A Case Report of Radiotherapy for Skull Lesions of Langerhans Cell Histiocytosis With Dural Invasion

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Abstract. Background: Langerhans cell histiocytosis (LCH) is a rare disease, especially in adults. It is often associated with non-fatal bone and skin lesions and has relatively good radiosensitivity. In contrast, brain and lymph node metastases from LCH lesions are considered to be less sensitive to radiotherapy. Case Report: At our institution, 30 Gy radiotherapy was used to treat bone lesions with dural invasion in a patient with adult-onset LCH. The patient was treated with chemotherapy and radiotherapy for 21 years since the initial diagnosis. After radiotherapy, the tumor shrank rapidly, and a complete response was achieved 1 year after treatment. The patient survived without local recurrence. Conclusion: Here, we report the details of this case, along with a review of the literature. We suggest that even with invasion of the tissues around the bone lesions in LCH, local recurrence can be prevented by middle radiation doses.

Langerhans cell histiocytosis (LCH), formerly known as histiocytosis X, has been classified as Hand–Schuller–Christian disease, Letterer–Siwe–Syndrome, and Langerhans cell granulomatosis. However, after the discovery that all of these diseases involve Langerhans cells, they were collectively defined as LCH. LCH is a disease characterized by the proliferation of myeloid dendritic cells, which express CD1a, the same antigen expressed in Langerhans cells in the skin. LCH is a relatively rare disease, especially in adults, with the highest incidence in infants and children (1, 2).

At our institution, we perform radiotherapy for bone lesions with suspected subdural invasion in patients with adult-onset LCH. In this report, we present the response of a patient to this treatment, along with a review of the literature.

Case Report

A 47-year-old woman was admitted to our department for radiotherapy. She had a long history of treatment for LCH. At 21 years before undergoing radiotherapy at our hospital (X-21), she noticed a swelling under her left jaw and visited her doctor. Biopsy revealed LCH at the referral hospital. As metastasis to other sites was not observed, the patient underwent mass excision and postoperative radiotherapy, followed by steroid pulse therapy. After that, no apparent recurrence had occurred until October X-5 when she experienced bilateral tonic convulsions and was examined. Positron emission (PET)–computed tomography (CT) revealed 18F-fluorodeoxyglucose accumulation in numerous bone lesions, including skull lesions and an intracranial lesion, as well as multiple lymph node swellings. In November, excision of the intracranial lesion was performed and relapse of the LCH was revealed. During the same month, postoperative radiotherapy was performed to treat the lesions in the cervical and thoracic spine. In January X-4, systemic therapy with 6-mercaptopurine combined with etoposide or vinblastine was administered until April. PET-
CT confirmed a complete response (CR) in May, after which she was followed-up regularly at the referral hospital, but in X-2, she changed her hospital visits to ours when she moved. PET-CT confirmed maintenance of the CR in October X-2 but revealed multiple bone lesions in April X-1. Systemic chemotherapy was considered for the bone lesions, but because the lesions were small, the patient was referred to our department for local treatment. All of the bone lesions showed osteolytic changes but no obvious subjective symptoms such as pain. Radiation therapy was administered to the left humeral head, left iliac and parietal bones at 20.0 Gy/10 fr, and good local control was obtained.

In August X, CT showed a punched-out lesion in the temporal bone, and magnetic resonance imaging (MRI) showed a mass with contrast enhancement in the same area. The mass was mainly subcutaneous, but some intracranial extension was observed, and a contrast effect was observed in the subdural area where subdural invasion was suspected (Figure 1).

We discussed the treatment plan with the medical oncology and neurosurgery departments. We decided to perform radiotherapy for the following reasons: the metastatic lesions were limited, the risk of incomplete surgical resection was high because of a suspicion of subdural invasion, and radiotherapy had been effective so far. The patient was scheduled to undergo radiotherapy starting in August X year and was prepared for treatment. Using a thermoplastic head shell, the patient's head was fixed to ensure reproducibility, and CT for treatment planning using 2.5 mm slices without intravenous contrast agent was performed. Treatment planning was conducted using the RayStation (RaySearch Laboratories, Stockholm, Sweden). The dose distribution is shown in Figure 2. Unlike the previous bone lesions, this lesion was treated with 30.0 Gy/10 fr because of its large size and the surrounding invasion.

During the treatment period, only radiation dermatitis of grade 1, according to CTCAE ver. 4.0, was observed (3). Hair loss at the irradiated area was observed starting 2 weeks after treatment, but the hair had almost returned at 4 months. No symptoms of increased intracranial pressure or cerebrospinal fluid leakage were observed during follow-up.

