Mononeuropathy Multiplex with Ulcerative Colitis

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We describe acute mononeuropathy multiplex in a patient with chronic ulcerative colitis. The symptoms of neuropathy were well correlated with the disease activity of colitis. Both electrophysiological study and sural nerve biopsy revealed axonal degeneration. Mononeuropathy multiplex may be an extraintestinal manifestation of ulcerative colitis.
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Key words: extraintestinal manifestation, axonal degeneration

Introduction

Ulcerative colitis has various extraintestinal manifestations (1–14). However, neurological involvement is relatively rare. In particular, there are few reports of peripheral neuropathy with ulcerative colitis (1, 2, 8–10, 14). We report the association of acute mononeuropathy multiplex and ulcerative colitis.

Case Report

A 40-year-old woman first developed rectal bleeding, tenesmus, diarrhea, and weight loss in July 1984. Barium enema, colonoscopy, and colonic biopsy established a diagnosis of ulcerative colitis, involving the intestine from the upper third of the ascending colon to the rectum. She responded to the initial therapy with oral salazosulfapyridine (SASP). The initial therapy dose and period of treatment of SASP were 3,000 mg/day and 6 years, respectively. She went into remission for 7 years. In March 1991 an exacerbation of the disease occurred, with bloody diarrhea and anemia. Therapy of oral SASP (4,000 mg/day) and steroid (prednisolone 30 mg/day) resulted in a partial response. On May 20, 1991, the oral SASP was suddenly discontinued because erythroblasts appeared in her peripheral blood, which might indicate a side effect of SASP. The next day her condition was exacerbated again, with fever, tenesmus, and severe bloody diarrhea. She simultaneously noted paresthesia and mild weakness of the right foot, which spread to both legs and the right hand within a week. She was bedridden until the re-start of SASP on June 30. Both her general and neurological symptoms gradually became better following the resumption of SASP. On July 16, she underwent neurological examination. General examination was unremarkable except for 31% ema-

ciation (height 156 cm, weight 35 kg). Mentation and cranial nerve functions were normal. She could stand by herself but could not walk without support. Weakness with a decrease of muscle tone was predominant in the distal legs, being more severe on the right side. Muscle strength was nearly normal in the arms, 3+ to 4+ in the left leg, and 2+ to 3+ in the right leg by manual muscle testing. Muscle atrophy was remarkable in the muscles of the right lower leg. Muscle stretch reflexes were absent at the knee and ankle. There was severe impairment of perception of joint positional and vibratory sensation below the left ankle and below the right knee. Soft touch and pin prick sensation were also severely impaired below the left ankle and below the right knee; these were moderately or mildly decreased up to the left knee and up to the right hip, as well as in the right hands up to the right wrist.

The hematocrit was 33% and the erythrocyte sedimentation rate was 22 mm/hr. Serum iron concentration and total iron binding capacity were 43 and 197 µg/dl, respectively. The following were normal or negative: serum vitamin B1, B2, B6, E, folate, blood sugar, hemoglobin A1c, immunoelectrophoresis, urine for Bence Jones protein, cryoglobulin, thyroid studies, and lupus erythematosus preparation. CSF protein was 68 mg/dl, without oligoclonal bands. Nerve conduction studies showed reduced amplitude of sensory potentials and mild prolongation of conduction velocity both in the arms and in the legs (Table 1). Motor potentials had normal amplitudes and latencies in the arms (Table 1). In the legs, motor thresholds were markedly increased at all of the tested sites of nerve stimulation, much more on the right side. Amplitudes of compound muscle action potentials were severely reduced at the right posterior tibial nerve and mildly reduced at the left tibial nerve, although motor nerve conduction velocity between the ankles and the knees

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Table 1. Motor and Sensory Nerve Conduction Studies

Nerve tested					Lower normal limit	
	pAMP (mV)	dAMP (mV)	CV (m/s)	CB/TD	dAMP (mV)	CV (m/s)
Motor nerves						
R median	19	20	55	—	10	46
L median	12	12	57	—		
R ulnar	19	20	60	—	10	46
L ulnar	15	16	52	—		
R peroneal	2.2	2.5	45	—	2	39
L peroneal	3.2	3.8	44	—		
R tib. pos.	1.3	1.7	50	—	6	39
L tib. pos.	3.0	3.5	50	—		
	AMP (μV)	CV (m/s)			AMP (μV)	CV (m/s)
Sensory nerves						
R median	5.8	49			10	50
L median	7.7	48				
R ulnar	7.0	47			10	50
L ulnar	8.9	47				
R sural	4.2	36			6	40
L sural	5.3	34				

pAMP: proximal amplitudes of CMAPs, which were evoked from sites of nerve stimulation at the elbow or knee, dAMP: distal amplitude of CMAPs, which were evoked from sites of nerve stimulation at the wrist or ankle, CMAPs: compound muscle action potentials, CV: nerve conduction velocity, CB: conduction block*, TD: abnormal temporal dispersion, R: right, L: left, —: negative, tib. pos.: posterior tibial nerve, AMP: amplitudes of sensory nerve action potentials.

