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CASE REPORT

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Sensorimotor polyneuropathy as an initial clinical manifestation of sarcoidosis

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Abstract A 45 year-old Japanese woman developed numbness and tingling of both hands and feet. Electrophysiological examination revealed sensorimotor polyneuropathy. She was diagnosed as suffering from sarcoidosis on the basis of the pathological findings from dermal biopsy. Steroid therapy effectively improved the clinical symptoms. Although sarcoid neuropathy is rare, this case suggests sensorimotor polyneuropathy is an important symptom of sarcoidosis and can represent the initial clinical manifestation of the disease.

Key words Axonal degeneration · Electromyography (EMG) · Sarcoidosis · Sensorimotor polyneuropathy

Introduction

Sarcoidosis is a disorder of unknown cause, which affects multiple organs with formation of granulomatous lesions and causes many different clinical manifestations including neurological signs. Among its various manifestations, sarcoid neuropathy is a rare complication of sarcoidosis. Here, we report a Japanese patient with sarcoidosis who showed progressive gait disturbance due to sensorimotor polyneuropathy.

Case report

A 45-year-old Japanese woman developed numbness and tingling of both hands and feet in March 2000. Magnetic resonance imaging of the spine was performed at another hospital and no major abnormality was observed. In April, she began to have painful legs with difficulty in walking. She was referred to our outpatient clinic for further examination in June 2000. At the time of admission, she had fever at 37°C and had pain in her lower extremities. She was a housewife with no alcohol habit and had never been exposed to any toxic chemical materials. On physical examination, there was slight edematous erythema in her feet. However, there was no facial erythema, xerostomia, scleroderma, muscle atrophy, or subcutaneous nodules. Neurological examination revealed symmetric muscle weakness in the plantar extensors and flexors, iliopsoas, hamstrings, and gastrocnemius muscles graded as 3–4/5, as well as painful paresthesia. Cutaneous sensation was impaired in glove and stocking distribution to the ankles and wrists. Brachioradialis and Achilles tendon reflexes were absent. However, there were no cranial nerve abnormalities.

Laboratory findings (Table 1) showed an erythrocyte sedimentation rate (ESR) of 39 mm/h; there was a normal urinalysis and blood count with no eosinophilia. Liver and renal functions were normal. The serum creatine kinase, calcium, vitamin B_{12}, and folic acid values were within the normal range. Serum angiotensin-converting enzyme (ACE) was 23.6 IU/l (normal 7.7–29.4 IU/l), but lysozyme was elevated to 12.5 μg/ml (normal 4.2–11.5 μg/ml). Hypergammaglobulinemia was found and C-reactive protein was slightly elevated to 0.24 mg/dl. Cryoglobulin, antineutrophil cytoplasmic autoantibodies (PR-3 ANCA, MPO-ANCA), and immune complexes were within normal limits. Anti-dsDNA, anti-SS-A, anti-SS-B, anti-RNP, anti-Jo-1 antibodies, and the tuberculin skin test were all negative.

In nerve conduction studies in June 2000 (Table 2), distal motor latencies were prolonged in the median and ulnar nerves. Compound muscle action potentials (CMAPs) were very low in amplitude in the tibial and peroneal nerves, and temporal dispersion and conduction block were not detected. Sensory nerve action potentials (SNAPs) of the median nerve were also low in amplitude. However, motor and sensory conduction velocities were relatively preserved

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Table 1. Laboratory data on admission

ESR	39 mm/h	Blood chemistry		Immunological	
Urinalysis		TP	7.0 g/dl	IgG	1880 mg/dl
Protein	(–)	Alb	3.6 g/dl	IgA	501 mg/dl
Sugar	(–)	BUN	12.3 mg/dl	IgM	245 mg/dl
Cast	(–)	Cre	0.6 mg/dl	CRP	0.24 mg/dl
CBC		Ca	9.2 mg/dl	C3	65 mg/dl
WBC	4400/μl	IP	3.1 mg/dl	C4	17 mg/dl
	(Band+Seg 65, Lymph 20, Mono 9, Eosino 5, Baso 1)	LDH	218 IU/l	IC (Anti-C3d)	11.8 μg/ml
RBC	4.02×10^6/μl	ALT	36 IU/l	RF	<10 IU/ml
Hb	12.2 g/dl	AST	31 IU/l	ANA	(–)
Ht	37.2 %	CK	48 IU/l	Cryoglobulin	(–)
Plt	25.2×10^4/μl	FBS	91 mg/dl	PR3-ANCA	(–)
		ACE	23.6 IU/l	MPO-ANCA	(–)
		Lysozyme	12.5 μg/ml	Anti-dsDNA	(–)
		Vitamin B_{12}	1090 pg/dl (233–914)	Anti-U1RNP	(–)
				Anti-SSA	(–)
				Anti-SSB	(–)
				Anti-Jo-1	(–)