After treatment, the patient was treated with cladribine from October X until June X+2. During treatment, a recurrent mass was found in the right temporal–occipital region, which was outside of the irradiated field in January X+2, and radiotherapy was performed again with 30.0 Gy/10 fr. The patient was followed up over 3 years after last treatment, and no obvious recurrent lesion was observed during follow-up.
MRI was performed at 1 and 4 months and 1 year after completion of treatment (Figure 3). The CR of the lesion was maintained, with no evidence of local recurrence.

**Discussion**

LCH is a rare disease that often manifests as single or multiple bone or skin lesions; bone and skin lesions occur in approximately 80% and 40% of patients, respectively (4). However, the lesions often involve soft tissue and the central nervous system, with mortality rates reaching 10–20% in some populations (5). In particular, pediatric cases of LCH with liver, spleen, and bone marrow involvement are classified as high risk because children have the highest risk of death from LCH (6).

LCH is classified into single-system and multi-system types according to the extent of the lesion. In general, good
results are obtained in elderly patients and patients with single-system LCH, whereas poor results tend to be obtained in younger patients and patients with multi-system LCH, organ dysfunction, or lung involvement (2).

Several randomized clinical trials of systemic chemotherapy for pediatric patients with multi-system LCH have been conducted and resulted in favorable outcomes (7, 8). However, for adult patients, in whom the estimated incidence of LCH is 1-2 cases per million people per year, treatment information for optimal care is limited to retrospective reports (2). Among the various treatment modalities, radiotherapy may be useful for patients at risk of pain and pathological fractures associated with tumor growth. The local control rate of bone lesions by radiotherapy is reported to be >90%, and radiotherapy is considered an effective treatment (9). However, in recent years, the use of radiotherapy in children with LCH has been gradually decreasing considering the long-term adverse effects such as bone growth inhibition due to radiation-induced cartilage damage and secondary cancers (10). On the other hand, in adult patients, such effects are less prevalent than in pediatric patients, and radiotherapy may still be an effective treatment if local pain and other symptoms are severe.

Laird et al. retrospectively analyzed the efficacy and toxicity of radiotherapy in 39 patients with LCH and found that bone lesions showed good local control and symptom relief even at low radiation doses such as 10.8 Gy, whereas extra-skeletal lesions showed high local recurrence rates and less symptom relief even at high doses (10). They also reported poor control of brain metastases at the same dose as that used effectively for bone metastases. In this case report, because the tumor was large with probable invasion of the surrounding area, it was irradiated with 30 Gy, resulting in good local control. The optimal dose for bone lesions, even those invading the brain, as in this case, is different from that for brain metastases, and the dose that we used for the bone lesions may have been sufficient.

In this case, there were no significant adverse events other than hair loss during the treatment course and we were able to do cladribine safely and obtain a long progression-free relapse period. In the past, however, adverse events associated with radiotherapy have been shown to be highly prevalent especially in children (11). Currently, CT-based treatment planning is the standard for radiotherapy, and the accuracy of radiotherapy has been improved by the combination of technological advances such as image-guided radiotherapy and particle therapy, and reduced adverse events (12, 13). In the future, more reports with high-precision radiotherapy will help confirm any reductions in adverse event rates even at increased dose. Consequently, radiotherapy will likely become established as an effective and safe treatment for LCH.

Conclusion

Medium-dose radiotherapy was performed on a patient with adult-onset LCH of the skull with invasion to surrounding soft tissue and dura. As treatment effect was satisfactory without severe adverse events, it is suggested that medium-dose radiotherapy may be effective as a local treatment for symptomatic LCH.

Conflicts of Interest

The Authors declare no conflicts of interest in relation to this report.

Authors’ Contributions

Conceptualization, Y.H. and Y.T.; methodology, Y.H.; formal analysis, T.S.; investigation, Y.H. and T.I.; resources, T.S.; data curation, M.M.; writing – original draft preparation, Y.H.; writing – review and editing, T.S. and H.K.; visualization, Y.H.; supervision, T.O. and H.S.; project administration, Y.T. All Authors have read and agreed to the published version of the manuscript.

Acknowledgements

This work was supported in part by Grants-in-Aid for Scientific Research(C)(19K08219) from the Ministry of Education, Science, Sports and Culture of Japan.

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Received November 6, 2021
Revised December 26, 2021
Accepted December 27, 2021