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Case Report

Mononeuritis multiplex in incomplete Behcet's disease: A case report and the review of the literature

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SUMMARY *A case of Behcet's disease with peripheral nervous system involvement is described. A 58-year-old female with a 16-year history of Behcet's disease was admitted to our hospital because of numbness in multiple areas in both the upper and lower extremities. A biopsy of the sural nerve revealed degeneration of the axons and a capillary lesion. This finding was compatible with mononeuritis multiplex. This case of Behcet's disease with biopsy-proved mononeuritis multiplex is a very rare one.*

Key words: Behcet's Disease, Peripheral Nerve, Mononeuritis

INTRODUCTION

Central nervous system (CNS) involvement is common in Behcet's disease (BD) and about 10% of BD patients have CNS problems. Peripheral nervous system involvement, however, is very rare in this disease. The purpose of the present report is to describe a documented case of peripheral nervous system involvement in BD.

CASE REPORT

A 58-year-old female was admitted to Teikyo University Hospital because of numbness and tingling sensation in both legs. She was well until 1971, when recurrent oral aphthae developed. In 1973 weakness in the legs and erythema-nodosa developed. In 1978 weakness in the legs became worse, and numbness in the distal portion of lower extremities developed. Thereafter, oral aphthae and weakness in the legs recurred intermittently. In 1983 arthralgia in the left knee developed. In May 1984, arthralgia in the left knee, numbness in the legs and hands, genital ulcers, and multiple folliculitis developed. In September 1984, the patient was referred to our clinic and the diagnosis of BD was made according to the criteria of the Japanese BD research commitee (1). Later the patient was admitted twice to our hospital because of severe numbness in the extremities. The patient never experienced ocular symptoms. In April 1986, the weakness and numbness in the extremities became worse and the patient was admitted to our hospital for the third time.

On admission, physical examination revealed that the patient had multiple folliculitis in the scalp. The patient had no ocular symptoms and there were no abnormalities observed on ophthalmologic examination. In the upper limbs, there was weakness of the right hand muscles, but no sensory loss was

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detectable apart from tingling paresthesias in the fingers of the right hand. Tendon reflexes were normal. The legs showed bilateral weakness, with the left leg being more affected, particularly concerning flexion and extension of the knee. There was no significant wasting away of the muscles. Both knee and ankle jerks in the legs were totally absent. Plantar response was flexor. Sensory testing displayed an extensive impairment for all modalities in the lateral and posterior portion of her left leg, being more severe distally along the course of the peroneal nerve. In the right leg, a mild stocking-type loss of the temperature sense was detected. There were tingling paresthesias on the feet, but, no cranial nerve abnormality was found.

Laboratory data disclosed that the erythrocyte sedimentation rate was 9mm/h, the erythrocyte count was $449 \times 10^4/mm^3$, the leukocyte count was $6,300/mm^3$, the C reactive protein (CRP) was negative, and the rheumatoid factor was negative. The fasting blood sugar was 78mg/dl, and there was no glucose in the urine. Antinuclear antibody, hepatitis B antigen, and cryoglobulin were negative. The beta-thromboglobulin was 120.7ng/ml (nl < 50), the platelet factor 4 was 62.3ng/ml (nl < 20), and the fibrinopeptide A was 27ng/ml (nl < 5). The skin pathergy test was negative. The electromyogram of both sides of the anterior tibial muscle revealed polyphasic motor unit action potentials having a long amplitude and duration, thus suggesting neurogenic abnormalities. Motor nerve conduction velocity in the right peroneal nerve was slightly reduced (40.5m/sec).