IC, immune complex

Table 2. Nerve conduction studies

	June 2000	January 2001	January 2003
Median nerve (rt)			
DLT (ms)	6.8	4.2	4.7
CMAP (mV)	4.0	9.9	13.4
MCV (m/s)	50.0	48.7	47.3
SNAP(μV)	12	18	49
SCV (m/s)	29.2	42.4	42.4
Ulnar nerve (rt)			
DLT (ms)	5.2	3.7	4.4
CMAP (mV)	7.0	17	18
MCV (m/s)	52.5	52.5	48.6
Tibial nerve (rt)			
DLT (ms)	N.E.	5.1	4.1
CMAP (mV)	N.E.	4.0	15.2
MCV (m/s)	N.E.	38.6	43.7
Peroneal nerve (rt)			
DLT (ms)	5.3	4.8	5.4
CMAP (mV)	0.2	–	64
MCV (m/s)	42.8	40.7	41.7

DLT, distal latency time; CMAP, compound muscle action potential; MCV, motor conduction velocity; SNAP, sensory nerve action potential; SCV, sensory conduction velocity; N.E., not evoked

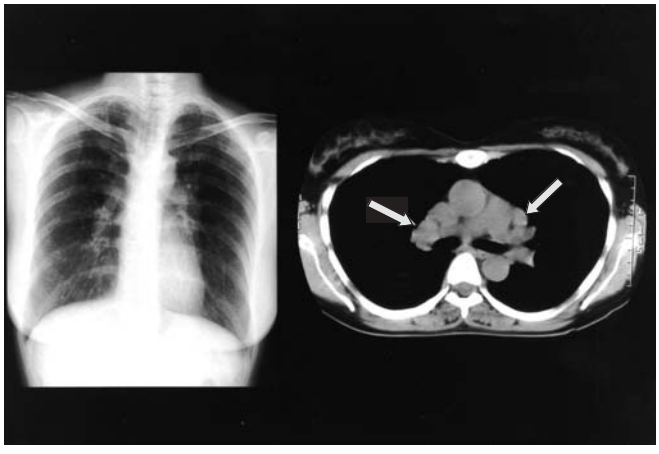

Fig. 1. Chest computed tomography findings on admission. Bilateral hilar lymphadenopathy was present (*arrows*)

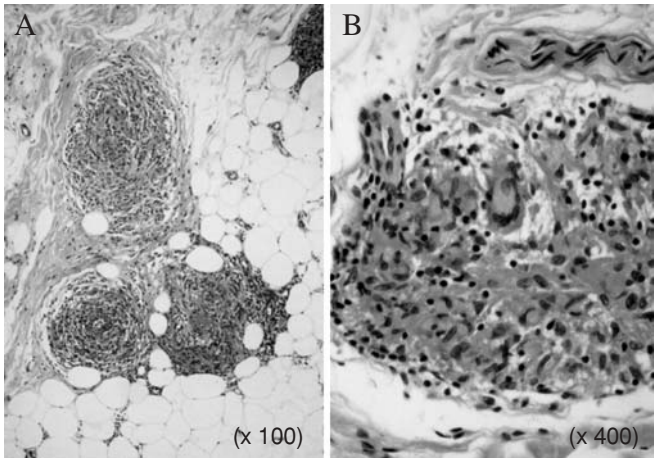

Fig. 2A,B. Histological sections of the erythematous dermal biopsy specimen (H&E staining; **A** ×100, **B** ×400). In higher magnification, non-caseating granuloma with infiltrating lymphocytes and a few giant cells are noted

in all nerves tested. In needle electromyography, denervation potentials were observed in the distal muscles. These findings were compatible with sensorimotor polyneuropathy due to axonal degeneration rather than segmental demyelination.

