Cauda Equina Involvement in Post-Radiation Lower Motor Neuron Syndrome

Nozomu Matsuda¹, Shunsuke Kobayashi¹, Hideyuki Matsumoto², Masayo Machii¹, Tomoko Soeda¹ and Yoshikazu Ugawa¹

Abstract

Post-radiation lower motor neuron syndrome (PRLMNS) is a rare neurological complication of radiation therapy and its pathogenesis is unclear. We herein report a patient with PRLMNS who developed leg weakness 17 years after craniospinal radiation as a treatment for suprasellar germinoma. The electrophysiological evaluation, via a novel magnetic stimulation method, indicated a prolonged cauda equina conduction time, suggesting focal demyelination of the nerve roots in the cauda equina. The distribution of the denervated muscles detected by magnetic resonance imaging was consistent with patchy motor nerve root lesions. These results support the hypothesis that PRLMNS originates from ischemic radiculopathy in the cauda equina.

Key words: post-radiation lower motor neuron syndrome, magnetic stimulation, cauda equina, skeletal muscle MRI, suprasellar germinoma

We recently developed a new magnetic stimulation technique for measuring the cauda equina conduction time (CECT) based on a specially devised powerful coil called a magnetic augmented translumbosacral stimulation (MATS) coil (9, 10). This technique is clinically useful for detecting abnormalities of the nerve roots at the level of the cauda equina.

We herein report a patient who developed PRLMNS 17 years after receiving craniospinal radiation as a treatment for suprasellar germinoma. We conducted a magnetic stimulation study with the aim of identifying the lesion site. We also performed skeletal muscle magnetic resonance imaging (MRI) of the lower extremities to map the distribution of the denervated muscles.

Case Report

A 20-year-old man developed polyuria in 1979 and was admitted to a hospital in Tokyo. The endocrinological testing revealed diabetes insipidus and hypopituitarism. Cranial computed tomography detected a suprasellar mass with a contrast enhancement effect. He was diagnosed with suprasellar germinoma and was treated with vincristine and...
subsequent high-dose radiation therapy to the suprasellar region (15 Gy), whole brain (84.9 Gy), and spinal cord (upper part, 63.4 Gy; middle part, 63.8 Gy; lower part, 27 Gy) during 1983 and 1984 (Fig. 1). Complete remission was achieved and the patient continued receiving nasal desmopressin and oral levothyroxine. In 2000, he noticed intermittent claudication and had difficulty walking up stairs. The patient’s leg weakness progressed gradually. On his first visit to our department in 2009, he was 50 years of age, and a physical examination revealed alopecia of the head and radiation dermatitis along the spine (Fig. 2). A neurological examination revealed that higher cognitive function was intact and the visual field was full. The cranial nerves were intact, including the bulbar function. The patient had leg weakness predominantly on the right side, but he had no weakness in the upper limbs and trunk. His muscle strength was diminished, and bilateral plantar responses were in mal and fasciculation was not detected. Only the right ankle in the right quadriceps femoris. The muscle tones were nor-
rior, and (3, 4) in the gastrocnemius, respectively. The mus-
femoris, (3, 4) in the hamstrings, (5, 5) in the tibialis ante-
proximal and distal sites by placing the edge of the coil over the spinous process of the L1 and S1 vertebrae, respec-
tively (9, 10). We stimulated the cauda equina at both the proximal and distal sites by placing the edge of the coil over the spinous process of the L1 and S1 vertebrae, respectively (Fig. 4). CMAPs were recorded from the right abduc-
torun communis. The lumbar MRI detected no structural abnormalities in the spinal cord or cauda equina. Contrast enhanced MRI was not performed.

We measured the CECT using a method previously de-
scribed (9, 10). We stimulated the cauda equina at both the proximal and distal sites by placing the edge of the coil over the spinous process of the L1 and S1 vertebrae, respectively (Fig. 4). CMAPs were recorded from the right abductor hallucis. The CMAP amplitude evoked by S1 stimulation was reduced. The CECT of control populations examined in previous studies was 3.7±0.7 ms (mean ± SD), with an upper limit (mean+2.5 SDs) of 5.5 ms (9, 10). The CECT of our patient was significantly prolonged to 6.4 ms. MRI of the lower extremities disclosed abnormal signals in the skeletal muscles of the buttock, thigh, and calf predominantly on the right side (Fig. 5). A conspicuous finding was that muscles even within the same myotome were often unevenly involved; for example, despite the marked T2 elongation in the right vastus lateralis and vastus intermedius, the rectus femoris and vastus medialis were mostly spared.
Figure 3. Myokymic EMG discharges. Myokymic discharges detected in the right tibialis anterior muscle on the needle EMG examination.