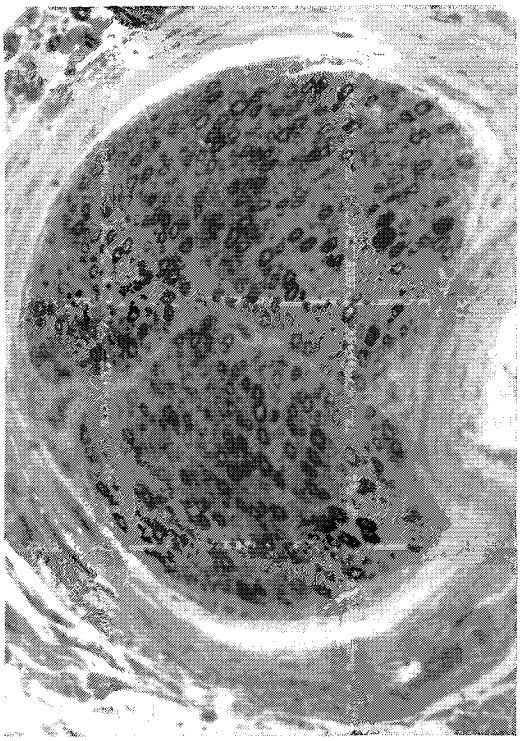

Fig. 1a: A photograph of semithin sections of sural nerve from the patient. There are some fibers showing acute degeneration (myelin ovoids) localized at the upper right edge in the fascicule (arrow). The density of myelinated fibers is relatively decreased around this area of the fascicule. This type of focal change suggests an ischemic process as the pathogenesis of neuropathy (toluidine blue stained, original magnification X42.5).

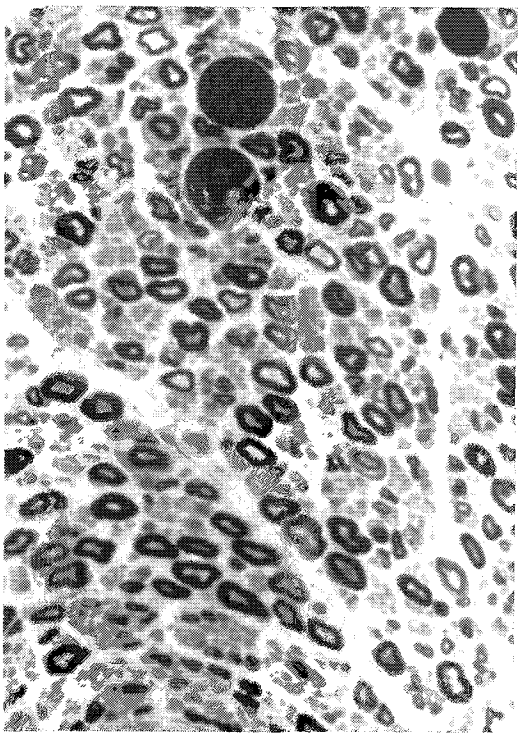

Fig. 1b: Another fascicule of the same nerve with the same kind of focal area of axonal degeneration shown as myelin ovoids (toluidine blue stained, original magnification X170).

The spinal fluid analysis revealed that the initial pressure was 130mm$H_2$0, the total protein was 42mg/dl, the glucose was 52mg/dl and the cell count was 7/mm^3. The computed tomography of the brain and the electroencephalogram indicated normal functioning.

In order to determine the type of the neuropathy, a biopsy of the sural nerve was performed. Figure 1 shows a semithin cross section of the tissue. Selective fascicular damage is not as conspicuous as in the neuropathy of ischemic arteritis. However, a patchy localized degeneration of fibers, identified by the presence of clustered ballooned myelin balls in two of the total fascicles of the nerve, suggested an ischemic process.

The number of myelinated fibers in the total fascicles was slightly low (6,900/mm^3). The diameter histogram of myelinated fibers showed a slight decrease of both large and small myelinated fibers.

Electron micrographs showed various stages of axonal degeneration on both myelinated and unmyelinated fibers (Fig. 2a, b). Significant thickening of the basement membrane in a capillary was seen at the periphery within a nerve fascicle also suggesting the ischemic pathology of nerves just as indicated on diabetic neuropathy (2) (Fig. 2c).

These data suggested that the patient suffered from mononeuritis multiplex. As a result, a large quantity of methylated vitamin

