CASE REPORT

Long-term remission after autologous stem-cell transplantation for relapsed histiocytic sarcoma

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ABSTRACT

Histiocytic sarcoma is diagnosed according to established criteria. However, treatment is controversial: although lymphoma chemotherapy regimens are often used, their impact on the natural history of the disease is unclear. Here, we report a disease-free survival of 2 years after autologous stem-cell transplantation in a patient with relapsed histiocytic sarcoma.

KEY WORDS

Histiocytic sarcoma, chemotherapy, stem-cell transplantation

1. INTRODUCTION

Histiocytic sarcoma (HS) is a rare malignancy that arises from histiocytes and that can occur at any site where histiocytes are present. Histiocytes bear surface markers that are detectable by immunohistochemistry, and those markers are variably retained in HS, thereby permitting diagnosis. Treating HS is challenging because of its rarity. No prospective studies have determined the efficacy of chemotherapy in patients with HS, and the published experience with allogeneic and autologous stem-cell transplantation for HS consists of only a few case reports, with limited follow-up1–3.

Here, we report a case of confirmed HS of the small bowel, with involvement of intra-abdominal lymph nodes. Although the patient responded initially to multiagent chemotherapy, nodal disease subsequently recurred. Autologous stem-cell transplantation was performed and resulted in complete remission, without disease recurrence, at the 24-month follow up.

2. CASE DESCRIPTION

Our patient, a 40-year-old woman, presented with recurrent abdominal pain for 3 years. A presumptive diagnosis of Crohn disease was made, and she was treated empirically with courses of steroids, without significant improvement. In January 2007, she presented with small-bowel obstruction. An urgent laparotomy for resection of a 7-cm ileal tumor was performed. Histopathologic examination revealed a proliferation of large, atypical cells with plump pleomorphic nuclei [Figure 1(a)]; immunohistochemistry analysis showed that the malignant cells were positive for vimentin, CD68, CD4, and lysozyme [Figure 1(b)]; variably positive for CD45 and S-100; but negative for CD2, CD3, CD5, CD7, CD8, CD20, CD21, CD23, CD23, CD30, CD43, CD1a, BCL-2, BCL-6, CK8-18, and keratin AE 1/3. In addition, no evidence of clonality of B or T cells was found on molecular analysis. The overall features were consistent with HS. The resection margins of the small bowel and two associated lymph nodes were free of malignancy. Computed tomography (CT) imaging showed paraesophageal, retroperitoneal, and retrocrural lymphadenopathies. Bone marrow aspiration and biopsy were normal.

The patient was treated with 6 cycles of chemotherapy. The CHOP chemotherapy regimen (cyclophosphamide 750 mg/m², doxorubicin 50 mg/m², vincristine 1.4 mg/m², prednisone 100 mg) was given every 21 days, although the first cycle of the regimen was replaced with inpatient administration of EPOCH (etoposide 50 mg/m² daily for 4 days, prednisone 60 mg/m² daily for 5 days, vincristine 0.4 mg/m² daily for 4 days, cyclophosphamide 750 mg/m², doxorubicin 10 mg/m² daily for 4 days) to watch for potential chemotherapy-induced bowel perforation. Post-treatment evaluation demonstrated no evidence of disease on history and physical examination, and CT imaging showed complete remission. Post-treatment surveillance was instituted.

One year later, the patient started to experience intermittent fever, night sweats, and marked fatigue. Physical examination revealed cervical and supraclavicular lymphadenopathies, no abnormality on cardiorespiratory examination, and no
hepatosplenomegaly. Restaging CT imaging showed enlarged retroperitoneal and retrocrural lymph nodes, with no other organ involvement. An excisional biopsy of a left cervical lymph node showed recurrent HS. There was no evidence of infiltration on bone marrow biopsy.

Second-line chemotherapy was initiated. The patient experienced a successful induction with 3 cycles of ESHAP (etoposide 60 mg/m² daily for 4 days, cisplatin 25 mg/m² daily for 4 days, methylprednisolone 500 mg daily for 4 days, cytarabine 2000 mg/m² on day 5). Post induction, CT imaging confirmed significant disease regression. Stem-cell mobilization and harvest were performed after the second cycle of ESHAP chemotherapy.

