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【 CASE REPORT 】

Retroperitoneal Bulky Histiocytic Sarcoma Successfully Treated with Induction Chemotherapy Followed by Curative Surgery

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Abstract:
Histiocytic sarcoma (HS) is a rare hematopoietic neoplasm. We report a patient with HS treated with induction chemotherapy followed by curative surgery. A 50-year-old man was referred to our hospital because of a retroperitoneal tumor. A computed tomography scan revealed a bulky retroperitoneal mass, infiltrating the surrounding organ. An excisional biopsy confirmed the diagnosis of HS. The tumor shrunk after multidrug chemotherapy. However, positron emission tomography showed uptake of fludeoxyglucose in the residual tumor. He underwent right nephrectomy to remove the tumor. Pathological examination showed complete response. Surgery combined with induction chemotherapy may be an effective way to manage HS.

Key words: histiocytic sarcoma, chemotherapy, surgery

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Introduction

Histiocytic sarcoma (HS) is an extremely rare hematopoietic neoplasm with a few hundred cases reported in the literature. HS is derived from phagocytic cells and histiocytes. HS is differentiated from other histiocytic disorders (dendritic cell tumors and Langerhans histiocytosis) by morphology and immunohistochemistry (1). HS involves any organ, and some cases present as advanced disease. There is no consensus regarding the treatment of HS because of its rarity. We report a patient with advanced stage HS successfully treated with induction chemotherapy followed by curative surgery.

Case Report

A 50-year-old man was referred to our hospital because of a retroperitoneal tumor founded incidentally during a yearly medical checkup. His vital signs were normal and he had a right quadrant abdominal mass on palpation. His performance status was two. Laboratory tests showed markedly elevated lactate dehydrogenase level of 2,577 IU/L, albumin level of 3.2 g/dL, hemoglobin level of 11.6 g/dL. Other laboratory tests were normal. A contrast enhanced CT revealed a bulky retroperitoneal mass of 14 cm ×11 cm, infiltrating the right pleural cavity, diaphragm, iliopsoas muscle, and ascending colon with high uptake of fludeoxyglucose by positron emission tomography (PET) (Fig. 1A, B). A ultrasonography (US)-guided needle biopsy of the tumor revealed atypical cells. However, immnohistochemical studies did not confirm a specific origin of the tumor, and an additional excisional biopsy was performed. A histopathological examination of the retroperitoneal mass revealed the proliferation of atypical cell with pleomorphic nuclei (Fig. 2A, B). Immunohistochemistry showed that the tumor cells were positive for CD10, CD68, and CD163 (Fig. 2C, D). On the other hand, the tumor cells were negative for CD3, CD20, CD56, CD138, and S-100. A diagnosis of HS was confirmed based on these findings. A stage of