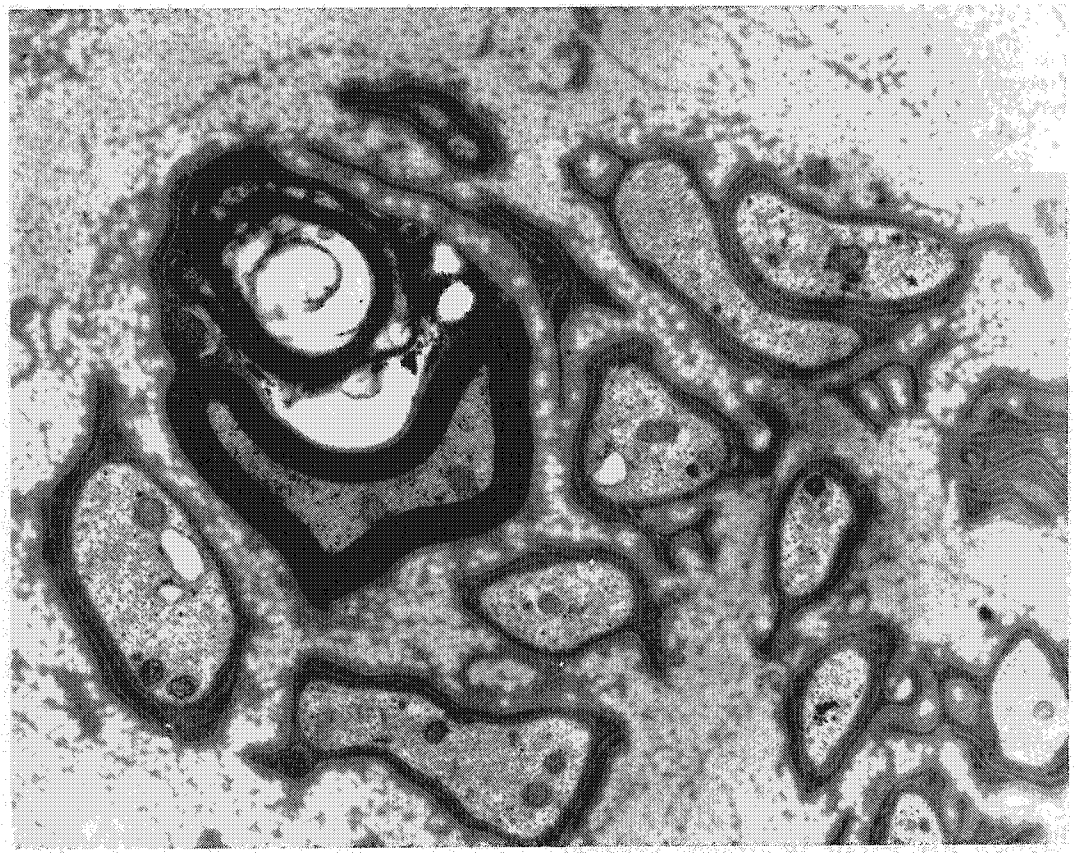

Fig. 2a:Electron micrograph of the biopsied nerve. A small myelinated fiber with myelin debris in the Schwann cell cytoplasm, surrounded by several unmyelinated fibers of almost the same diameter. The repeated process of regeneration and degeneration of myelinated fibers is suggested. Scattered are a lot of collagen pockets and flattened Schwann cell processes devoid of axons suggesting unmyellinated fiber degeneration going hand in hand with myelinated fiber change (original magnification X6000).

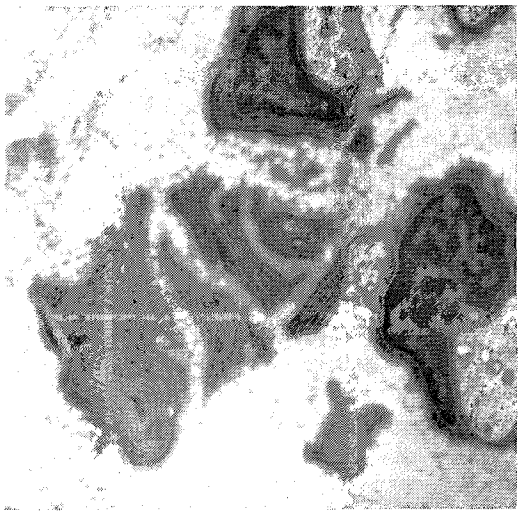

Fig. 2b: A magnified view of a flattened Schwann cell processes indicating the degeneration of unmyelinated fibers (original magnification X10000).

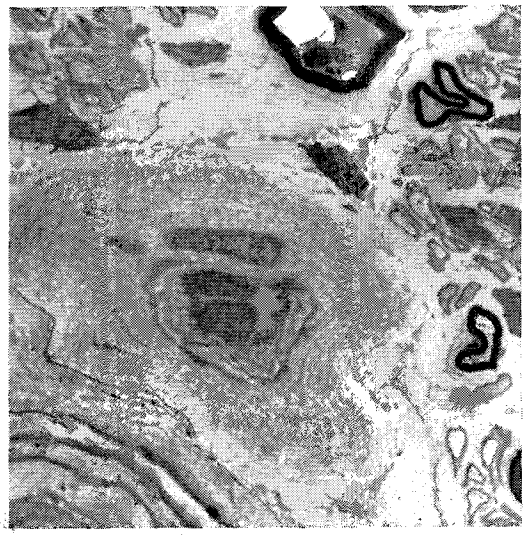

Fig. 2c: Thickening of the basal lamina of a capillary is significant (original magnification X2100).

