Successful Salvage Therapy of Irinotecan for Relapsed Hodgkin’s Lymphoma

Kazuhisa Urushihata, Tomonobu Koizumi, Toshimichi Kaneki, Shinji Yamaguchi, Keisaku Fujimoto and Keishi Kubo

Abstract

A 30-year-old man, who had a repeated history of relapsed Hodgkin’s lymphoma over 7 years, developed bilateral pleural effusion and chest wall involvement. He was treated with weekly irinotecan hydrochloride (CPT-11; 80 mg/m²/week). Partial response was observed after two cycles of irinotecan. Neutropenia and diarrhea were tolerable. This case demonstrated that irinotecan has a therapeutic effect in patients with relapsed Hodgkin’s lymphoma.

Key words: CTP-11, chemotherapy

Introduction

Irinotecan hydrochloride (CPT-11), a DNA topoisomerase-1 inhibitor, has been shown to have strong antitumor activity against several tumors (1–3). Several clinical studies have shown that irinotecan has beneficial effects in patients with malignant lymphoma, especially relapsed and/or refractory non-Hodgkin’s lymphoma (4–6). However, the dose and schedule are still controversial. In addition, little information has been reported on the efficacy of irinotecan in patients with Hodgkin’s lymphoma. We present here a case of relapsed Hodgkin’s lymphoma who showed a good outcome with irinotecan.

Case Report

In November 1994, a 24-year-old man was admitted to our hospital because of chest pain. His chest radiograph showed an anterior mediastinal mass surrounding the vessels. Laboratory findings including human chorionic gonadotropin and α-fetoprotein were normal. Percutaneous biopsy was performed. Although the specimens were too small to make a definite diagnosis, germ cell tumor or Hodgkin’s lymphoma was suspected. He was treated with 3 cycles of cisplatin and etoposide (PVP) chemotherapy. Good partial response was achieved and thoracic radiotherapy (46 Gy) followed. The first relapse occurred in October 1998. He developed left cervical lymph node swelling and lower abdominal huge mass. The histological diagnosis of Hodgkin’s lymphoma (mixed cellularity type) was made by cervical lymph node biopsy. He was treated with 6 cycles of ABVD (adriamycin 25 mg/m², bleomycin 10 mg/m², vinblastine 6 mg/m², dacarbazine 375 mg/m², day 1 and 15, respectively) chemotherapy and radiotherapy for the abdominal mass (40 Gy). Complete remission was achieved after the therapy. However, right cervical lymph node swelling was again found in August 2000. Radiotherapy for a right neck lesion (46 Gy) was performed. However, body weight loss and emaciation developed. He developed right chest pain, cough and dyspnea in October, 2000. A radiograph showed a pleural effusion in right lung side. Thoracocentesis was performed twice and right pleural effusion was drained. The cytology was class II. However, subsequent radiograph revealed a pleural effusion in both sides and a right chest wall mass (Fig. 1). Chest computed tomography also showed similar findings (Fig. 2). Laboratory findings were: white blood cell (WBC) count 7,020/μl, hemoglobin (Hb) 10.8 g/dl, lactate dehydrogenase (LDH) 299 U/ml. Soluble interleukin 2 receptor (SIL-2R) was 7,980 U/ml. He was treated with irinotecan (80 mg/m²) therapy biweekly without recurrence for 10 months. There were no significant toxicity. However, pleural effusion in both sites was again increased in October 2001.

Discussion

Several clinical and experimental studies have suggested a lack of cross-resistance between irinotecan and other anticancer agents (1–3). Irinotecan has shown a good response in patients with relapsed and/or refractory malignant lymphoma (4–6). With regard to therapeutic efficacy of irinotecan in patients...
with Hodgkin's lymphoma, there is little information. One of three patients with Hodgkin's lymphoma in early phase II (4) and 0 of 4 patients in late phase II study (5) achieved partial response. The response rates seem to be low compared with those of non-Hodgkin's lymphoma (42%; 26/62 cases) (4). However, the present case suggested that CPT-11 is efficacious.

Figure 1. Chest radiographic findings before chemotherapy, showing bilateral pleural effusion.

Figure 2. Computerized tomography of the chest before chemotherapy, showing bilateral pleural effusion and multiple mass shadows in the right lung field (A), one such infiltrate on the chest wall (B).

Figure 3. Chest radiogram after chemotherapy revealed no tumor mass or pleural effusion.
in the salvage treatment of Hodgkin’s lymphoma. Further clinical trials of the treatment with irinotecan are warranted as an alternative strategy.

We used 80 mg/m² of irinotecan weekly every 3 weeks, because weekly administration is suitable for the treatment of outpatients. This regimen has been the frequency used in patients with solid tumors. Although the present case had a good response with this treatment regimen, the dose and the schedule of irinotecan should be discussed.

Antitumor activity of SN-38, the active metabolite of irinotecan, has been thought to be 100 to 1,000 times stronger than that of irinotecan (1). Based on clinical studies by Nakano et al, intravenous administration of irinotecan produced adequate distribution of irinotecan and SN-38 in pleural fluid, and SN-38 showed a higher concentration than irinotecan in the pleural space (7). In addition, we have previously shown that SN-38 has better transfer into lung lymph circulation following intravenous administration of irinotecan in an animal model (8). The extent of the disease in the present case was mainly in the intrathoracic region. We speculate that the beneficial outcome by irinotecan in the present case is related to these pharmacokinetic characteristics of irinotecan.

In summary, the present case demonstrated that irinotecan has a therapeutic effect in patients with refractory and relapsed Hodgkin’s lymphoma. Although the dose and schedule of irinotecan are still undetermined, our case may provide optional information into the chemotherapeutic strategy for refractory malignant lymphoma.

References