Case report

Allogeneic and autologous stem cell transplantation in advanced small round cell sarcomas

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Introduction

Small round cell sarcomas (SRSs) comprise a heterogeneous group of malignant neoplasms with similar cytomorphology characterized by small, round, relatively undifferentiated cells; the group includes Ewing family sarcomas and rhabdomyosarcoma.1 These malignancies are chemotherapy-sensitive and potentially curable, and are treated by multimodality, dose-intensive, neoadjuvant protocols.2,3

For Ewing family sarcomas and rhabdomyosarcoma, actinomycin D-based chemotherapy combined with vincristine and cyclophosphamide is widely accepted as a standard therapy regimen.2,3 Since the beginning of the 1970s, such regimens have significantly improved the patients' prognosis.4,5 However, even after induction of these regimens, few patients with overt metastasis at diagnosis or with localized but extensive unresectable primary lesions of the trunk are cured. Most high-risk patients initially respond to treatment, but most of them eventually suffer a recurrence of the tumor and die of disseminated disease.6–9

To try to improve systemic control, hematopoietic stem cell transplantation (HSCT) has been considered as a possible approach.10,11 Autologous blood stem cell transplantation, such as peripheral blood cell transplantation (PBSCT), rescues patients who are myelo-suppressed following high-dose chemotherapy.10–13 Allogeneic blood stem cell transplantation, such as umbilical cord blood transplantation (UCBT), may have the advantage of having graft-versus-tumor (GVT) effects.14

Here, we report two cases of patients with SRS who suffered a refractory recurrence and systemic metastasis of their tumor. Without any consolidation therapy, we could not prevent complete paralysis (case 1) or general dissemination (case 2). We performed high-dose chemotherapy rescued by autologous PBSCT (auto-PBSCT) and UCBT. Our treatment produced a marked response and induced a partial remission. We describe the courses of the patients and the residual problems associated with our treatment. All the treatments were performed after informed consent was obtained from the patients and their families, and approval of the chief of our institution was obtained according to the institutional code of ethics. The patients and their families were informed that data from the case would be submitted for publication and gave their consent.

Case reports

Case 1

An 18-year-old woman was referred to our clinic with complaints of numbness of the trunk and a urination problem. Radiography and magnetic resonance imaging (MRI) showed a tumor around her thoracic spine that compressed the spinal cord. We performed an open biopsy and diagnosed the tumor as Ewing sarcoma (Fig. 1). We started chemotherapy consisting of two courses of etoposide (100 mg/m² × 5 days) and ifosfamide (2 g/m² × 5 days) and three courses of the combination of vincristine (1.5 mg/m² × 1 day), doxorubicin (75 mg/m² × 2 days), and cyclophosphamide (1200 mg/m² × 1 day). Even though intensive chemotherapy was performed, the response was progressive disease. At the time, her European Cooperative Oncology Group (ECOG) performance status was 2. Her tumor did not stop growing and thus compressed the spinal cord, which resulted in motor disorder (Fig. 2A). Therefore, we decided to perform a laminectomy and HSCT.

We initiated high-dose chemotherapy consisting of carboplatin (400 mg/m² × 4 days), melphalan (90 mg/m²
and motor disorder disappeared, and she had no difficulty walking or driving a car. The patient maintained complete donor chimerism with limited chronic GVHD, such as localized skin involvement. Prednisolone was tapered off on day 336.

On day 359 after the PBSCT (day 183 after the UCBT), she had a fever of 38°C, diarrhea, and bilateral leg edema. Her abdomen was distended. On day 391 (day 215 after the UCBT) she suffered acute interstitial pneumonia (IP) (Fig. 3). Laboratory data showed elevated aspartate aminotransferase (AST) (169 U/ml), alanine aminotransferase (ALT) (44 U/ml), total bilirubin (4.9 mg/dl), and fibrin degradation product (FDP) (12.5 mg/ml). β-D-Glucan was negative, and we could not identify any microorganism in blood or sputum cultures. We assessed that the IP was possibly caused by chronic GVHD and started pulsed steroid therapy (prednisolone 1000 mg/day) and assisted ventilation. Despite the treatment, the patient did not recover from the acute respiratory disorder. She died of IP 3 days after the onset.

**Case 2**

A 25-year-old woman was referred to our clinic with a history of rhabdomyosarcoma in her right hand. The surgeon who had treated her previously had resected the tumor with a marginal margin 2 weeks previously. After the resection, he found that the tumor was histologically malignant, and intensive chemotherapy was required (Fig. 4). We started 11 cycles of a combination chemotherapy of vincristine (2 mg/m² × 1 day), actinomycin D (0.5 mg/m² × 5 days), and cyclophosphamide (3000 mg/m² × 1 day), according to the IRS protocol. Over 6 months, she received the full cycles of chemotherapy and was discharged with no evidence of disease.

Three months later a new axillary lymph node metastasis was found. We performed a lymph node dissection.