INTERNAL MEDICINE

□ CASE REPORT □

Demyelinating Peripheral Neuropathy Due to Renal Cell Carcinoma

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Abstract

Renal cell carcinoma (RCC) patients who develop a paraneoplastic syndrome may present with neuromuscular disorders. We herein report the case of a 50-year-old man who suffered from progressive gait disturbance and muscle weakness. The results of a nerve conduction study fulfilled the criteria of chronic inflammatory demyelinating polyneuropathy. An abdominal CT scan detected RCC, the pathological diagnosis of which was clear cell type. After tumor resection and a single course of intravenous immunoglobulin therapy, the patient's symptoms drastically improved over the course of one year. The patient's neurological symptoms preceded the detection of cancer. A proper diagnosis and the initiation of suitable therapies resulted in a favorable outcome.

Key words: demyelinating polyneuropathy, paraneoplastic syndrome, renal cell carcinoma, chronic inflammatory demyelinating polyneuropathy

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Introduction

Paraneoplastic syndrome develops in approximately 10-40% of renal cell carcinoma (RCC) patients. Neuromuscular disorders, such as paraneoplastic syndrome related to RCC are extremely rare (1). We herein report the case of a patient who initially presented with gait disturbance due to polyneuropathy, which was defined as chronic inflammatory demyelinating polyneuropathy (CIDP) related to RCC. We discuss the possible risk factors for demyelinating peripheral neuropathy as a paraneoplastic syndrome.

Case Report

The patient originally came from Bangladesh and lived in Tokyo. At the age of 50, he noticed general fatigue. Two weeks later, he had difficulty going up and down stairs because of weakness in his bilateral lower limbs. One month after the onset of symptoms, he was unable to walk long distances without muscle cramps in the bilateral lower limbs; furthermore, he showed muscle atrophy on both femurs, and lost 7 kg of body weight. After presentation to our hospital, he was admitted. During the first set of neurological examinations, the symptoms related to the patient's cranial nerves showed normal findings. He showed a wide-based gait and was unable to perform tandem gait or squat. Muscle weakness was found in the bilateral lower limbs (manual muscle test (MMT); right: left = 4:4). Muscle atrophy was observed on the proximal side of the lower limbs. The patient's deep tendon reflexes were diminished at both knees and Achilles tendons. Abnormal sensations such as hypoesthesia and numbness appeared on the peripheral side of both of the lower limbs. A cytobiochemical examination of the patient's cerebrospinal fluid revealed a high protein level (150 mg/dL; normal, ≤45 mg/dL), a normal level of glucose (71 mg/dL; normal, ≤75 mg/dL), and a normal cell count (4/μL; normal, ≤5 μL). The patient's myelin basic protein level and IgG index value were within the normal range. The cytology of the cerebrospinal fluid presented no abnormal findings, including malignancy. We also used a Euroimmun scan (Euroline, Euroimmun, Luebeck, Germany) to evaluate antibodies against amphiphysin, CV2, Ma2/Ta Ri, Yo, Hu, recoverin, SOX1, titin, zic4, GAD65,

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Table 1. The Results of the Nerve Conduction Study before and after Treatment.

Nerve	Site		Limit of normal values	On admission		Two months after admission, before Ivg, and post operation	Six months after admission	One year after admission
				Left	Right	Right	Right	Right
Median N.	wrist-elbow	MCV	> 48m/s	47.7	48.7	59.1	49.2	53.4
		Amp	> 5mV	11.5	10.26	6.49	7.37	9.13
		DL	< 4.5ms	9.39	8.73	10.62	8.58	8.04
		FWL	< 31.4ms	35.6	35.55	40.8	30.95	33.6
Ulnar N.	wrist-below groove	MCV	> 46 m/s	48.8	47.9	55.2	48.8	61.3
		Amp	> 4.7mV	6.28	9.53	6.99	6.7	5.97
		DL	< 3.6ms	7.65	8.67	9.06	8.37	7.38
		FWL	< 31.7ms	38.6	38.75	43.05	37.15	32.65
Tibial N.	ankle-knee	MCV	> 36m/s	32.8	34	38	35.9	43
		Amp	> 5.6mV	6.7	3.19	0.98	0.84	1.15
		DL	< 5.9ms	17.35	17.45	19.5	17.85	14.7
		FWL	< 56.8ms	64.4	67.9	81.6	70.7	67.7
Peroneal N.	ankle-head of fibula	MCV	> 37.1m/s	35.7	39.8	32.5	33.9	39.9
		Amp	> 0.7mV	3.39	0.76	0.63	0.22	0.57
		DL	< 6.2ms	16.6	15.55	16.75	16.6	13.55
		FWL	< 55.3ms	74.65	66.2	NA	NA	68.1