Slit-lamp biomicroscopy revealed that the patient had uveitis. Swelling of bilateral hilar lymph nodes was observed by chest computed tomography (Fig. 1), and gallium scintigraphy disclosed abnormal uptake of bilateral hilar lymph nodes that was consistent with the finding of active sarcoidosis. The dermal biopsy of leg erythema showed non-caseating granuloma with infiltration of lymphocytes and a few giant cells, but no eosinophils (Fig. 2). Diseases possibly causing peripheral neuropathy due to axonal

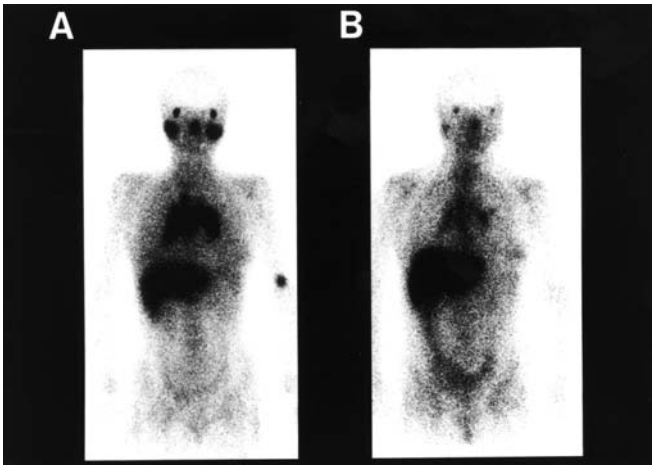

Fig. 3. Gallium scintigraphy of the whole body before (**A**) and after (**B**) steroid treatment. Abnormal uptake in the bilateral hilum improved markedly after treatment

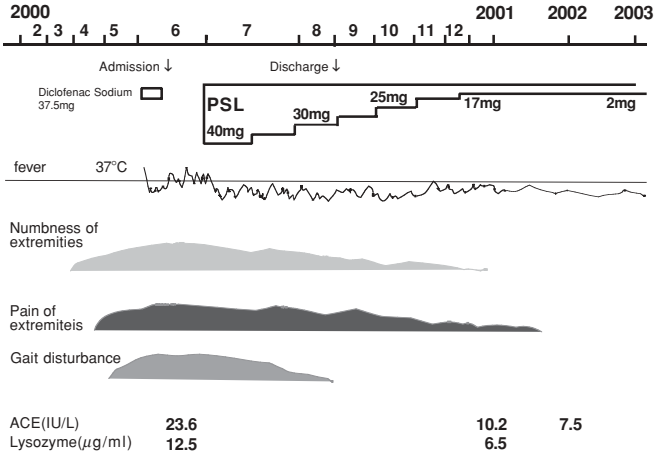

Fig. 4. Clinical course of this case. After prednisolone (*PSL*) treatment, numbness and pain of the extremities and gait disturbance were improved. Serum levels of angiotensin-converting enzyme (*ACE*) and lysozyme were also decreased

degeneration, such as metabolic diseases, toxic diseases, chronic inflammatory demyelinating polyneuropathy, infectious diseases, Vitamin B_{12} deficiency, and other collagen diseases, were all absent.

In July 2000, the diagnosis of sarcoidosis was made and the patient was started on 40mg daily of prednisolone (PSL), resulting in partial improvement of numbness and painful difficulty in walking. The following nerve conduction studies in January 2001 and January 2003 showed a marked improvement in CMAPs in the median, ulnar, tibial, and peroneal nerves, and SNAPs in the median nerve (Table 2). Abnormal uptake in the bilateral hilum also improved greatly after treatment (Fig. 3). Although the PSL dose was tapered gradually, her symptoms of peripheral neuropathies have been well controlled for 3 years. She continued to take the low dose of PSL (2mg daily) with no severe adverse events (Fig. 4).

Discussion

This is a case of sarcoidosis that showed sensorimotor polyneuropathy as an initial clinical manifestation. Neurological involvement in sarcoidosis has been reported to occur in 5%–15% of cases.[1,2] Moreover, in the context of neurological involvement, the prevalence of peripheral neuropathy including cranial nerve abnormality is estimated to occur in 4%–14% of cases,[3] although a recent study reported a higher incidence of peripheral nerve involvement.[4]

Previous studies have reported similar cases of sarcoidosis indicating spinal peripheral neuropathy (Table 3).[5–13] Of these, clinical features of 16 cases, including ours, are available for comparison. Ten of these 16 patients (63%) presented with peripheral neuropathy associated with sarcoidosis as an initial manifestation.[5–10,13] Thirteen (81%) cases had pulmonary symptoms during their course.[5,7–9,11–13] All patients were given corticosteroid therapy with improvement of their symptoms with only one exception. The patterns of neuropathy were variable, as seen in the previous studies.[4,6] Eight of 16 (50%) had sensorimotor polyneuropathy, four (25%) multifocal sensorimotor neuropathy, three (19%) multifocal sensory neuropathy, and one (6%) multifocal motor neuropathy.

