Concomitant use of radiotherapy and two topoisomerase inhibitors to treat adult T-cell leukemia with a radiotherapy-resistant bulky disease: a case series

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Abstract: Concomitant chemoradiotherapy is established as the standard treatment to improve the prognosis of several types of solid tumor, but has not been the general practice for hematological malignancies. Here, I report two cases of adult T-cell leukemia (ATL) with a radiotherapy-resistant bulky disease treated with concomitant radiotherapy and two topoisomerase inhibitors: etoposide (VP-16) and irinotecan (CPT-11). Patient 1 was a 78-year-old man with chemotherapy-resistant inguinal bulky mass. Radiotherapy (total 40 Gy) for this inguinal lesion was started; however, the bulky disease was found to be resistant to radiotherapy and progressed. VP-16 and CPT-11 were administered in addition to radiotherapy (after a total of 20 Gy of radiotherapy). Patient 2 was a 71-year-old man with a solitary bulky mass in left cervical lesion. Various previous chemotherapy and radiotherapy approaches had not been able to control the disease. Six months after first radiotherapy, the bulky disease rapidly progressed with the occurrence of pain. Second radiotherapy (30 Gy) was started with simultaneous administration of CPT-11 and VP-16. In both cases, the bulky disease gradually regressed and completely disappeared by the end of radiotherapy. Thus, flexible adaptation of concomitant chemoradiotherapy including two topoisomerase inhibitors may offer a potential therapeutic option for radiotherapy-resistant bulky diseases, even in hematological malignancies.

Keywords: Adult T-cell leukemia, topoisomerase, radiotherapy

Introduction

Concomitant chemoradiotherapy is established as the standard treatment to improve the prognosis of several types of solid tumor [1, 2], but has not been generally practiced for hematological diseases because of the favorable response of hematological diseases to radiotherapy and the expectation of severe adverse effects [3]. However, we sometimes experience radiotherapy-resistant hematological bulky diseases. These synergistic effects derived from concomitant chemoradiotherapy may offer an attractive option to control some radiation-resistant hematological diseases. Adult T-cell leukemia (ATL) is one of the most aggressive hematological diseases and is frequently resistant to various treatment modalities. Here, I report two cases of lymphoma-type ATL with a radiotherapy-resistant bulky disease treated with concomitant radiotherapy and two topoisomerase inhibitors: etoposide (VP-16) and irinotecan (CPT-11). This combination therapy induced a favorable response and may offer an attractive option for these radiation-resistant diseases.

Case presentations

Two patients with lymphoma-type ATL were recruited (Table 1). Both patients showed anti-human T-lymphotrophic virus-1 antibodies and a bulky disease that was diagnosed as peripheral T-cell lymphoma. ATL usually presents as an extended systemic disease, but both patients had solitary bulky disease although their peripheral blood contained a small number of leukemic cells.

Patient 1 had a hard solitary bulky mass in inguinal lesion, which was 20 cm in diameter (Figure 1A). One course of terarubicin, cyclo-
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was started, and CPT-11 (40 mg/day/2 weeks, a total of 3 times as shown in Figure 1B, intravenous infusion) and VP-16 (100 mg/day/2 weeks, a total of 2 times as shown in Figure 1B, intravenous infusion) were administered simultaneously with radiotherapy. Concomitant chemoradiotherapy led to favorable lasting control of radiotherapy-resistant bulky disease (Figure 1B). Adverse effects including mucositis were limited. This patient also showed a favorable clinical course for a while, but died of other systemic diseases six months after the concomitant chemoradiotherapy.

Discussion

The concomitant use of radiotherapy and topoisomerase inhibitors was effective in controlling these radiotherapy-resistant diseases of ATL. Since moderate doses of chemotherapy were administered, adverse effects including mucositis were limited; therefore, further increase in the intensity of chemotherapeutic agents can be considered.

Information is limited with regard to the use of chemotherapeutic agents in concomitant therapy. The synergistic effects of CPT-11 and VP-16 [4], and their individual radiation-enhancing effects [5, 6] have been reported previously. Furthermore, Jae-Sung et al. reported the enhancement of radiation therapy in lung cancer with the combined use of CPT-11 and VP-16. Topoisomerase is considered to play an important role in the repair of DNA damage [7, 8]. Thus, topoisomerase inhibitors are an apposite adjuvant to radiotherapy. The timing and sequence of radiation and drug administration are reported to be important in radiation enhancement [4, 5, 9] and should be further explored in the present regimen. Carboplatin (CBDCA), one of the most important salvage agents, is also reported to show synergistic effects with radiotherapy [10]. Concomitant use of CBDCA and topoisomerase inhibitors in addition to radiotherapy may be a powerful alternative for controlling radiotherapy-resistant diseases.

Recently, the usefulness of this concomitant therapy for nasal NK/T-cell lymphoma was reported [11]. Nasal NK/T-cell lymphoma is known as one of the most aggressive hematological malignancies, so this concomitant trial involving was performed. Flexible adaptation of

<table>
<thead>
<tr>
<th>Table 1. Patient characteristics</th>
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<tr>
<td>Patient</td>
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<tr>
<td>Age, gender</td>
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<tr>
<td>Type</td>
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<tr>
<td>Bulky disease</td>
</tr>
<tr>
<td>WBC (× 10^9/L)</td>
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<tr>
<td>Ab lym (%)</td>
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<td>LDH (IU/L)</td>
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<td>Time from onset to concomitant therapy</td>
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<td>HTLV-1 provirus DNA</td>
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Laboratory data are from the time of concomitant therapy. WBC, white blood cell; Ab lym, abnormal lymphocytes; HTLV-1, human T-lymphotrophic virus 1.
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the concomitant use of radiotherapy and topoisomerase inhibitors may offer a potential therapeutic option for therapy-resistant bulky diseases, even in hematological malignancies.

Disclosure of conflict of interest

None.

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References


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