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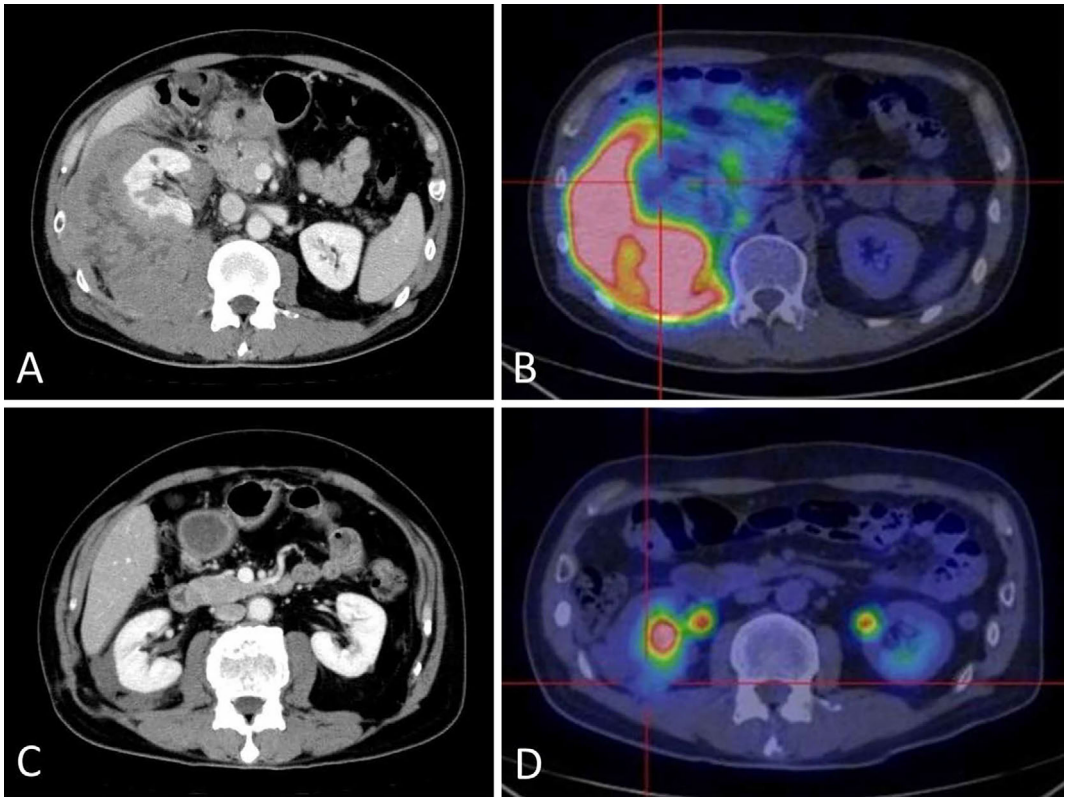

Figure 1. **A contrast enhanced CT and PET-CT before treatment shows bulky retroperitoneal mass with high uptake of fluorodeoxy glucose (FDG) (A, B). A contrast enhanced CT and PET-CT after treatment shows shrinkage of the tumor with weak uptake of FDG (C, D).**