MCV: motor conduction velocity, Amp: amplitude of the muscle action potential on wrist or ankle stimulation, DL: distal latency, FWL: F wave minimum latency on wrist or ankle stimulation, R: right, L: left, NA: not assessed

and Tr related to paraneoplastic syndrome. All of the levels were normal.

A nerve conduction study fulfilled the criteria for CIDP (Table 1) (2). The patient displayed a prolonged motor distal latency of ≥50% above the upper limit of the normal values in four nerves. Conduction blocks were seen in three nerves on the right and left sides of the ulnar nerve and at the right side of the peroneal nerve. These were defined as >50% reduction in the amplitude of the proximal negative peak compound muscle action potential relative to the distal side (2). Lumbar MRI showed high intensity in the area of the medullary cone to the cauda equina with gadolinium enhancement and the increased thickness of the spinal nerve roots from T8 to the lower lumbar levels (Figure a, b and c). Abdominal CT scans revealed RCC in the right kidney (63 mm) without direct invasion to the spinal cord (Figure d). Twenty-two days after admission, the patient underwent laparoscopic surgery to resect the tumor in the right kidney. The pathological diagnosis was clear cell carcinoma (Figure e). We initiated additional therapy with intravenous immunoglobulin (IVIg) due to the mild weakness of the patient's lower limbs. One month after the administration of IVIg, the patient was able to move his limbs with full power, squat, and walk for long distances. His MMT fully recovered. After one year of follow-up, he was healthy with no recurrence of the tumor or polyneuropathy. The patient's nerve conduction study (NCS) results indicated a partial improvement (Table 1).

Discussion

Our patient had a favorable outcome after tumor resection and single round of IVIg therapy over the course of one year. Although our case did not have any specific antibodies related to RCC, he was diagnosed with paraneoplastic neurological syndrome because of the clear improvement after tumor resection. We summarized the findings from five previous reports that mentioned the association between RCC and polyneuropathy in Table 2 (3-7). The cases shared common clinical features: (i) symptoms of the lower limbs involving sensory or motor neuropathy, (ii) an NCS result revealing demyelinating polyneuropathy, and (iii) the pathological appearance of clear cell carcinoma. Half of the patients showed good responses to immunomodulation therapy and tumor resection. Interestingly, the neurological symptoms preceded the detection of cancer in the majority of patients (5/6) with paraneoplastic neurological disorders due to RCC. Neurological symptoms may imply the existence of malignancies among patients with paraneoplastic syndrome.

The marked delay of minimal F wave latencies in multiple nerves also supported diffuse dysfunction in the root nerves and the cauda equina. Lumbar MRI revealed gadolinium enhancement of the cauda equina and the dorsal roots in the lower spine. These findings are characteristic of CIDP