*Conduction block was defined as a reduction in the ratio of proximal-to-distal CMAP amplitudes to <0.60 without abnormal temporal dispersion.

was normal (Table 1). Proximal nerve conduction velocity using F wave was mildly reduced in the legs (45–47 m/s). In electromyographic studies, motor unit potentials were increased in amplitude and duration (4–6 mV in amplitude, 8–12 ms in duration). However, no denervation potentials were evident.

Right sural nerve biopsy revealed active axonal degeneration (Fig. 1). Myelinated fibers (MF) were moderately decreased (2,205 MF/mm²), with a more prominent loss of the larger fibers (Fig. 1). The loss of MF was not diffuse; rather it was accentuated multifocally (Fig. 1). There were many myelin ovoids, and vacuolation of axons and myelin sheaths, as well as atrophy of axons (Fig. 1). Thinly myelinated fibers were few in number, and no onion bulb formation was observed. Inflammatory cell infiltrates or vasculitis were not evident. In the single teased fiber study, many fibers showed rows of myelin ovoids (Fig. 2), indicating axonal degeneration, but rare segmental demyelination.

A daily dosage of 60 mg of prednisolone was administered in addition to SASP. The patient gradually improved in both general and neurological status. In September 1991, she could walk unassisted and had nearly normal muscle strength, but continued to have moderate or mild sensory impairment. The severity of the neuropathy symptoms were well correlated with

her illness of ulcerative colitis.

Discussion

The clinical features of the neuropathy found in this patient with ulcerative colitis was acute mononeuropathy multiplex. The neurological symptoms developed with distinct asymmetry, which predominated on the right side. Nerve conduction studies supported this asymmetry (Table 1). Nerve conduction studies and sural nerve biopsy revealed the main process of the neuropathy to be axonopathy. The reduction of the amplitudes of the sensory and motor potentials, and biopsy findings (moderate loss of myelinated axons and many degenerated axons, such as myelin ovoids) implied axonal degeneration. In addition, other aspects of the biopsy findings (few thinly myelinated fibers and segmental demyelination in the teased study) indicated the presence of some demyelination. The neuropathy was primary axonal degeneration with some secondary demyelination.

The characteristic in this patient was that the development and course of the neuropathic manifestations were well correlated with the disease activity of ulcerative colitis. This indicated that the association between ulcerative colitis and the

Fig. 1. Cross-section of the biopsied sural nerve. Numerous myelin ovoids show breakdown of axons and myelin sheaths (a). The loss of myelinated fibers is not diffuse, but appears multifocal (b). (Epon-embedded section stained with toluidine-blue, a: $\times 506.6$, b: $\times 161.4$)

Fig. 2. Single teased fiber study showing rows of myelin ovoids ($\times 162.9$).

neuropathy was not coincidental. Guillain-Barré syndrome could be ruled out, because the neuropathy in this patient showed primary axonal degeneration. This syndrome typically reveals acute demyelinating polyneuropathy. Malnutritional neuropathy due to exacerbation of ulcerative colitis could be ruled out, since this neuropathy usually occurs in accordance with vitamin deficiency (15) and vitamin deficiency polyneuropathy shows chronic polyneuropathy, and the serum vitamin levels were normal in the present patient. Since the patient gradually improved following the administration of

SASP, sensorimotor neuropathy due to SASP (16) was also unlikely.

There are few reports of peripheral neuropathy with ulcerative colitis. Subacute autonomic neuropathy (1), chronic polyneuropathy clinically similar to chronic inflammatory demyelinating neuropathy (CIDP) (2, 8), perineuritis (2), and Guillain-Barré syndrome (9, 10, 14) have been documented. However, acute mononeuropathy multiplex with axonal degeneration as found in the present case, has not yet been described.

Almost one-third of all adults with the clinical syndrome of mononeuropathy multiplex have a clear-cut picture of a demyelinating disorder, typically with multiple foci of persistent conduction block on electrodiagnostic examination, which represents part of the spectrum of CIDP (17). The remaining two-thirds of patients with mononeuropathy multiplex have an electrodiagnostic examination showing axonal involvement, and about one-half of these patients have vasculitis of the vasa nervorum (17). Although the vasculitis of vasa nervorum was not evident in the sural nerve biopsy of the present patient, the pattern of multifocal fiber loss suggested ischemic changes, as is frequently observed in vasculitic neuropathy (18). Ulcerative colitis has various extraintestinal manifestations associated with systemic vasculitis, i.e. pulmonary vasculitis (3, 4), perineuritis (2), giant cell arteritis and sensory neural deafness (5), cerebral arteritis (6, 11), vasculitis of the skin (7) and the penis (12), and multiple large vascular lesions similar to Takayasu's arteritis (13). Therefore, we conclude that her neurological symptoms were associated with ulcerative colitis. Acute mononeuropathy multiplex may be an extraintestinal manifestation of ulcerative colitis, probably due to vasculitis associated with ulcerative colitis.

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