CASE REPORT

Post-irradiation Skin Changes Associated with Lumbosacral Radiculopathy

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Abstract

We herein describe the cases of two patients with post-irradiation lumbosacral radiculopathy. The patients underwent postoperative radiation therapy to the abdomen due to testicular neoplasms 20 and 25 years prior to the onset of weakness, respectively. On physical examinations, asymmetric lower limb weakness and areflexia without apparent sensory loss were observed in both patients. Interestingly, artificial and squared atrophy of the skin and subcutaneous tissue, thought to correspond to the radiation fields, were observed in the lower back, and electromyography revealed selective motor axon loss localized to the lower extremities. The detection of skin changes in the area being irradiated is a valuable clue for diagnosing post-irradiation lumbosacral radiculopathy.

Key words: post-irradiation lumbosacral radiculopathy, post-irradiation lower motor neuron syndrome, post-irradiation skin atrophy, radiation dermatitis, lower motor neuron syndrome

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Introduction

Post-irradiation lumbosacral radiculopathy (also known as post-irradiation lower motor neuron syndrome) is a rare complication of radiation therapy to the abdomen for urological neoplasms or malignant lymphoma. Asymmetric lower motor neuron syndrome localized to the lower limbs, absent or minimal sensory impairment and rarely bladder and/or rectal disturbance, is included in the common clinical presentation (1-5), and gadolinium enhancement of the anterior portion of the cauda equina on MRI is a supportive feature for diagnosis. Due to the non-specific symptoms and varied incubation period, which ranges from three months to 27 years after the completion of radiation therapy (6), making an accurate diagnosis is often difficult. Post-irradiation skin atrophy associated with post-irradiation lumbosacral radiculopathy has not been reported previously. We herein describe two patients with post-irradiation lumbosacral radiculopathy and atrophy of the lumbar skin and subcutaneous tissues that corresponded to the radiation field.

Case Reports

Patient 1

A 44-year-old man developed lower limb weakness on his right side. He had a history of testicular neoplasm and had undergone left orchiectomy followed by radiation therapy at 24 years of age. Details regarding the level of radiation or the radiation field were not available. The patient’s symptoms slowly progressed, and he experienced difficulty in climbing stairs at 48 of age. On a physical examination conducted at 49 years of age, the patient presented with lumbago and leg weakness on the right side. His muscle strength was scored as grade 4 in the iliopsoas, gluteus maximum, tibialis anterior and hamstring muscles on the manual muscle testing (MMT) grading scale. Muscle atrophy was also observed in the weakened muscles and the quadriceps muscle on the right side. Tendon reflexes were normal in the upper limbs and diminished in the lower limbs bilaterally. The patient’s sensory function was intact, and no vesicorectal impairment was observed. The serum creatinine kinase (CK) level was 740 IU/L.
(normal <244 IU/L), and a cerebrospinal fluid examination revealed an increased protein level of 48 mg/dL (normal <45) with normal cellularity. A nerve conduction study demonstrated low-amplitude compound muscle action potentials (CMAPs) in the bilateral peroneal nerves. However, the sensory nerve action potentials exhibited normal amplitudes in the superficial peroneal, saphenous and sural nerves. No motor conduction block was observed in any of the tested nerves. The F-waves in the tibial nerves demonstrated 100% persistence with a normal latency (44.6 ms on the right and 45.4 ms on the left). A-waves with a latency of 40.0 ms were recorded on the left side. On needle electromyography, fibrillation potentials and positive sharp waves were detected in the peroneus longus and gluteus maximum muscles. High-amplitude motor unit potentials were observed in the paraspinals at the L5 level, iliopsoas, quadriceps femoris, tibialis anterior, peroneus longus and gluteus maximum muscles on the right side. In contrast, the upper limb muscles and paraspinals at the T10 level were intact. No fasciculation potentials were found in any of the muscles tested, and short latency somatosensory evoked potentials of the tibial nerves were completely normal bilaterally. The electrodiagnosis at that time was lower motor neuron syndrome. The patient displayed squared skin and subcutaneous tissue atrophy with pigmentation on the lower back (Fig. 1A). Following the restriction of strenuous exercise and sports, his symptoms remained nearly unchanged over the subsequent 6-year follow-up period.