B_{12} (5,000μg/day) was given for 2 weeks in order to improve the myelin sheath. Clinical symptoms and signs gradually subsided so that the patient could be discharged in September of 1986.

DISCUSSION

There are four major symptoms of BD: oral aphthae, cutaneous lesions, ocular impairment, and genital ulcers (3). In addition, other organs may sometimes be involved. Neurological involvement is especially important because it is one of the main causes of death in BD sufferers (3). Clinically neurological manifestations include hemiplegia, headaches, and paraplegia (4). Laboratory data of BD patients show increases in the cell number and the protein in the spinal fluid, abnormal electroencephalograms, and low density areas as determined by computed tomography and nuclear magnetic resonance (5).

It is interesting to note that lesions of neuro-Behcet mainly occur in the brain and instances of peripheral nerve involvement are rare. The cases with peripheral nervous system involvement are summarized in Table I. In 1958 Ardouin et al reported a 49-year-old male with BD who had paresthesia in his legs and lost Achilles tendon reflex (6). In 1971 O'Duffy reported a 49-year-old housewife who had diminution of two-point discrimination and of temperature sensation in the feet with bilateral facial weakness (7). Since then there were more than 10 reports about peripheral nervous system involvement in Behcet's disease. Some patients had CNS involvement in addition to peripheral nervous system involvement (6,12,17).

There are many types of peripheral nervous system involvement. Some patients had neuropathy (7,8,9,15,21), another had mononeuritis multiplex (12,19,20), and others had radiculitis (11). In two cases vasculitis was proved by the biopsy (8,20). In our case, the patient had weakness of the muscles of the right hand and tingling paresthesias in the fingers of the right hand, as well as left leg weakness with an extensive sensory impairment localized in the lateral and posterior portion of her left leg. The distribution of sensory disturbance and weakness was absolutely asymmetrical. Therefore, the diagnosis

Table I *Peripheral nervous system involvement in BD*

Year	Reporter	Age	Sex	Symptoms	Reference
1958	Ardouin	49	M	paresthesia, loss of tendon reflex, meningoradiculoneuritis	(6)
1971	O'Duffy	43	F	diminution of sensation, peripheral neuropathy	(7)
1972	Lobo-Antunes	37	M	loss of tendon reflexes, glove-stocking type neuropathy, biopsy-proved vasculitis	(8)
1972	Kitajima			polyneuropathy	(9)
1973	Aggarwal	32	F	facial paralysis	(10)
1973	Faldi		3 cases	sciatic pain, areflexia, motor weakness, radiculitis	(11)
1975	Wakayama	28	M	mononeuritis multiplex	(12)
		42	M	CNS involvement	
1975	Murakami	42	F	cranial nerve involvement	(13)
1977	Fujiwara		7 cases	decreased sensation	(14)
1980	Afifi		2 cases	peripheral neuropathy	(15)
1982	Rougmont		1 case		(16)
1983	Yorita	50	M	paresthesia CNS involvement	(17)
1984	Bakouche	21	F	polyradiculitis	(18)
1986	Hashimoto	24	M	mononeuritis multiplex	(19)
1986	Tsubata	52	M	mononeuritis multiplex, vasculitis	(20)
1987	Namer	46	F	weakness and paresthesia in legs, peripheral neuropathy	(21)

M = male, F = female.

of polyneuropathy or polyradiculopathy was excluded. Diagnosis of mononeuritis multiplex might have been considered when the sensory disturbance in the hands and the right leg was not detected. The detailed and careful neurological evaluation of this patient resulted in the diagnosis of mononeuritis multiplex.

Pathological examination also suggested mononeuritis multiplex. As shown in Fig. 1, the patchy or multifocal degeneration of nerve fibers indicates the presence of ischemia (22,23).

The thickening of capillary basement membrane is known as a characteristic of diabetic neuropathy for many years, and recently diabetic neuropathy was proved to be induced by ischemia, which causes focal fascicular lesions proximally due to microangiopathy and diffuse symmetrical polyneuropathy distally. Therefore, the finding of basement membrane can also be an indication of ischemic neuropathy (24,25). In addition to diabetes, such a kind of pathological change has already been demonstrated in BD as well. Fujiwara (14) and Afifi (15) showed exactly the same kind of capillary change as ours in their papers on neuro-Behcet's disease. Therefore, this finding may have a pathogenetical role as mononeuritis multiplex with neuro-Behcet's disease.

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