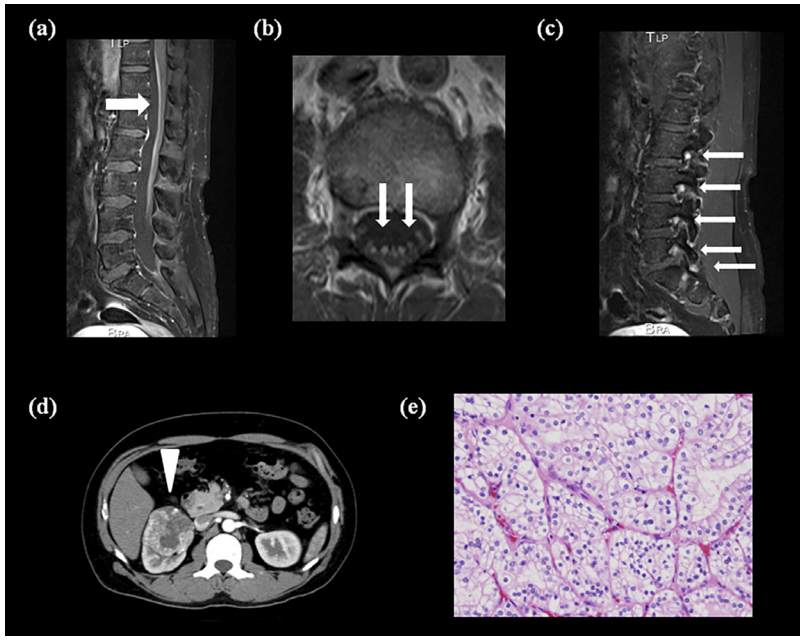

Figure. **(a) and (b) The sagittal and axial views, respectively, of lumbar T1-weighted MRI with gadolinium enhancement demonstrate longitudinal high intensity on the cauda equina (white arrows). The axial view indicates prominent enhancement on the anterior side of the cauda equine at L2. (c) The dorsal roots (white arrows) show high intensity in the sagittal view. (d) Abdominal CT scans with ioversol enhancement reveal an RCC on the right kidney (white triangle). (e) The pathological findings were consistent with clear cell carcinoma (Hematoxylin and Eosin staining).**

Table 2. **A Summary of the Previous Studies Describing Peripheral Neuropathy Due to Renal Cell Cancer.**

Gender / age	Initial symptom	Precedence of neurological symptoms	Deep tendon reflex	Nerve conduction study	Clinical diagnosis of neurological symptom	Pathology	Treatments	Prognosis	Reference
Male / 48	pain and paresthesia in the legs	yes	absent	NA	Polyneuropathy, motor and sensory neuropathy	Clear cell	resection of tumor	improved	[4]
Male / 57	progressive wakeness and dysesthesia in upper and lower limbs	yes	absent	NA	Peripheral neuropathy, motor and sensory neuropathy	Clear cell	resection of tumor	complete recovery	[5]
Female / 71	Prgressive weakness of the lower limbs	yes	absent	Demyelinating peripheral neuropathy	Sensory and motor neuropathy	Clear cell	resection of tumor, IVIg, high doses of prednisone	worsened, finally died	[6]
Male / 63	progressive weakness in righ upper and lower limbs	No	hyporeflexia in ankle jerks	Demyelinating and axonal neuropathy	Peripheral neuropathy, motor and sensory neuropathy	Clear cell	resection of tumor	worsened, finally died	[7]
Male / 65	Progressive weakness in bilateral lower limbs, dysesthesia in lower limbs	yes	absent	Demyelinating polyradiculo neuropathy	Peripheral neuropathy, motor and sensory neuropathy	NA	IVIg	improved	[3]
Male / 50	Progressive weakness in bilateral lower limbs, dysesthesia in lower limbs	yes	absent	Demyelinating polyradiculo -neuropathy	Peripheral neuropathy, motor neuropathy	Clear cell	IVIg	improved	

or Guillain-Barré syndrome (8). This phenomenon occurred due to the non-specific disturbance of the blood-nerve barrier by a T-cell-mediated process. Paraneoplastic motor neuropathy and Hodgkin's lymphoma have been reported to cause gadolinium enhancement of the lumbar spine (9). Gadolinium enhancement of the lumbar spine has not previously been reported among patients with RCC and polyneuropathy (3-7). Although the type of malignancy in this previous case was different from the findings in our case, lumbosacral gadolinium enhancement may be a common characteristic of paraneoplastic neuropathy.

One of the limitations of the present study is that we could not strictly exclude the possible co-incidence of RCC and demyelinating peripheral neuropathy, as we could not detect any specific antibodies related to RCC. Although the efficacy of our treatments was good, it remains unclear which of the treatments, IVIg or tumor resection, was effective. However, we emphasize that RCC is rarely complicated by demyelinating peripheral neuropathy, which shows the favorable efficacy of the treatments. Furthermore, previous reports and our own patient showed the same symptoms and clinical course.

In conclusion, malignancies may be complicated with paraneoplastic neurological disorders. The proper diagnosis and initiation of suitable treatments can yield a favorable outcome.

The authors state that they have no Conflict of Interest (COI).

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