**Patient 2**

A 51-year-old man noticed leg weakness. He gradually began to walk unsteadily and experienced difficulty in climbing stairs independently at 58 years of age. He had a history of treatment with left orchectomy for testicular anaplastic seminoma followed by postoperative radiation therapy at 26 years of age. The level of radiation and radiation field were unknown. On a physical examination performed at 61 years of age, squared atrophy of the subcutaneous tissue was observed on the lower back, mostly ranging from the first to fourth lumbar spine approximately 8 cm in width (Fig. 1B). The cranial nerve function was intact, although the muscle strength in the lower limbs was asymmetrically weak: grade 4/4 (right/left) in the iliopsoas and gluteus maximus, 3/4 in the gluteus medius, 4/4 in the hamstrings, 3/1 in the tibialis anterior, 2/1 in the soleus and 1/1 in the extensor hallucis longus muscles on the MMT grading scale. Tendon reflexes were normal, except for diminished bilateral Achilles tendon reflexes; pathological reflexes were absent. The patient was able to walk with a foot drop, although he required support. Sensory impairment was absent, and he did not complain of any difficulties with urination.

The laboratory findings revealed an elevated CK level of 301 U/L. The cerebrospinal fluid protein level was also increased at 113 mg/dL, with normal cellularity. A nerve conduction study showed normal results for the upper limbs. Reduced-amplitude CMAPs were observed in the left peroneal nerve (0.2 mV; normal, >3 mV), whereas the right peroneal nerve and tibial nerve remained normal. F-waves in the right tibial nerve demonstrated 100% persistence with normal latency (46.4 ms). The left tibial nerve was not tested.

The sensory nerve action potentials in the superficial peroneal and sural nerves were within the normal ranges bilaterally. Needle electromyography revealed no abnormalities in the upper limb or paraspinals muscles at the T10 level. Meanwhile, fibrillation potentials and positive sharp waves were detected in the paraspinals at the L4 level and in the tibialis anterior muscles, and high-amplitude motor unit potentials with the reduced recruitment of motor unit potentials.
was observed in the paraspinalis at the L4 level as well as in the iliopsoas and tibialis anterior muscles. No fasciculation potentials were found in the tested muscles, and somatosensory evoked potentials of the tibial nerves were within normal ranges bilaterally. Uroflowmetry disclosed mild detrusor overactivity. Gadolinium-enhanced MRI demonstrated enhancement of the anterior portion of the cauda equina in addition to L3/4 disk herniation (Fig. 2). The patient’s symptoms remained unchanged during the 6-month follow-up period, without any medical treatment.

Discussion

Our patients each had a history of hemi-orchiectomy for testicular neoplasms and postoperative radiation therapy to the abdomen administered at different hospitals. In addition, both patients showed asymmetric lower limb weakness without sensory impairment 20 and 25 years after receiving radiation therapy, respectively. One patient presented with mild detrusor overactivity on a urology study, without any subjective symptoms. Furthermore, neurophysiological studies revealed chronic motor neuron loss, without fasciculation potentials, localized to the lower extremities asymmetrically in both patients, while MRI disclosed enhancement of the cauda equina in one patient. Based on these clinical features, a diagnosis of post-irradiation lumbosacral radiculopathy was made in each case. The prolonged progression and preservation of the upper limbs, in addition to the spontaneous discontinuation of symptom progression in Patient 1, distinguish these presentations from those of other motor neuron syndromes. Interestingly, both patients exhibited similar patterns of artificial squared skin and subcutaneous tissue atrophy on the lower back (Fig. 1). The use of abdominal para-aortic lymph node radiation subsequent to orchiectomy for stage I seminoma is a well-accepted therapy (7). The radiation field is usually set from the upper edge of the 11th or 12th thoracic spine to the lower edge of the fifth lumbar spine along the vertical axis and both edges of the transverse processes along the horizontal axis (7), consistent with the fields of skin atrophy observed in our patients. We therefore concluded that their skin changes were caused by irradiation.

Since Greenfield and Stark first reported the condition in 1947 (1), more than 75 patients developing lower motor neuron syndrome after radiation therapy have been reported (2-4). As sensory impairment is minimal or absent, post-irradiation lower motor neuron syndrome is the most commonly used name. However, a pathological study of an autopsied case reported prominent hyalinization with a loss of smooth muscle cells in the arterioles within the cauda equina, whereas spinal anterior horn cells were preserved (3, 5). Therefore, the proximal nerve roots were considered to be the site of the main pathological lesion, and the term post-irradiation lumbosacral radiculopathy was suggested (3). Microvascular damage in the cauda equina and the breakdown of the blood-nerve barrier, followed by the activation of cytokines, is considered to be a possible mechanism of motor axon damage (8-10). Because the symptoms associated with this condition are non-specific and affected patients occasionally experience long periods of
incubation, making an appropriate diagnosis is often difficult.