Induction was followed by autologous stem-cell transplantation. In September 2009, the patient received conditioning with BEAM (carmustine 300 mg/m², etoposide 200 mg/m², cytarabine 200 mg/m², melphalan 140 mg/m²) followed by stem-cell infusion. She has now been in complete remission for 24 months.

3. DISCUSSION AND CONCLUSIONS

Because of the small number of HS cases reported, it is difficult to characterize prognostic factors or to establish an optimal therapeutic approach. The disease can present with a broad range of clinical manifestations, depending on the organs involved. Nodal and extranodal sites can both be affected. Clinical features range from general constitutional symptoms and signs (fever, night sweats, and weight loss) to organ-specific manifestations such as hepatosplenomegaly, solitary masses, pancytopenia, and skin lesions.

The diagnosis is made using a combination of histologic and immunohistochemical features to confirm the histiocytic lineage and to exclude other poorly-differentiated large-cell malignancies, including B- or T-cell lymphomas, melanomas, and carcinomas. In 2002, the International Lymphoma Study Group recommended the use of a panel of immunohistochemical markers (CD68, CD1a, CD21, CD35, S-100) for the correct identification of HS. On immunophenotyping, HS cells express one or more histiocytic markers (CD163, CD68, lysozyme) typically with an absence of markers for Langerhans cells (CD1a, langerin) and myeloid cells (CD33, CD13, MPO). In addition, CD45, CD45RO, and HLA-DR are usually positive.

Prognosis is variable, although most patients die from disease progression. Radiation therapy can be used in localized disease. For advanced stages, non-Hodgkin lymphoma treatment protocols have been used despite a lack of prospective data. Allogeneic and autologous stem cell transplantation have both been described in case reports. However, some of those cases date back to the 1990s, when many of the specific immunohistochemistry stains for histiocytes were not available, raising questions about the accuracy of the diagnosis.

Autologous stem-cell transplantation has been used in relapsed or refractory disease. In the International Lymphoma Study Group study 6, only 1 of 18 patients with HS underwent autologous stem-cell transplantation for relapse, and that patient was alive at 3 years’ follow-up. No details were provided about stage at presentation, initial treatment, or disease status after transplantation. A more recent report described a 64-year-old woman who received CHOP chemotherapy and thalidomide for 3 months, followed by autologous stem-cell transplantation because of an only partial response to initial chemotherapy. She also received thalidomide maintenance therapy for residual disease. At 6 months’ follow-up, she had no evidence of disease.

Figure 1. (A) Medium-power microphotograph of a representative section of the patient’s histiocytic sarcoma at recurrence. Note the large, plump cells (compared with lymphocytes in the upper left corner), with large irregular nuclei and moderately abundant cytoplasm. Hematoxylin and eosin stain, 200× original magnification. (B) Medium-power microphotograph of histiocytic sarcoma cells stained for lysozyme, showing variable staining of a moderate number of cells. 200× original magnification.
The diagnosis in our patient was confirmed using modern immunohistochemistry. She had advanced disease at presentation, but attained complete remission after CHOP chemotherapy. Autologous stem-cell transplantation was performed at relapse after response to ESHAP salvage chemotherapy. At 24 months, she remains in complete remission, confirmed by CT imaging. This follow-up is one of the longest reported, and the present publication adds to the evidence that, in the absence of prospective trial results, it is reasonable to treat HS as an aggressive lymphoma. Autologous stem-cell transplantation may be an effective option for patients with relapsed HS. We do not know how effective the approach would be compared with allogeneic transplantation, nor whether high-dose therapy followed by transplantation might benefit newly diagnosed patients. Given the rarity of HS, randomized controlled trials will be challenging to perform, and publication of case reports and case series will likely remain an important source of information.

4. CONFLICT OF INTEREST DISCLOSURES

The authors have no financial conflicts of interest to disclose.

5. REFERENCES


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