MR Imaging of Radiation-Induced Lumbosacral Plexopathy, as a Rare Complication of Concomitant Chemo-Radiation for Cervical Cancer

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INTRODUCTION

Radiation-induced lumbosacral plexopathy (RILSP) is an uncommon but serious complication of radiation therapy that can result in different degrees of sensory and motor deficits. An age 59 female with cervical cancer, who had received combined chemotherapy and radiation therapy two years before, presented with bilaterally symmetric lower-extremity weakness and tingling sensation. The magnetic resonance imaging showed diffuse T2 bright signal intensity and mild enhancement along the bilateral lumbosacral plexus with no space-occupying masses. RILSP was diagnosed after the exclusion of malignant and inflammatory plexopathies.

Keywords: Radiation plexopathy; Lumbosacral plexus; Radiotherapy; Magnetic resonance imaging; Cervical carcinoma

CASE REPORT

An age 59 female was admitted to our hospital because of a history of vaginal bleeding and cervical cancer, which had been diagnosed using punch biopsy.
Fig. 1. Contrast-enhanced hip MRI two years after the completion of CCRT. Coronal MRI at the first sacral foramen level reveals bilateral, symmetric, and diffuse T2 hyperintensity of LSP on coronal FS T2WI (a, arrows). The consecutive coronal FS T2WIs in the posterior direction demonstrated extensive involvement of LSP (b, c, arrows). Also, diffuse mild enhancement of the impacted LSP at the first sacral foramen level is depicted on T1WI (d, arrows) and contrast-enhanced T1WI (e, arrows). Note the asymmetric T2 signal change (pronounced on the right side) of the bilateral piriformis muscle (f, arrows). FS = fat suppressed; LSP = lumbosacral plexus
Histopathology revealed non-keratinized, invasive squamous cell carcinoma (SCC) with a positive polymerase chain reaction for human papillomavirus 18. The initial imaging revealed International Federation of Gynecology and Obstetrics stage Ib cervical cancer involving the uterine cervix and mid-luteal phase of the corpus luteum with a metastatic left internal iliac lymph node (T2b, N1, M0; tumor size: 52 × 49 × 40 mm). Following a multidisciplinary tumor board discussion, curative CCRT was performed with 40 mg/m²/week of cisplatin and external radiotherapy (total dose: 5400 cGy), followed by intracavitary brachytherapy with radiotherapy to the tumor mass (total dose: 3000 cGy). The treatment was well tolerated without significant adverse effects. The six-month follow-up pelvic CT revealed complete resolution of the cervical cancer.

Two years after the completion of the CCRT, the patient was admitted because of progressive, bilaterally symmetric lower-extremity weakness and tingling sensation, requiring a walker for ambulation. Neurologic examination revealed decreased motor function in the bilateral hip flexion and knee extension (IV/IV) and in the ankle dorsiflexion and plantar flexion (III/III). Additionally, diminished senses of pain, touch, and temperature and no sense of vibration below the bilateral L2 dermatomes were noted. The pelvic CT revealed complete resolution of the primary tumor without evidence of recurrence. Cervical cytology was negative, and the level of serum SCC antigen was within the normal range (0.47 ng/mL). Routine blood and urine laboratory examinations were unremarkable, other than an elevation in the erythrocyte sedimentation rate (ESR) (73 mm/h). However, the elevated ESR with normal C-reactive protein and fibrinogen levels was a non-specific inflammatory marker and insufficient for a conclusive medical decision. Also, the ESR decreased continuously in the follow-up without treatment. The cerebrospinal fluid (CSF) analyses were unavailable because of poor cooperation from the patient. On admission day three, contrast-enhanced hip MRI was performed with a 3.0-T MRI scanner (MAGNETOM Vida 3T®, Siemens, Erlangen, Germany) with a flexible 18-channel body coil, including turbo spin echo T1-weighted image (T1WI) and T2-weighted image (T2WI), DIXON-based fat suppression T2WI, and contrast-enhanced T1WI. MRI demonstrated diffuse T2 bright signal intensity and mild enhancement along the bilateral lumbosacral plexus (LSP) with no space-occupying masses. Additionally, patchy T2 bright infiltrations were detected in the bilateral piriformis and iliacus muscle without definite atrophic changes (Fig. 1). These findings were newly defined compared to the pre-CCRT baseline pelvic protocol MRI two years before (Fig. 2). Treatment-related (specifically, radiation) lumbosacral plexopathy was suggested first, and electrophysiologic findings from an additional electromyogram (EMG) test and a nerve conduction study were also compatible with the bilateral lumbosacral plexopathy. Finally, the attending physician and requested neurologist diagnosed the patient with RILSP rather than chronic inflammatory demyelinating polyneuropathy in view of muscle weakness at the disease onset, prominent pain, and disease progression to a nadir in less than four weeks. After steroid pulse therapy for five days (methylprednisolone: 1000 mg/day, I.V.), the patient