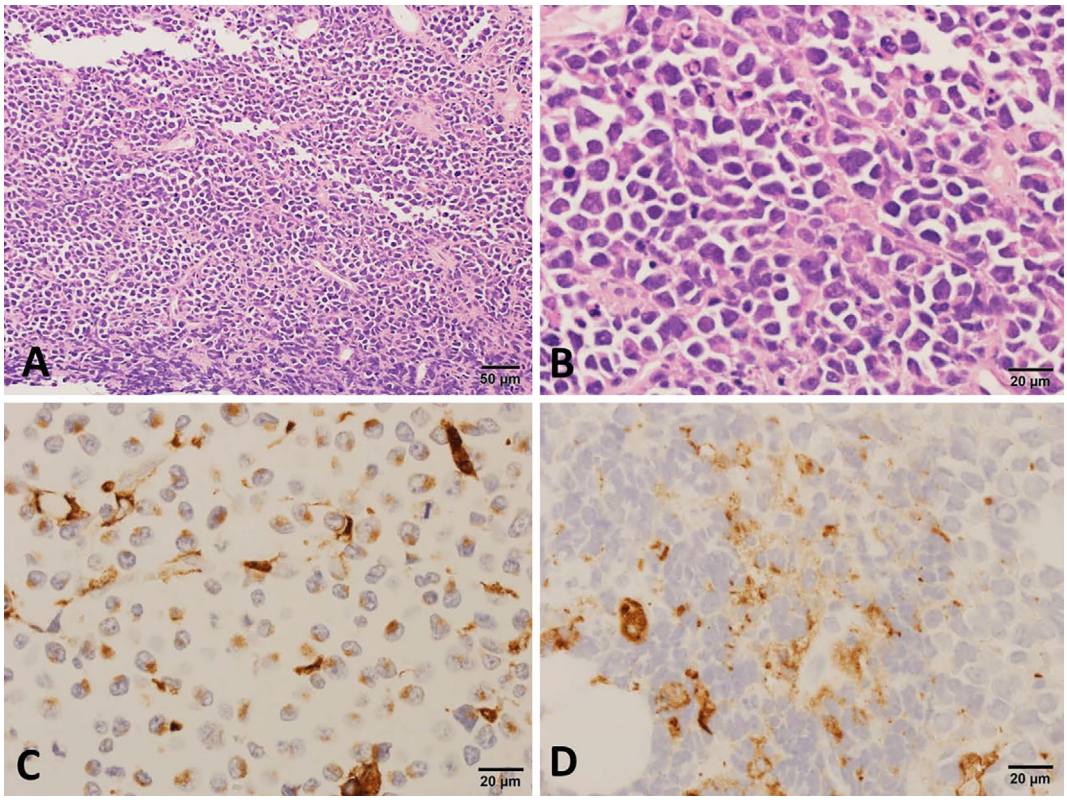

Figure 2. **Histopathological features of the surgical specimen obtained from retroperitoneal mass. A Hematoxylin and Eosin staining (A, B) and immunohistochemistry for CD68 (C) and CD163 (D) are displayed.**

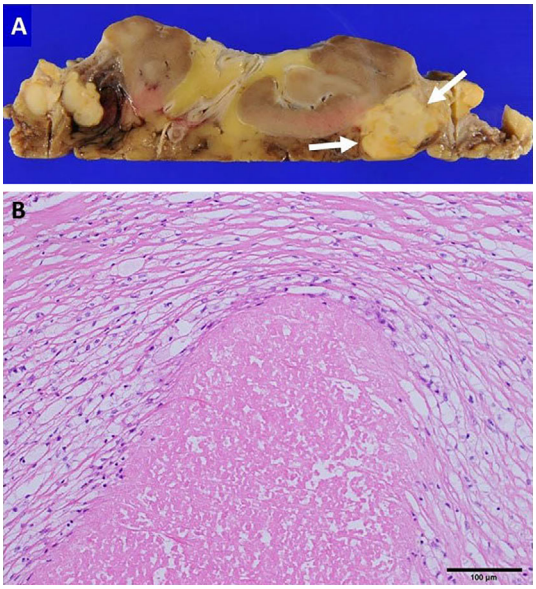

Figure 3. Clinical features of the resected retroperitoneal tumor. A macroscopic appearance (A) and Hematoxylin and Eosin staining (B) are displayed. There was yellowish tumor in the adipose tissue surrounding the right kidney (arrows). A histopathological examination demonstrated necrotic tissue and reactive granuloma.

histiocytic sarcoma was considered stage 3 according to the staging system of malignant lymphoma and six to eight courses of chemotherapy was planned. Induction chemotherapy consisting of adriamycin, vincristine, cyclophosphamide, and prednisolone was started (CHOP: cyclophosphamide 750 mg on day 1, doxorubicin 50 mg on day 1, vincristine 1.4 mg on day1, prednisone 100 mg on days 1-5, cycle length: 21 days). After chemotherapy was started, the retroperitoneal mass shrank rapidly. A CT after three course of chemotherapy patient showed partial remission of the tumor. However, multiple lesions including ascending colon and psoas muscle remained and additional five course of chemotherapy was started. Adverse events during chemotherapy were neutropenia (grade 3) and peripheral neuropathy (grade 3). A CT performed after eight courses of CHOP therapy showed partial remission of the tumor (Fig. 1C). The residual tumor was localized around the right kidney and infiltration into other organs had disappeared completely. A PET scan showed weak uptake of fludeoxyglucose in the residual tumor (standardized uptake value max=2.2) (Fig. 1D), which indicated refractory disease. We offered the patient three options for treatment; salvage chemotherapy with upfront peripheral blood stem cell transplantation, radiation therapy, and nephrectomy. The patient declined additional chemotherapy because he was suffering from peripheral neuropathy and decided to undergo right nephrectomy with curative intent. Macroscopically, there was yellowish tumor in the adipose tissue surrounding the right kidney (Fig. 3A). A histopathological examination of the residual tumor demonstrated only necrotic tissue and reactive granuloma, which indicated pathological complete remission (Fig. 3B). Creatinine levels increased from 0.75 mg/dL to 1.51 mg/dL after nephrectomy. The patient is alive without recurrence at 2 year after treatment.

