Int J Clin Exp Med 2020;13(9):7086-7091
www.ijcem.com /ISSN:1940-5901/IJCEM0110629

Case Report

Myeloid sarcoma derived from the sacral vertebrae: a case report and literature review

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Received March 10, 2020; Accepted June 18, 2020; Epub September 15, 2020; Published September 30, 2020

Abstract: We reported a case of isolated myeloid sarcoma (MS) derived from the sacral vertebrae and reviewed the relevant literature. A 22-year-old female had constant pain in the left hip and leg for a month. Magnetic resonance imaging (MRI) revealed a mass lesion on the left side of the sacral vertebrae. H&E and immunohistochemical staining showed the characteristics of MS. After two cycles of acute myeloid leukemia-type induction chemotherapy, the MRI scan revealed a significant reduction in the mass size. She then received a cycle of high-dose cytarabine for consolidation. A second cycle of the same consolidation chemotherapy and local radiation therapy were scheduled. However, the patient voluntarily stopped both treatments due to financial constraints and died at 13 months after first symptom onset. The prognosis of isolated MS involving the spine is poor. Standardized chemotherapy and radiotherapy should be performed to improve the prognosis.

Keywords: Myeloid sarcoma (MS), acute myeloid leukemia (AML), sacral vertebrae, chemotherapy, idarubicin, cytarabine

Introduction

Myeloid sarcoma (MS), also known as granulocytic sarcoma or chloroma, is an extramedullary tumor composed of mature or immature myeloid blast cells [1]. According to the World Health Organization (WHO), MS is categorized as a subtype of acute myeloid leukemia (AML) [2]. The MS can arise before the diagnosis of intramedullary AML without evidence of blood or bone marrow disease, which is defined as isolated, primary, or non-leukemic MS [3]. The isolated MS are a rare disease with an incidence of 2 in 1,000,000 adults [4], accounting for only 0.7% of all AML cases [3]. According to a large study of 746 patients in a national dataset [5], isolated MS may develop at any anatomical site, and the most common site is the soft tissues (31.3%). By contrast, only 4.9-6.6% of isolated MS are derived from the bone [3, 5]. Especially, isolated MS involving the spine are extremely rare. Here, we report a case of isolated MS from the sacral vertebrae and review the relevant literature. This study was approved by the institutional review board of the Third Affiliated Hospital of Southern Medical University, Guangzhou, Guangdong, China. Written informed consent was obtained from the patient.

Case presentation

A 22-year-old female was admitted to the Third Affiliated Hospital of Southern Medical University (Guangzhou, Guangdong, China) due to constant pain in the left hip and leg for a month. She could not walk and sleep as usual and had difficulty in defecation. She had no history of AML, injury, or prior surgery. Physical examination revealed unremarkable findings. She had tenderness and percussion pain on the left Ischial tuberosity, as well as hypoesthesia in