The previous reports[1,6,7,11,12] indicated that sarcoidosis could elicit both compressive neuropathy due to perineural granuloma formation and ischemic neuropathy due to periangitis. Typically, complete compression causes Wallerian degeneration followed by demyelination, while vasculitis induces segmental demyelination first because Schwann cells are more vulnerable to ischemia. Although we did not perform sural nerve biopsy, the electrophysiological findings suggested that the main mechanism involved in this case was axonal degeneration. It is likely that sarcoid nodules observed in the specimen of skin biopsy compress the myelinated and unmyelinated neural fibers. Moreover, granulomatous vasculitis or vessel occlusion due to granulomas might also be involved in the neurological manifestations. In general, neuropathies due to vasculitis indicate mononeuritis multiplex. However, symmetrical polyneuropathy was also seen in previous reports.[5–7,14] Our case suggested symmetrical sensorimotor polyneuropathy. This might have been due to the severity and duration of the disease or the effects of systemic inflammation causing vasculitis.

We were able to perform nerve conduction tests before and after treatment. The electrophysiological parameters showed improvement after treatment. This suggests that nerve conduction studies are useful for evaluating the efficacy of treatment even when marked improvement of physiological symptoms is not seen.

Corticosteroid therapy is recommended for the peripheral neuropathy of sarcoidosis and is effective in most patients, although a placebo-controlled double-blind trial has not been performed. The improvement of electrophysiological parameters might be a consequence of the decreased ischemia due to vasculitis as well as reduction of

Table 3. Clinical manifestation of published neurosarcoidosis only manifesting the spinal peripheral neuropathy

First author/year[Ref.]	Age (years)/ sex	Initial manifestation	Pattern of neuropathy	Other symptoms	Therapy	Efficacy of PSL
Oh/1979[5]	58/F	Peripheral nerve	Sensorimotor polyneuropathy	Lung	100 mg	(+)
Nemni/1981[6]	29/F	Peripheral nerve	Sensorimotor polyneuropathy	(–)	150 mg every 2 days	(+)
Galassi/1984[7]	70/M	Peripheral nerve	Sensorimotor polyneuropathy	Lung	100 mg every 2 days	(+)
	54/M	Peripheral nerve	Sensorimotor polyneuropathy	Lung	High dose	(+)
Okada/1986[8]	25/M	Peripheral nerve Skin	Multifocal sensory neuropathy	Lung/skin/eye	60 mg every 2 days	(+)
Yamane/1986[9]	53/F	Peripheral nerve Skin	Sensorimotor polyneuropathy	Lung	40 mg	(–)
Krendel/1992[10]	39/F	Peripheral nerve Skin	Sensorimotor polyneuropathy	Skin	40 mg	(+)
Iwata/1993[11]	58/F	Lung	Multifocal sensory neuropathy	Lung/skin/eye	30 mg	(+)
Sharma/1996[12]	40/M	N.A.	Sensorimotor polyneuropathy	Lung/skin/heart	(+)	(+)
	33/M	N.A.	Multifocal motor neuropathy	Lung/skin/eye	(+)	(+)
	48/M	N.A.	Multifocal sensory neuropathy	Lung/lymph node	(+)	(+)
	50/M	N.A.	Multifocal sensory neuropathy	Lung	(+)	(+)
	46/F	N.A.	Multifocal sensory neuropathy	Lung/skin	(+)	(+)
Said/2002[13]	63/M	Peripheral nerve	Multifocal sensorimotor neuropathy	Lung	1 mg/kg	(+)
	69/M	Peripheral nerve	Multifocal sensorimotor neuropathy	(–)	(+)	(+)
Present study	45/F	Peripheral nerve Skin	Sensorimotor polyneuropathy	Lung/skin/eye	40 mg	(+)

N.A., not available

compression injury due to resolution of granulomatous lesions.

Sarcoidosis shows a wide variety of clinical features and its diagnosis is difficult in the absence of clinical manifestations such as cutaneous or pulmonary involvement. Any of the preceding neurologic manifestations can occur without any evidence of systemic features of sarcoidosis.[5–7,9,10] It is therefore important to consider the possibility of systemic disease including sarcoidosis even when only peripheral neuropathy is found.

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