Radiation-induced neuropathic pain successfully treated with systemic lidocaine administration

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Abstract: Radiation-induced neuropathic pain is a rare but devastating complication following cancer treatment. It is often progressive, refractory to conservative treatment, and sometimes irreversible. The exact mechanism of radiation-induced neuropathic pain is unknown, but it is associated with perineural fibrosis, atrophy, and ischemia. Systemic administration of local anesthetics is known to be effective for various acute and chronic painful diseases, such as neuropathic pain, as well as inflammatory and nociceptive pains. We report a patient with generalized radiation-induced neuropathic pain successfully treated with systemic lidocaine administration.

Keywords: cancer, complication, lidocaine, pain, neuropathy

Introduction

Radiation treatment is a mainstay of cancer therapy. Although radiotherapy has improved the survival of cancer patients, it unfortunately can harm exposed areas. Ionizing radiation not only breaks down cancer cells but may also affect adjacent noncancerous cells by releasing various cytokines and inflammatory mediators from killed cancer cells. The inflammatory reaction can cause fibrosis, atrophy, and ulceration of the tissues, including vessels and nerves, and consequently nerve damage may result.1 Although radiation-induced neuropathy is known to be caused by this complex interaction, the exact mechanism of this painful disease is still unclear. Methodologically sound trials for radiation-induced neuropathy are scarce, and few case reports have been published. Radiation-induced neuropathic pain is often progressive, unresponsive to conservative treatment, and sometimes irreversible. We report on a case of intractable radiation-induced neuropathic pain successfully treated with systemic lidocaine administration.

Case report

Written Informed consent for publication was obtained from the patient. A 60-year-old male patient visited our pain clinic, referred from a tertiary hospital, with a complaint of chronic burning, itching, aching pain, and restlessness of the whole body, mainly in both arms and legs, and concomitant myalgia and chills during pain attacks (numeric rating of 9 on a scale of 10) for about 6 years. The patient had received a liver transplant because of hepatocellular carcinoma 10 years before, but just a few years later, metastatic cancers of his lung and adrenal gland were detected in turn, and right-upper-lobe wedge resection of the lung and an adrenalectomy were performed uneventfully. Then he had to get radiation treatment for metastatic cancer of the left iliac bone. Radiation treatment was performed with a total dose of 50 Gy in ten fractions using external-
A month after completing the radiation treatment, he had experienced both pelvic and perineal pain radiating to the groin and penis, with a feeling of itching and aching. The pain had progressively spread into the whole body for 2 years, and the intensity of the pain worsened continuously.

Even though he had received ganglion impar neurolysis and superior hypogastric plexus neurolysis several times and had been taking many useful medications, including high-dose opioids, his pain was refractory to the treatments. He said that neurolytic treatments had a limited effect for only a day. On the visit to our clinic, he was taking pregabalin 450 mg/day (Pfizer Inc., New York, NY, USA), milnacipran 100 mg/day (Bukwang Pharm. co., Seoul, Korea), high-dose transdermal fentanyl 350 μg/hour (LTS Lohmann Therapie-Systeme AG, Andernach, Germany), and other strong opioids, such as sublingual fentanyl (Menarini Korea Ltd., Seoul, Korea), tramadol–paracetamol (Janssen Korea Ltd., Seoul, Korea), and oxycodone (Mundipharma Korea Ltd., Seoul, Korea), for the breakthrough intractable pain. He also complained of cutaneous itching and aching. The pain had progressively spread into the whole body for 2 years, and the intensity of the pain worsened continuously.

After 14 days, the patient reported much more substantial pain relief, with a pain score of 3 and = a much smaller dose (150 μg/hour) of transdermal fentanyl, but he still complained of residual, vague, and fluctuating pain of the whole body, so a third therapy was performed. After 14 days, the patient reported that his pain had markedly decreased to a pain score of 0 and remained stable, a mild heating sensation only remained, and 87 μg/hour transdermal fentanyl was being delivered. He remained stable and was satisfied with the treatment result.