Post-irradiation lumbosacral radiculopathy produces severe motor axon loss with minimal or absent sensory impairment. The cause of this phenomenon is uncertain. However, motor selectivity is a key clinical characteristic of this condition. Neurophysiological examinations play an important role in confirming the diagnosis of post-irradiation lumbosacral radiculopathy. Abraham and Drory described finding low-amplitude CMAPs in the lower limbs in most patients, while only two of 45 (4%) patients assessed in their study presented with abnormal sensory nerve conduction (6). Because Bowen et al. did not differentiate between anterior and posterior roots in their autopsy study (3), the pathological selectivity of motor axons was not revealed. One explanation for this condition is possible differences in vulnerability to radiation between motor and sensory nerves. However, patients with post-irradiation brachial plexopathy commonly exhibit sensory deficits (11), and there is no evidence indicating a difference in radiation tolerance among nerve cells. Another explanation is the location of neuron cell bodies. Motor neuron cell bodies are located in the spinal anterior horn, which is positioned at the center of the radiation field. In contrast, sensory neuron cell bodies are located in the dorsal root ganglion, which exists at the edge of the radiation field. Therefore, motor neurons are more heavily affected by radiation, whereas sensory neuron cell bodies and post-ganglionic sensory nerve fibers are not exposed to as much radiation and therefore tend to survive. In the systematic review conducted by Abraham and Drory, 12 of 45 (27%) patients presented with sensory symptoms. However, seven of these 12 subjects demonstrated normal sensory nerve action potentials (two exhibited abnormal potentials and the details were not reported in the other patients) (6), suggesting that several sensory cell bodies in the dorsal root ganglia survived, whereas the proximal sensory tract was affected. In order to clarify this observation, further studies are required to evaluate the proximal portion of the sensory nerves during the acute stage of the disease using assessments of somatosensory evoked potentials or other examinations.

Post-irradiation lumbosacral radiculopathy often presents with asymmetric weakness. Both of the current patients also showed asymmetry. Although the radiation fields were not identified in our patients, the side of seminoma did not match the dominated side of weakness in Patient 1. In the systematic review performed by Abraham and Drory, 15 of 50 (30%) patients showed apparent asymmetry (6). Moreover, post-irradiation lumbosacral radiculopathy possibly causes monomelic amyotrophy (12). The radiation fields in these patients were not available, and the reason for asymmetry is uncertain. We consider that the presence of such asymmetry supports the credibility of the microvascular theory.

The possibility arises that our patients received excessive doses of radiation. The epidermal tissue is continually renewed, although neurons are not regenerated. Therefore, according to the Bergonie-Tribondeau law, the radiation sensitivity of the skin tissue is higher than that of differentiated neurons or vascular tissue (13). Previous reports have shown that post-irradiation lumbosacral radiculopathy occurs following treatment with a standard dose of radiation (6). Moreover, post-irradiation skin changes may develop at radiation doses of 20 to 25 Gy, which are below the generally accepted doses of radiation therapy (6, 14). In fact, the development of varying degrees of skin changes is an unavoidable complication of radiation therapy. Although the doses of radiation applied in our patients were not identified, it is unlikely that both patients were subjected to excessive doses of radiation at two separate hospitals. Due to the absence of reports on these skin changes, we believe that characteristic skin changes may be underestimated.

Because our patients demonstrated long-term steady courses, we deferred the administration of any specific treatments. Indeed, the symptoms in Patient 1 remained unchanged, except for the need for restriction of strenuous exercise and sports during the 6-year follow-up period. Based on the hypothesis that microvascular damage and the activation of cytokines are possible mechanisms underlying this condition, the use of anticoagulation therapy with warfarin or heparin, glucocorticoid therapy and/or combination therapy is recommended (15, 16). However, the effectiveness of each of these treatments remains inconclusive. Nevertheless, when patients present with an unsteady clinical course, these treatments should be considered.

The detection of the characteristic pattern of skin atrophy on the back is a valuable clue for making a diagnosis of post-irradiation lumbosacral radiculopathy in the differential diagnosis of lower motor neuron syndrome.

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

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