Isolated Mediastinal Myeloid Sarcoma Successfully Treated with Chemoradiotherapy Followed by Unrelated Allogeneic Stem Cell Transplantation

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Abstract

A 22-year-old man was diagnosed with isolated mediastinal myeloid sarcoma which radiologically mimicked primary mediastinal lymphoma. Despite administration of standard remission induction chemotherapy with daunorubicin and cytarabine, and three cycles of intensive high-dose cytarabine-based consolidation, chemo-resistant hypermetabolic lesions were persistently detected in the highest mediastinum and in the supraclavicular area. However, complete remission and long-term survival were achieved by curative radiotherapy followed by unrelated allogeneic stem cell transplantation.

Key words: mediastinum, myeloid sarcoma, radiotherapy, hematopoietic stem cell transplantation

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Introduction

Myeloid sarcoma (MS) is an extramedullary localized tumor composed of immature myeloid cells. MS usually occurs concomitantly with, or after the diagnosis of, acute myeloid leukemia (AML) (1). Isolated MS has been rarely described in previous case reports to initially present in the skin, bone, breast, pancreas, conjunctiva, spine, gastrointestinal, cervix, and vagina (1-9). However, isolated mediastinal MS is extremely rare (10, 11). Here, we describe the first case of chemo-resistant isolated mediastinal MS mimicking primary mediastinal lymphoma. We achieved long-term disease-free survival by radiotherapy followed by unrelated allogeneic stem cell transplantation.

Case Report

A 22-year-old man was admitted in January 2009 complaining of rapidly progressive shortness of breath during rest and chest discomfort. On auscultation, rapid and coarse breathing sounds were detected with localized rales in the right lower lung field. Simple chest X-rays revealed mediastinal widening, and blunting in the right costophrenic angle (Fig. 1A). A contrast-enhanced chest computed tomography (CT) scan demonstrated a huge infiltrative mass on the anterior mediastinum which compressively extended in the aorta, superior vena cava, and heart, with right-sided pleural effusion. In addition, enlargement of supraclavicular, right internal mammary, and supradiaphragmatic lymph nodes were observed, which initially led to a strong suspicion of primary mediastinal lymphoma (Fig. 1B).

Blood tests showed a white blood cell count of 3,890/mm3, 77.7% neutrophils, 21.2% lymphocytes, 0.4% eosinophils, 0.1% basophils, 11.1 g/dL hemoglobin, a platelet count of 254,000/mm3, and 1.6% reticulocytes. Blood chemistry tests showed a total protein content of 7.6 g/dL, 3.9 g/dL albumin, 175 mg/dL cholesterol, 12 IU/L aspartate aminotransferase, 30 U/L alanine aminotransferase, 122 IU/L L alkaline phosphate esterase, 0.32 mg/dL total bilirubin,
3004

Figure 1. A: Simple chest X-rays revealed mediastinal widening, and blunting in the right costophrenic angle. B: A contrast-enhanced CT scan demonstrated a huge infiltrative mass on the anterior mediastinum which compressively extended in the great vessels, and heart with right-sided pleural effusion.

Figure 2. A: large myeloblasts with prominent nucleoli and eosinophil precursors (Hematoxylin and Eosin staining, ×400). B, C: positive findings for MPO (2-B) and CD68 (2-C). D: negative findings for LCA.

12.6 mg/dL BUN, 0.89 mg/dL creatinine, 9.1 mg/dL calcium, 3.2 mg/dL phosphate, and 7.0 mg/dL urate.

Pathological evaluation of needle aspiration and biopsy of the anterior mediastinal mass demonstrated homogenous malignant infiltration containing large round nuclei, dispersed chromatin, prominent nucleoli, ill-defined eosinophilic cytoplasm, and frequent mitotic features (Fig. 2A). Immunohistochemically, malignant cells were positive for myeloperoxidase (MPO) and CD68 (Fig. 2B, C), but negative for S-100, CD117, LCA, CD3, CD20, and CD138, compatible with MS (Fig. 2D).

On bone marrow aspiration and biopsy, no evidence was found regarding leukemic infiltration and normal trilineage hematopoiesis with age-adjusted normal cellularity. No cytogenetic abnormality was detected in the bone marrow and myeloid sarcoma tissue. Based on these findings, we diagnosed the patient with isolated mediastinal MS. Remission induction chemotherapy consisting of daunorubicin [90 mg/m²/day intravenously (i.v.) on days 1, 2, and 3] and cytarabine (200 mg/m² continuous i.v. on days 1-7) was admin-
istered. A follow-up contrast-enhanced chest CT scan revealed a markedly decreased size of the anterior mediastinal mass combined with other lymph nodes and the disappearance of right-sided pleural effusion, indicating a partial response according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria.

Despite an intensive three cycles of consolidation chemotherapy with high-dose cytarabine (2,000 mg/m² every 12 hours i.v. on day 1, 3, 5, and 7), etoposide (100 mg/m² i.v. on days 1, 3, 5, and 7), and cisplatin (20 mg/m² i.v. on days 1, 3, 5, and 7), contrast-enhanced chest CT and positron emission tomography (PET) showed a persistent partial response, with a hypermetabolic lesion of the left supraclavicular and highest mediastinal lymph nodes, as a chemoresistant disease (Fig. 3A). After curative radiotherapy on the highest mediastinum, supraclavicular area, and left sternocleidomastoid muscle (5,000 cGy/25 fractions), contrast-enhanced CT revealed a slightly decreased previous persistent lesion.

