	29.8
Left ulnar	3.8	8.1	52.6	30.3
Right median	5.6	6.09	52.1	Not done
Right ulnar	4.2	7.62	60	Not done
Left peroneal	5	5.88	52.5	Not done

TD = temporal dispersion.

the neuropathy was probably directly related to *Borrelia* infection, rather than to an immune-mediated process. Similar improvement with antibiotic treatment has also been described in the distal symmetric neuropathy that occurs with chronic Lyme infection.[4,5]

Demyelinating neuropathy in the context of Lyme disease has not been well documented. Severe conduction slowing and conduction block consistent with chronic demyelination in a patient with Lyme infection and two other patients with possible acute demyelinating neuropathy have been described.[2,3] It is unclear whether those patients responded to immunosuppression or to treatment of the infection.

Our case indicates that a demyelinating neuropathy occurs with chronic *Borrelia* infection and provides a rationale for routine Lyme testing in such patients. Unlike the immune-mediated demyelinating neuropathies, it responds to antibiotic therapy. Early recognition is important given the excellent response to treatment.

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IMPROVEMENT OF TICS AFTER SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION

Deep brain stimulation (DBS) of the medial thalamic nuclei and globus pallidus internus (GPi)[1,2] has been tried in the treatment of medically refractory Tourette syndrome (TS). Subthalamic nucleus (STN) is the target most commonly used for DBS in Parkinson disease (PD). A double-blind randomized study has shown the efficacy of STN-DBS in obsessive compulsive disorder (OCD),[3] which is considered within the spectrum of TS.

We report a patient with PD who also had a history of TS in whom bilateral STN-DBS improved both PD and tics.

Case report. A 38-year-old man with an 8-year history of PD was referred for DBS consideration. He had a history of tics that began at the age of 7 and improved by the age of 12. Tics increased in adulthood prior to the diagnosis of PD. No changes of tics were noticed following the onset of PD or dopaminergic medication. No treatment for tics was ever prescribed. Prior to surgery he had motor and phonic tics and compulsion of checking that doors were locked. A single exon 5 deletion in the parkin gene was detected. Quadripolar 3389 DBS electrodes (Medtronic, Minneapolis, MN) were implanted bilaterally in the STN under local anesthesia and connected a few days later to a pulse generator (Kinetra®, Medtronic). The position of each electrode's contact was calculated using preoperative and postoperative stereotactic MRI and the software Framelink (Medtronic). The active contacts were located in the dorsal tip of the STN on the left side and adjacent to the medial border of the center of the STN on the right. Stimulation was monopolar with pulse width 60 μsec and frequency 130 Hz. Ampli-

Table UPDRS motor part scores and tics quantification

	Preoperative		Postoperative							
			OffM/OnS		OffM/OffS		OnM/OnS		OnM/OffS	
	OffM	OnM	6 mo	1 y	6 mo	1 y	6 mo	1 y	6 mo	1 y
UPDRS III	49	19	17	21	43	57	11	10	NA	NA
Tics*										
Motor/phonic	160/43	173/91	15/8	5/0	65/6	47/1	33/21	12/3	52/9	47/2
Total	203	264	23	5	71	48	54	15	61	49

The table shows the clinical scores of the Unified Parkinson's Disease Rating Scale (UPDRS) motor part and tics quantification, counted on a 10-minute videotape preoperatively and at 6 months and 1 year after DBS. Postoperatively, parkinsonian symptoms and tics were assessed in different conditions of medication and stimulation. Off-medication was defined by 1 night of dopaminergic medication withdrawal. Off-stimulation assessments were done after 15 minutes of turning the stimulation off.
*10-minute videotape (5 min observed/5 min unobserved) for each condition following the rush video protocol.
OffM = off medication; OnM = on medication; OnS = on stimulation; OffS = off stimulation; NA = not available.

tude was progressively increased over time to 3.0 volts for the left STN and 3.2 for the right, in parallel with a reduction in dopaminergic medication. The patient reported a subjective amelioration of tics before stimulation was started. An improvement of both tics and parkinsonian symptoms was observed once the stimulation was initiated. At 1 year, STN DBS produced a 57% improvement in the motor part of the Unified Parkinson's Disease Rating Scale and allowed a 56% reduction in dopaminergic medication dosage. Tics frequency diminished by 89% at 6 months and 97% at 1 year, counted on a 10-minute videotape by a blinded investigator. Switching off the stimulation produced an immediate increase in tic frequency (table). The compulsion improved but did not resolve completely.

Discussion. Coexistence of TS and PD has previously been described, with the evolution of PD or dopaminergic medication having variable effects on TS manifestations.[4] Although the more than 50% reduction in dopaminergic medication could in part explain the improvement of tics, the immediate deterioration in tics frequency after switching off the stimulation suggests a direct impact of STN stimulation. The remaining improvement observed in the off-stimulation assessment compared to preoperative could be explained by a long-term tic-suppressant effect of STN DBS, as stimulation was left off only for 15 minutes. A microlesion effect could account for the amelioration reported by the patient prior to stimulation onset.

From a physiologic perspective, STN occupies a privileged position influencing both output nuclei of the basal ganglia, GPi and substantia nigra (SN) reticulata. Several findings link the STN with behavioral changes that may improve with STN-DBS.[3] François et al.[5] found that stereotyped behaviors in nonhuman primates, resembling tics and compulsive disorders, were related to dysfunction of the limbic parts of the globus pallidus externus, the STN, and the SN reticulata, rather than to dysfunction of the GPi. Involvement of the SN in TS was also found in a functional MRI study.[6] Furthermore, stimulation of the anterior STN was effective in reducing stereotypes in a primate model of behavioral disorder[7] and STN DBS in PD can also result in behavioral changes. Indeed, the small size of this nucleus may allow modulation of abnormal neuronal activity of both limbic and sensorimotor territories, more easily than GPi or thalamic DBS.

This report suggests that the STN may be a potential target for DBS in TS. STN-DBS would allow modulation of both limbic and sensorimotor territories and may provide a quicker relief of symptoms than medial thalamic nuclei or GPi stimulation.

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