Discussion
Pain in cancer survivors is a growing concern as survival rates increase. In fact, persistent and chronic pain, even after a cancer cure, is the unsolved problem, which is a great burden to patients psychologically as well as physically, and is well known to influence quality of life negatively and increase health care costs. Harrison et al revealed that 89% of patients with persistent pain after tongue cancer treatment with radiotherapy suffered from moderate–severe distress. The causes of pain after cancer treatment are many. Pain may develop after chemotherapy (chemotherapy-induced peripheral neuropathy), radiotherapy, surgery (persistent postsurgical pain), hormone therapy, or stem-cell transplantation, with an overall prevalence of approximately 30%. Radiation treatment is one of the mainstays of cancer therapy. Mechanisms of ionizing radiation for killing cancer cells are direct and indirect DNA damage, associated with reactive oxygen species production and inhibited DNA repair. Radiation exposure can induce breakdown of cancer cells, causing the release of various cytokines and inflammatory mediators, and can also affect noncancerous cells. This inflammatory reaction causes fibrosis, atrophy, and ulceration of the related tissue, including vessels and nerves. Perineural fibrosis and ischemia, subsequently developing myelin destruction and axonal injury, are attributed to the main mechanism of radiation-induced neuropathic pain, such as radiation-induced brachial plexopathy after radiotherapy for breast carcinoma.

In addition, radiation treatment may produce various types of postradiation chronic pain syndromes, including peripheral nerve entrapment, radiculopathy, myelopathy, noncardiac chest pain, pelvic pain, osteonecrosis, and other soft-tissue damage at the sites exposed. Above all, pelvic pain after radiotherapy can arise from pelvic insufficiency fracture, enteritis, abdominal visceral pain, or neural injury. Andreyev et al defined pelvic radiation disease as a transient or long-term problem, affecting the bowels, urinary tract, sex organs, bones, or skin after radiotherapy to tumors of pelvic origin. However, in our case, there was no evidence of pelvic radia-
Lidocaine for radiation-induced neuropathic pain

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Abstract

Lidocaine can act as an analgesic by blocking peripheral sodium channels on the cell membranes of injured peripheral nerves producing ectopic discharge, dorsal root ganglia, and adjacent neurons. The fact that systemic lidocaine treatment can help to reduce opioid consumption and relieve pain in patients with intractable radiation-induced neuropathic pain is often unresponsive to conservative treatment and sometimes irreversible. We think that systemic lidocaine is worth applying in a patient with intractable radiation-induced neuropathic pain, even if it is a centrally sensitized state, as a rescue-treatment modality.

Meanwhile, it is notable that systemic lidocaine treatment can help to reduce opioid consumption. In fact, increasing dosages of opioids are routinely chosen to relieve chronic intractable pain by many physicians, because opioids reduce pain immediately and strongly for most patients without a ceiling effect. Moreover, opioids have been accepted as safe analgesic medication for cancer patients, with little possibility of aberrant drug-related behaviors, such as addiction. However, for patients with noncancer pain, including cancer survivors, long-term opioid medications may have harmful effects, such as opioid-use disorder, overdosing, and life-threatening adverse effects. Higher opioid doses may contribute to an increased risk of opioid-related death.

As our findings demonstrate, systemic lidocaine treatment can help to reduce opioid consumption and relieve pain in patients with intractable radiation-induced neuropathic pain.

Pain in cancer survivors should be evaluated precisely and treated by multimodal methods. First, an exact medical history, including prior cancer treatment and complicated problems and other physical or psychological disease, should be taken. Various imaging modalities, neurologic tests, or diagnostic block methods if possible may help diagnose the cause of pain. Additionally, other potential causes of pain should be considered, not only cancer-treatment-related pain syndromes but also other specific painful diseases, such as musculoskeletal disorders, neuropathies, or other medical diseases, whenever there are inexplicable changes in the nature, location, or intensity of pain. Multimodal approaches, including pharmacological, psychosocial, and interventional approaches, can be used for symptom improvement and functional recovery. Our experience with this patient suggests that systemic drug-infusion therapy may be a valuable part of the treatment strategy for radiation-induced neuropathic pain refractory to conventional pharmacological treatment.

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Author contributions

All authors contributed toward data analysis, drafting, and critically revising the paper, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.
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