In September 2009, the patient underwent unrelated allogeneic peripheral blood stem cell transplantation (PBSCT) following conditioning with busulfan (3.2 mg/kg i.v. on days -7 to -4) and cyclophosphamide (60 mg/kg i.v. on days -3 to -2). Additionally, he achieved stable engraftment. Bone marrow aspiration and biopsy also showed normal trilineage hematopoiesis without leukemic cell and full donor chimerism confirmed by short tandem repeat (STR)-polyme- rase chain reaction (PCR). However, severe ileus and skin rash developed on day 17 post-transplantation, which is compatible with grade 4 acute graft-versus-host disease (GVHD). High-dose glucocorticoid and tacrolimus were started to control the acute GVHD, and finally immunosuppressive agents were switched to mycophenolate mofetil (MMF; 1,000 mg daily) and low-dose glucocorticoid to control chronic GVHD. A follow-up contrast-enhanced CT (Fig. 3B) and PET-CT scan showed complete resolution of the disease site and metabolic complete remission was achieved 2 months after allogeneic PBSCT. Two years and 5 months after diagnosis of isolated mediastinal MS, the patient is well on regular follow-up at the outpatient clinic to control chronic GVHD, with no evidence of MS.

**Discussion**

Because primary mediastinal MS is extremely rare, most cases of isolated MS of the mediastinum are initially misdiagnosed as a malignant lymphoma, thymoma, and mediastinal germ cell tumor radiologically, and most MS develops within the first year preceding the occurrence of acute myeloid leukemia (AML), or concomitant with AML or at relapse of AML (1, 12).

Pathologically, the variable morphological appearance and absence or recognizable myeloid differentiation can be misleading (13, 14). The present patient’s disease radiologically mimics primary mediastinal lymphoma. However, immunohistochemical studies showed weak positivity for myeloperoxidase and strong positive results for CD68, but negative results for S-100, CD117, leukocyte common antigen (LCA), CD3, CD20, and CD138, compatible with MS. These immunohistochemical findings are compatible with a monoblastic or myelomonoblastic variant of myeloid sarcoma. The best treatment option is not yet established in isolated MS (1, 12).

Previous studies have suggested that patients with isolated MS should receive AML-like induction chemotherapy (1-15). However, local modalities such as surgical removal or radiotherapy might play an important role to control residual disease following systemic chemotherapy.

American investigators reported a review of 20 cases of nonleukemia MS in various locations from the MD Anderson Cancer Center in which combination treatment with radiotherapy and chemotherapy resulted in better treatment failure-free survival than chemotherapy alone (16).

According to two previously reported cases of isolated mediastinal MS (10, 11), no complete response was observed following induction chemotherapy with or without consolidation of high-dose cytarabine, and additional radiotherapy was needed for local control of chemo-resistant re-
sidual disease after systemic chemotherapy (Table 1). These findings suggest that multimodality approaches of both systemic and local treatment might be the best strategy to achieve better outcomes compared with standard AML chemotherapy alone.

The role of hematopoietic stem cell transplantation has been rarely elucidated in isolated MS and its efficacy is still unknown. However, there have been a few previous studies of isolated MS successfully treated with hematopoietic stem cell transplantation (12, 17). In a retrospective study that analyzed the characteristics, treatment, and overall survival of all patients presenting with isolated MS or MS with concomitant AML compared with AML treated during the same period, patients with MS at diagnosis benefited from upfront aggressive treatment with hematopoietic stem cell transplantation (12, 17). Although a single comparative study has previously shown that isolated MS may be associated with superior event-free survival and overall survival as compared to AML when patients receive AML-like therapy (18), the treatment outcome and overall survival of isolated MS are generally poorer than those of AML (16, 19, 20). Thus, further investigation is necessary to weigh the risk and benefit of hematopoietic stem cell transplantation in patients with isolated MS.

In conclusion, radiotherapy followed by allogeneic stem cell transplantation is considered to be a salvage treatment in patients with chemo-resistant isolated mediastinal MS. However, further prospective randomized studies are necessary to evaluate the efficacy and role of radiotherapy and hematopoietic stem cell transplantation in isolated MS, and particularly in chemo-resistant MS.

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

References


Table 1. Review of the Literature

<table>
<thead>
<tr>
<th>Case (reference)</th>
<th>Gender/ Age</th>
<th>Initial symptom</th>
<th>Induction CT</th>
<th>Consolidation</th>
<th>Response after CT</th>
<th>RT following CT</th>
<th>HSCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (14)</td>
<td>F/40</td>
<td>Chest pain, nocturnal fever</td>
<td>Daunorubicin + cytarabine</td>
<td>None</td>
<td>PR</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>2 (16)</td>
<td>M/40</td>
<td>Painless cervical lymph node</td>
<td>Idarubicin + cytarabine</td>
<td>High-dose cytarabine</td>
<td>PR</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>Our case</td>
<td>M/22</td>
<td>Progressive shortness of breath, chest discomfort</td>
<td>High-dose daunorubicin + cytarabine</td>
<td>High-dose cytarabine, etoposide, and cisplatin</td>
<td>PR</td>
<td>Yes</td>
<td>UPBSCT</td>
</tr>
</tbody>
</table>

CT: chemotherapy; F: female; M: male; RT: radiotherapy; HSCT: hematopoietic stem cell transplantation; UPBSCT: unrelated peripheral stem cell transplantation.


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