Figure 4. The electrophysiological study. The results of the motor nerve conduction studies by electrical stimulation of the tibial nerve at the ankle and knee were normal (top two traces). By contrast, magnetic stimulation at the S1 and L1 levels revealed a CECT of 6.4ms (bottom two traces), which significantly exceeded the normal range (3.7±0.7ms). The latencies of the compound muscle action potentials were 4.6ms (ankle), 14.6ms (knee), 24.7ms (S1), and 31.1ms (L1).

Furthermore, the long head of the right biceps femoris and semitendinosus showed T2 elongation, whereas the semimembranosus muscle appeared normal, even though all of these muscles belong to myotomes of L5, S1, and S2 and are all innervated by the sciatic nerve. The involved muscles exhibited high-intensity signals on both T1- and T2-weighted images, but they exhibited isointense signals on short tau inversion recovery (STIR) images.

The patient’s leg weakness progressed slowly, and he was required to use a walking stick in 2013. During the follow-up, serum CK was constantly elevated within the range of 300 to 900 IU/L.
The case of PRLMNS reported herein developed 17 years after radiation therapy. Recurrence of germinoma and neoplastic infiltration at the nerve root or plexus were excluded based on the clinical course, neuroimaging, and cerebrospinal fluid findings (11). Multifocal motor neuropathy, which predominantly affects the distal upper limb, was excluded, because: (i) his symptoms were limited to the lower limbs for 13 years after the onset, (ii) there was no evidence of conduction block, and (iii) serum anti-ganglioside antibodies were absent, including anti-GM1 IgM antibody. The diagnosis of PRLMNS was supported by the typical clinical manifestation of delayed and progressive motor symptoms. Our patient received radiation greater than 65 Gy at the middle segment of the spinal cord, which exceeds the cutoff dose of 40 Gy suggested to cause PRLMNS (2). The observed needle EMG findings, in particular the myokymic discharges, are characteristic of PRLMNS (11, 12). The mild elevation of serum CK was interpreted to be secondary to denervation rather than a primary myopathic process. Mild hyperCKemia was also reported in a previous study of PRLMNS (7). Additionally, we found reduced SNAP amplitude of the sural nerve and intrinsic sensory SEP, suggesting delayed and progressive loss of sensory axons distal to the dorsal root ganglion. This may have been due to subclinical toxic axonal neuropathy related to previous treatment with vincristine.

Even though PRLMNS was first reported in 1948 by Greenfield and Stark (3), the literature on PRLMNS remains...
very limited. Bowen et al. examined an autopsy case of PRLMNS and concluded that ischemic injury of the cauda equina nerve roots is caused by radiation-induced small vessel vasculopathy (2). However, the cauda equina pathology is often difficult to identify in vivo. In the present case, the conduction study of the tibial nerve showed mild delay of minimum F-wave latency and normal conduction velocity of the distal motor nerve. These results suggest focal proximal demyelination. However, by using the conventional methods, it is hard to further localize the lesion site. High-voltage electric stimulation at different vertebral levels can be used to detect proximal conduction delay at the cauda equina, but this procedure induces some degree of pain (13). The MATS coil is much better tolerated and it has been successfully applied to measure the CECT in chronic inflammatory demyelinating polyradiculoneuropathy and polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes (POEMS) syndrome (10, 14). In the present study, primary damage in the cauda equina was suggested by a markedly prolonged CECT. In addition, it is likely that the cauda equina damage caused secondary axonal degeneration and remyelination of the motor nerves, because the CMAPs induced by proximal stimulation showed temporal dispersion and reduced amplitude (bottom 2 traces, Fig. 4) and active denervation potentials were revealed on needle EMG.

It is unknown why motor disturbances are predominant and sensory symptoms are often mild in PRLMNS. It may be explained by the differences in sensitivity and vulnerability between the sensory and motor nerves, presumably associated with factors such as ischemic tolerance and vascularization level. However, it should be noted that sensory involvement was previously suggested in PRLMNS (2). In addition, in the present case, delayed SSEP and normal peripheral conduction time suggested damages in the sensory system proximal to the dorsal root ganglion.

Skeletal muscle MRI was also found to be useful for the assessment of PRLMNS in the present case. The pattern of abnormal MRI signals (high intensity on T1- and T2-weighted images and isointensity on STIR images) indicates chronic neurogenic changes with fat replacement in the lower extremity muscles (15, 16). Denervated muscles were characterized by a patchy distribution that deviated from the myotomal innervation patterns (17). The distribution was not compatible with combined peripheral nerve lesions but suggestive of patchy nerve root injuries within the cauda equina as reported previously (2, 7, 8).

The present and previous results together indicate that PRLMNS is characterized by motor impairment and mild (or no) sensory symptoms. This clinical presentation differs from that of cauda equina syndrome with other causes, such as compression, trauma, and inflammation, which commonly manifest sensory and autonomic symptoms, including saddle anesthesia and bladder dysfunction. The CECT measure and skeletal muscle MRI may be useful for the early detection of the latent syndrome and is suitable for application in prospective longitudinal cohort studies.

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

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**References**