

Case Report

Intraparenchymal Myeloid Sarcoma and Subsequent Spinal Myeloid Sarcoma for Acute Myeloblastic Leukemia

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Myeloid sarcoma is a solid, extramedullary tumor composed of leukemic myeloblasts or immature myeloid cells. Intraparenchymal myeloid sarcoma without the involvement of the skull or meninges is extremely rare. Here, we present the case of a 49-year-old man who developed intraparenchymal myeloid sarcoma on the left cerebellum after allogeneic bone marrow transplantation (BMT). He received radiotherapy after complete removal of intraparenchymal myeloid sarcoma, but he was diagnosed spinal myeloid sarcoma three month later. Nine months after the operation, new intracranial and spinal myeloid sarcoma were diagnosed and the patient's condition had been worsened rapidly. Although the spinal myeloid sarcoma was not histologically diagnosed, this report provides valuable insights into the clinical course of progression of intraparenchymal myeloid sarcoma.

Key Words : Myeloid sarcoma · Acute myeloid leukemia · Bone marrow transplantation.

INTRODUCTION

Myeloid sarcoma is a solid, extramedullary tumor composed of leukemic myeloblasts or immature myeloid cells¹⁾. The synonyms of this pathological entity include granulocytic sarcoma, chloroma, myeloblastoma, chloromyeloma, chloromyelosarcoma, granulocytic leukosarcoma, or myelosarcoma¹⁵⁾. In the 2002 World Health Organization classification of myeloid neoplasms, the terms "granulocytic sarcoma" and "chloroma" that were commonly used to refer to such tumors were replaced with "myeloid sarcoma"¹⁸⁾. Myeloid sarcoma involves almost all tissues, including those of the skin, lymph nodes, spine, orbit, and bone⁵⁾. Although the invasion of central nervous system (CNS) by leukemic cells could be attributed to leptomeningeal involvement, intraparenchymal myeloid sarcoma without the involvement of the skull or meninges is rare¹⁶⁾. Here, we report the case of intraparenchymal myeloid sarcoma on the left cerebellum and subsequent spinal myeloid sarcoma within a short interval after allogeneic bone marrow transplantation (BMT).

CASE REPORT

A 49-year-old man was diagnosed with acute myeloblastic leukemia (AML) in September 2003. Complete remission was achieved after induction chemotherapy using cytosine arabinoside (Ara-C) and idarubicin, and after consolidation chemotherapy using high dose Ara-C in October 2004. However, he relapsed in September 2005. After induction and consolidation chemotherapy using the mitoxantrone, etoposide, and Ara-C (MEC) regimen, he underwent an HLA-identical sibling donor allogeneic BMT as post-consolidation therapy in the second complete remission in March 2006. The patient's clinical condition was satisfactory until October 2008, when he exhibited progressive dizziness and cerebellar ataxia. The results of the hematological studies were normal with no evidence of leukemic relapse. Cranial magnetic resonance (MR) images revealed a 33×21×28 mm round mass without dural attachment that was isointense on T2-weighted images and hypointense on T1-weighted images in the left superior cerebellar hemisphere and vermis. Strong homogeneous contrast enhancement was observed following the administration of the contrast agent (Fig. 1). No tumor except intracerebellar mass was noted following spinal MR images, whole body computed tomography (CT), and positron emission tomography (PET) examinations. The tumor was completely removed by suboccipital craniectomy and a transcranial approach. Histological examination revealed myeloid sarcoma characterized by a diffuse proliferation of myeloblasts (Fig. 2).

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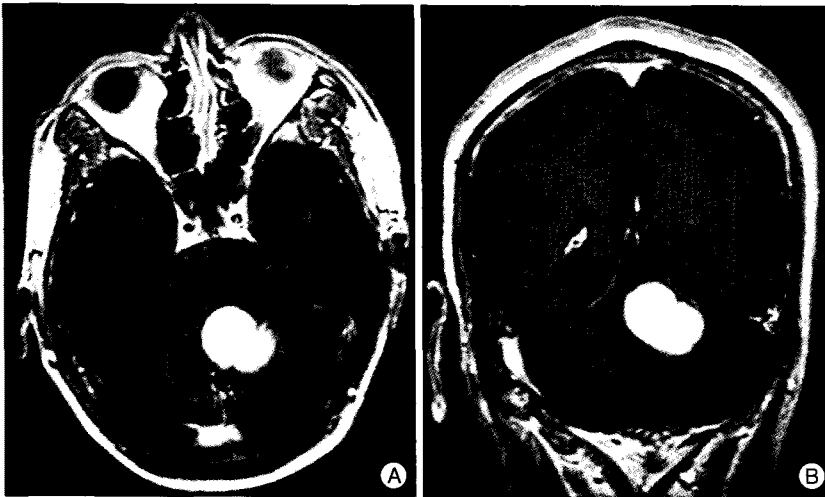


Fig. 1. Gadolinium-enhanced axial (A) and coronal (B) T1-weighted magnetic resonance images on October 2008 showing a 33×21×28 mm round homogeneously enhanced mass within the left superior cerebellar hemisphere and vermis without dural attachment.