Fig. 2. The MR feature of the LSP before CCRT. The pre-CCRT pelvic protocol MRI (a, axial T2WI; b, oblique coronal T2WI perpendicular to the cervix) reveal normal bilateral LSP at both of the sciatic foramen (arrows). Newly defined diffuse thickening of the bilateral LSP after CCRT completion can be heightened by comparing the images acquired before and after the CCRT. LSP = lumbosacral plexus
was discharged with relieved pain and stabilized motor symptoms, which persisted without significant improvement or progression at the last outpatient visit two months after the discharge.

DISCUSSION

In the treatment for gynecologic cancers with radiation therapy, it is crucial to maximize the ability of locoregional tumor control and minimize the risk of treatment-related complications. For radiotherapy only, the tolerance of LSP is 47 and 60 Gy (tolerance dose is the radiation dose that has 5% probability of serious sequelae in introduced patients within five years of the treatment). RILSP may have a higher dose of 70–80 Gy in full-volume irradiation (3). However, concomitant chemotherapy is likely to increase the radiosensitivity of the peripheral nerves and RILSP at far lower doses (50–60 Gy) (4).

The main pathophysiology of RILSP is delayed damage to the mature nerve tissue in the following complex stages, starting from initial microvascular injury and inflammation to radiation-induced fibrosis (5). Delanian et al. (6) reviewed the pathophysiology of radiation-induced neuropathy. The recent concepts focus on the endothelial reaction to the radiation therapy contrary to the old vascular theory based on gradual ischemia–hypoxia due to radiation-induced capillary network destruction. Particularly, procoagulant and pro-inflammatory impact of thrombin–altered microvascularization and factors against intermittent hypoxia induce neoangiogenesis. However, the role of these vascular dysfunctions seems indirect to the fibrotic phase, and the synergistic impact of continuous attacks by free radicals generate fibrogenesis (7).

The incidence of RILSP is approximately 0.8–3.0%, and the median symptom-free interval of RILSP is five years after treatment completion, with a range of 1–31 years (8). The main clinical presentation is painless weakness in one leg or both legs. In contrast, pain is present in only 10% of the patients when the initial neurologic symptom is evaluated. Weakness is usually bilateral (ratio of bilateral to unilateral illness, 5:1) but can be asymmetric. Paresthesia occurs in 50–75% of the patients at a more severe degree in comparison with motor impairment.

Among diagnostic imaging modalities, the MRI is more sensitive than the CT in detecting tumor recurrence (2). The MRI often determines if the mass is intrinsic or extrinsic to the plexus. Imaging features of the radiation-induced plexopathy include diffuse, symmetric, uniform swelling, and T2 high signal intensity of the plexus within the irradiation field. The T2 hyperintensity of the nerves can be well-demonstrated on fluid-sensitive sequences. Radiation fibrosis generally shows low signal intensity on T1- and T2-weighted images. Soldatos et al. (9) suggested a combination of 2D and 3D high-resolution MRI based on spin-echo sequences as 3.0-T MRI neurography of the LSP. Axial fat-suppressed T1- and T2-weighted 2D images can demonstrate in detail the fascicular pattern of the LSP and peripheral branches. Also, the coronal T1-weighted, short inversion time inversion recovery and proton density-fat-suppressed images facilitate side-by-side comparison of bilateral LSP, providing delineation of the lesions at the long axis of the nerves. Additionally, the conventional T1-weighted images can depict fat planes surrounding the LSP and distal branches. Fluorodeoxyglucose positron emission tomography can facilitate confirmation of metastases and better depict metastases at other sites. Since RILSP is a diagnosis of exclusion, the full work-up should include routine laboratory tests, CSF analysis, and EMG without evidence of malignancy, infection, or other inflammatory disease.

Currently, in the clinical practice, the treatment of RILSP is symptomatic. Medications include non-opioid analgesics, tricyclic antidepressants, and anti-epileptics. Physical therapy is crucial in maintaining the function and preventing joint problems. According to the stepwise pathophysiology of various levels, the restriction of several defined aggravating factors has been suggested, including anti-inflammatory drugs, such as corticosteroids. RILSP usually results in chronic irreversible motor and sensory deficits, which may show slow improvement with time. However, reversible neurologic symptoms have been reported in only a few case series.

In conclusion, RILSP is a rare but serious complication, which can devastate the quality of life in the impacted patients. Therefore, more surveillance is essential to understand the concise pathophysiology, incidence in global population, well-established diagnostic methods, and optimal treatment. Radiologists should understand and be familiar with the MRI features of RILSP for accurate diagnosis.

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REFERENCES