Discussion

HS is an extremely rare hematopoietic neoplasm that is derived from phagocytic cells and histiocytes. The World Health Organization (WHO) classification divided histiocytic and dendritic cell neoplasms into six categories, histiocytic sarcoma, Langerhans cell histiocytosis, Langerhans cell sarcoma, follicular dendritic cell sarcoma, interdigitating dendritic cell sarcoma, and dendritic cell sarcoma not otherwise specified (2). HS is diagnosed by histopathological examination including morphology and immunohistochemical studies. HS must be distinguished from other histiocytic malignancies, malignant lymphoma, metastatic carcinoma, and melanoma. Immunohistochemical analyses have shown that HS typically expresses CD68 and lysozyme but not CD1a, CD21/35, or S100 (3). CD163 is a glycoprotein belonging to the scavenger receptor cysteine-rich superfamily (4), and it is frequently used to identify monocyte and macrophage lineages. In this case, US-guided needle biopsy did not confirm HS because of a lack of specific immunohistochemical markers. An additional excisional biopsy revealed tumor cells that were positive for CD68 and CD163 but negative for S-100, lymphoid markers, myeloid markers, and epithelial markers. We diagnosed HS based on these immunohistochemical findings. It is necessary to obtain abundant tissue by excisional biopsy to make an accurate diagnosis of HS.

There is no standard treatment for HS because of the rarity of the disease. Patients with advanced disease usually receive multidrug chemotherapy used for aggressive lymphoma. However, there are no prospective trials regarding the best regimen and data regarding treatment are limited to small case series. The commonly used regimens are ifosfamide, carboplatin, and etoposide with mesna (ICE) and CHOP. HS generally has primary resistance to chemotherapy or relapses early after treatment (5). Recently, case reports have been published on the use of high-dose chemotherapy with autologous stem cell transplantation to overcome poor prognosis (6-8). In these three case reports, all patients achieved remission. Due to patient's poor performance status, we started CHOP considering the toxicity of high dose chemotherapy.

This patient received eight courses of chemotherapy due to advanced stage at presentation. The optimal strategy for treatment of residual tumors after chemotherapy is unknown. We undertook surgery because the residual tumor had activity despite eight courses of chemotherapy. The main disadvantage of surgery in this case was the loss of right kidney. The patient is alive without recurrence at 2 years, but he still has risk of relapse. A dose reduction of salvage chemotherapy will be mandatory in case of recurrence.

There is little data regarding the prognosis of HS. Hornick et al. reported 14 extranodal histiocytic sarcoma

cases (9). Six patients were treated with postoperative radiation and seven with chemotherapy. During median follow-up of 24 month, two patients died of progressive disease. Gounder et al. reported 53 cases of dendritic cell and histiocytic sarcomas (10). Among these cases, 15 patients had HS, with nine cases of metastatic disease. It is notable that there was no significant difference in overall survival between localized or metastatic disease, with 5-year overall survival of 70%. This finding was not observed in other dendritic cell tumors. This patient showed rapid response to chemotherapy, and the residual tumor was resected completely, which may indicate relatively good prognosis despite advanced disease at initial presentation.

In conclusion, we report a patient with advanced stage HS successfully treated with induction chemotherapy followed by surgery. HS generally has limited sensitivity to chemotherapy. Surgery combined with chemotherapy may be the effective way to manage HS.

The authors state that they have no Conflict of Interest (COI).

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