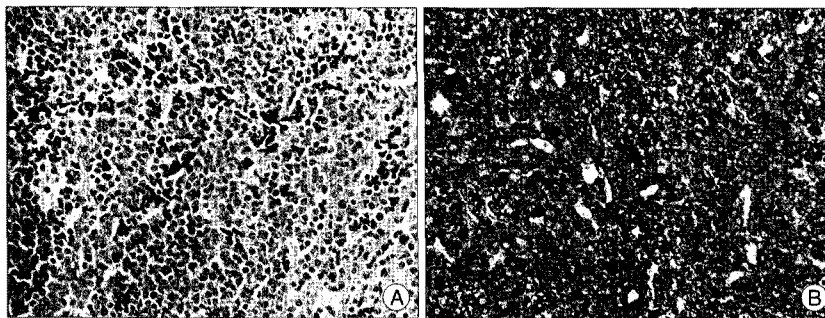


Fig. 2. Histological examination of the surgical specimen showing diffuse proliferation of myeloblasts with round nuclei and scanty cytoplasm and included numerous areas of mitosis (H&E; original magnification ×400) (A) and immunohistochemical staining showing positive for myeloperoxidase (Original magnification ×400) (B).



Fig. 3. Gadolinium-enhanced sagittal T1-weighted magnetic resonance images of the lumbar spine on January 2009 showing diffuse thickening with subtle enhancement along the surface of the spinal cord and nerve roots of cauda equina, and homogeneously enhanced nodules in the epidural space at the L3 level (arrow).

Immunohistochemical findings were positive for myeloperoxidase, CD56, and terminal deoxynucleotidyl transferase (TdT). The tumor was negative for CD99 and Pan CK stainings. The Ki-67 labeling index was approximately 70%. Subsequently, the patient received whole-brain radiotherapy with a total dose of 3,000 cGy and intrathecal treatment with methotrexate (MTX).

In January 2009, the patient presented with lower back pain, progressive weakness of the lower limbs, and unsteady gait. Spinal MR images revealed diffuse thickening with subtle enhancement along the surface of the spinal cord and nerve roots of cauda equina, and homogeneously enhanced nodules in the epidural space at the L3 level (Fig. 3). The bone marrow examination was normal. He was given a whole-spine radiotherapy with a total dose of 3,750 cGy and intrathecal retreatment with MTX, although the patient's symptoms were not alleviated. In July 2009, the patient developed headache and pain on left upper extremity. Cranial MRI revealed a round and strong homogeneous contrast enhancing mass in right frontal cortex with vasogenic edema (Fig. 4A). Cervical MRI revealed large soft tissue mass measuring 43 mm in craniocaudal diameter from

the C5 to C7 vertebral levels with spinal cord compression. Moreover, it revealed an inhomogeneous diffuse enhancement following the administration of a contrast agent (Fig 4B). We recommended an excisional biopsy for masses in right frontal cortex and cervical spinal canal, but the patient and his family refused the operation and treatment. The patient's condition continued to deteriorate and he was referred to another hospital.

DISCUSSION

Myeloid sarcoma is generally observed as a complication of AML, myelodysplastic syndromes, or myeloproliferative disorders, and it may be perceived as a *de novo* tumor without marrow involvement or as a tumor associated with leukemia in the marrow, and as a site of leukemia relapse^{6,7,10,17}. Myeloid sarcoma has been associated with 3.1-9.1% of AML cases¹¹. Recent evidence suggests that the frequency of myeloid sarcoma incidence is exceedingly increasing because of improved antileukemic therapy and longer remission in patients with AML¹⁴. Although myeloid sarcoma can occur anywhere in the body, intracranial involvement is unusual. Intracranial involvement has been associated

with the passage of leukemic cells from the bone marrow of the skull to the dura, and subsequently to the subarachnoid and Virchow-Robin spaces, thereby resulting in brain surface invasion².

Allogeneic BMT is often used for the treatment of AML, acute lymphoblastic leukemia (ALL), and chronic myeloid leukemia (CML). Myeloid sarcoma is a rare complication observed in AML patients after BMT and may be the first sign of relapse⁹; myeloid sarcoma may also precede the onset of systemic disease^{3,11}. In a 10-year survey conducted by the European BMT Registry, the incidence rate of myeloid sarcoma associated with AML was 0.65%⁴. Furthermore, relapse of myeloid sarcoma in the brain after BMT is an extremely rare complication. All levels of the spine may be affected by myeloid sarcoma. The thoracic spine was most commonly involved (73%) followed by the lumbar (34%), sacral (23%), and cervical (5%) regions. Multiple spinal lesions have been diagnosed in only 18% of patients⁹. However, myeloid sarcoma without bone marrow involvement is rare and only a few cases have been presented with spinal involvement¹³. There have been no reported cases of spinal myeloid sarcoma without bone marrow involvement after surgical resection of intraparenchymal myeloid sarcoma.

Although a histological examination was not conducted, the spinal tumor was clinically considered a spinal myeloid sarcoma based on spinal tumor characteristics as indicated by MR images. Our case was characterized by the occurrence of a spinal myeloid sarcoma after intraparenchymal myeloid sarcoma within a short interval; however, it is very difficult to draw conclusions about the time elapsed between the occurrence of intraparenchymal myeloid sarcoma and spinal myeloid sarcoma. In order to understand the development of spinal myeloid sarcoma, two possible pathogeneses have been postulated. First, no lesion was detected in the whole spine on the spinal MR images performed prior to the surgical excision of intraparenchymal myeloid sarcoma.

Therefore, we considered the possibility of spinal leptomeningeal metastases of the leukemic cell through the cerebrospinal fluid (CSF) pathway during the surgical excision of intraparenchymal myeloid sarcoma. Second, we could not rule out the possibility of the recurrence of multiple myeloid sarcomas to have multicentricity and different temporal varieties. The period to onset of the second spinal myeloid sarcoma was too short.

Combined chemotherapy and radiation therapy is the first choice in the treatment of isolated intracranial myeloid sarcoma¹⁹. The effect of surgical excision still remains controversial. Surgical excision is not indicated except in the presence of progressive neurological deficits which are uncontrollable by the conservative treatment⁸. Nishimura et al.¹² reported that surgi-

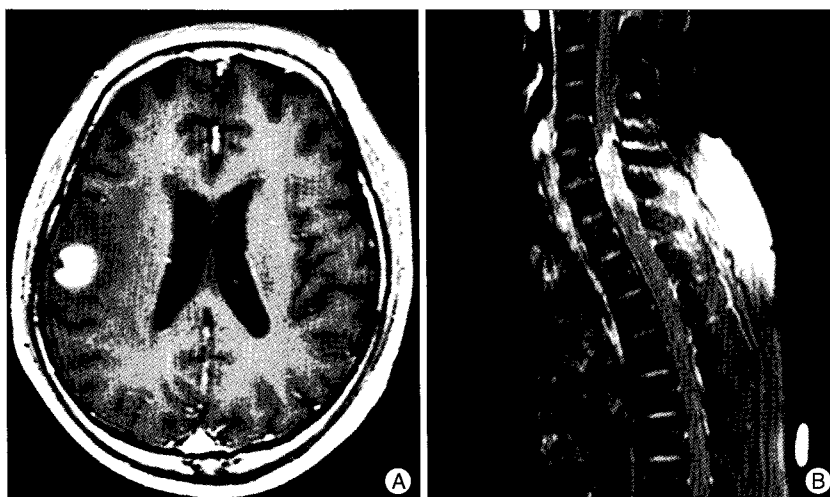


Fig. 4. The follow-up gadolinium-enhanced T1-weighted magnetic resonance images (MRI) after operation on July 2009. A : Cranial MRI showing a round and strong homogeneous contrast enhancing mass in right frontal cortex with vasogenic edema. B : Cervical MRI showing large, diffuse, inhomogeneous contrast enhancing mass from the C5 to C7 vertebral levels with spinal cord compression.

cal excision has no advantage over chemotherapy and radiation therapy. Moreover, surgery could increase the risk of infection and central nervous system dissemination. However, it has been documented that surgery of early-stage tumor may lead to a long symptom-free period and good response to external radiation—even though surgical excision and/or irradiation may only achieve local control, with no influence on survival⁸. In our case, the patient was admitted with complaints of progressive dizziness and cerebellar ataxia. He received radiotherapy after complete removal of intraparenchymal myeloid sarcoma, but he developed spinal myeloid sarcoma three month later. Nine months after the operation, new intracranial and spinal myeloid sarcoma was diagnosed and the patient's condition had been worsened rapidly. Seen from the perspective described above, it is thought that the surgical excision for intraparenchymal myeloid sarcoma of our patient had no noticeable advantages. Moreover, we cannot rule out the possibility of the CSF metastases from surgical excision of intracranial myeloid sarcoma.

CONCLUSION

Intraparenchymal myeloid sarcoma without skull or meningeal involvement is a rare complication of AML. Exact pathogenic mechanism remains unclear. Although the spinal myeloid sarcoma was not histologically diagnosed, this report provides valuable insights into the clinical course of progression of intraparenchymal myeloid sarcoma. Future studies should clarify the clinical characteristics and advantage of surgery of this rare tumor.

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