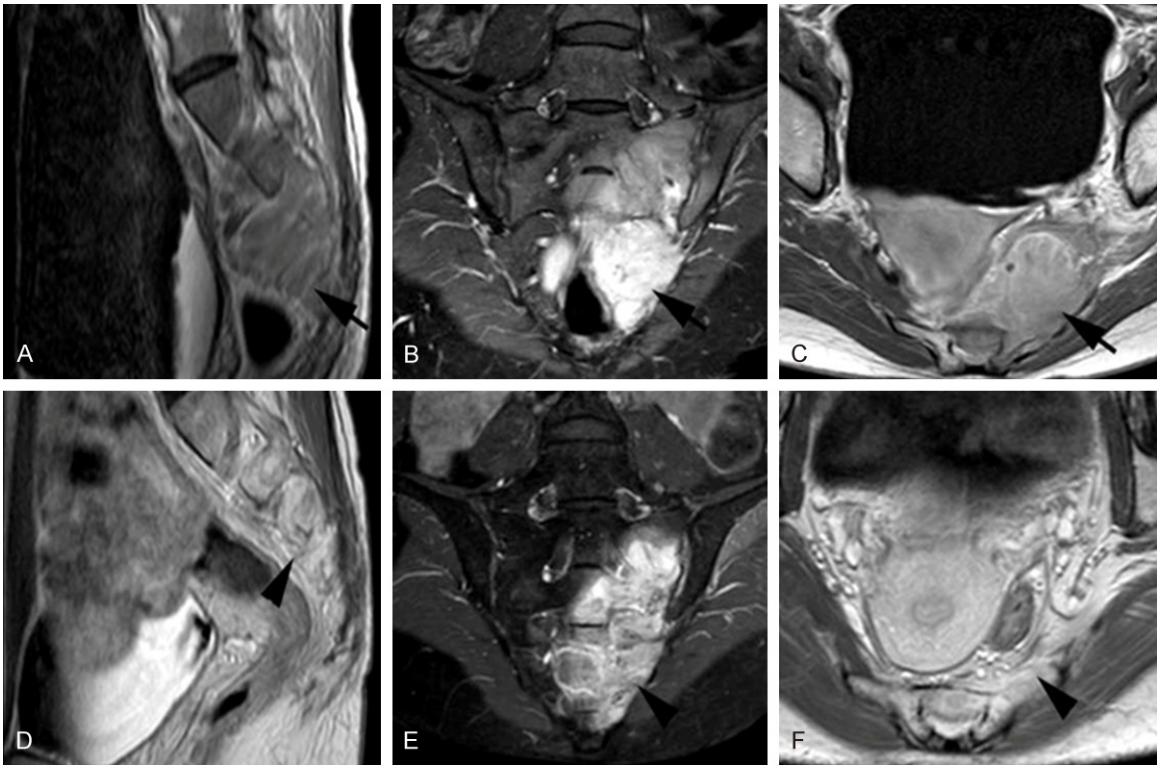

Figure 1. Sagittal, coronal, and axial T1WI and contrast-enhanced MRI scan of the spinal mass before (A-C) and after (D-F) two cycles of the induction chemotherapy. The sagittal scans revealed a mass on the sacral vertebrae with a clear margin and intermediate enhancement (arrow, A). The coronal T1WI SPIR and contrast-enhanced images showed that the mass was on the left side of the S3-S5 sacral vertebrae, with hyperintense upon enhancement (arrow, B). This was re-confirmed by the axial images (arrow, C). The tumor shrank remarkably after two cycles of induction with idarubicin and cytarabine (arrowheads, D-F). T1WI, T1-weighted; MRI, magnetic resonance imaging.

the perineum and lower left extremities. The muscle strength of the anal sphincter was declined. Both knee jerk reflex and ankle tendon reflex were increased, and no pathological reflex was found. Other neurological examination results were unremarkable.

The routine blood test showed a white blood cell count of 6.8×10^9/L, a red blood cell count of 4.67×10^{12}/L, a hemoglobin level of 128 g/L, and a platelet level of 281×10^9/L. Other laboratory results, including prothrombin and partial thromboplastin times, liver function, and renal function tests were all within the normal range. T1-weighted (T1WI) and contrast-enhanced magnetic resonance imaging (MRI) images of the spine showed a mass (9.9×5.8×4.0 cm) on the left side of S3-S5 sacral vertebrae with a clear margin and hyperintense enhancement (arrow, **Figure 1A-C**). A computed tomography (CT)-guided biopsy was performed on the mass and the hematoxylin and eosin (H&E) staining showed diffuse infiltration of small primitive cells among the trabecular bone. The cells were morphologically identical and were round, oval, or irregular in shape. The cells had delicate chromatin and small nucleoli, and only a small proportion of cells underwent mitosis (**Figure 2A** and **2B**).

The immunohistochemical staining results were as follows: cluster of differentiation (CD)3 (-), CD20 (-), CD34 (-), CD99 (+), CD117 (+), CD235a (-), myeloperoxidase (MPO) (+), Vimentin (-), CK (-), leukocyte common antigen (LCA) (-), terminal deoxynucleotidyl transferase (TdT) (-), Fli-1 (-), insulin-like growth factor II mRNA-binding protein 3 (IMP3) (-), and a Ki67 index of 15% (**Figure 2C-G**, for CD20, CD34, CD99, CD117, and MPO, respectively). No evidence of AML, chronic myeloid leukemia (CML), myelodysplastic syndrome (MDS), or myeloproliferative neoplasm (MPN) was found in the bone marrow aspirate (**Figure 2H**). The diagnosis of isolated myeloid sarcoma of the sacral vertebrae was then established.

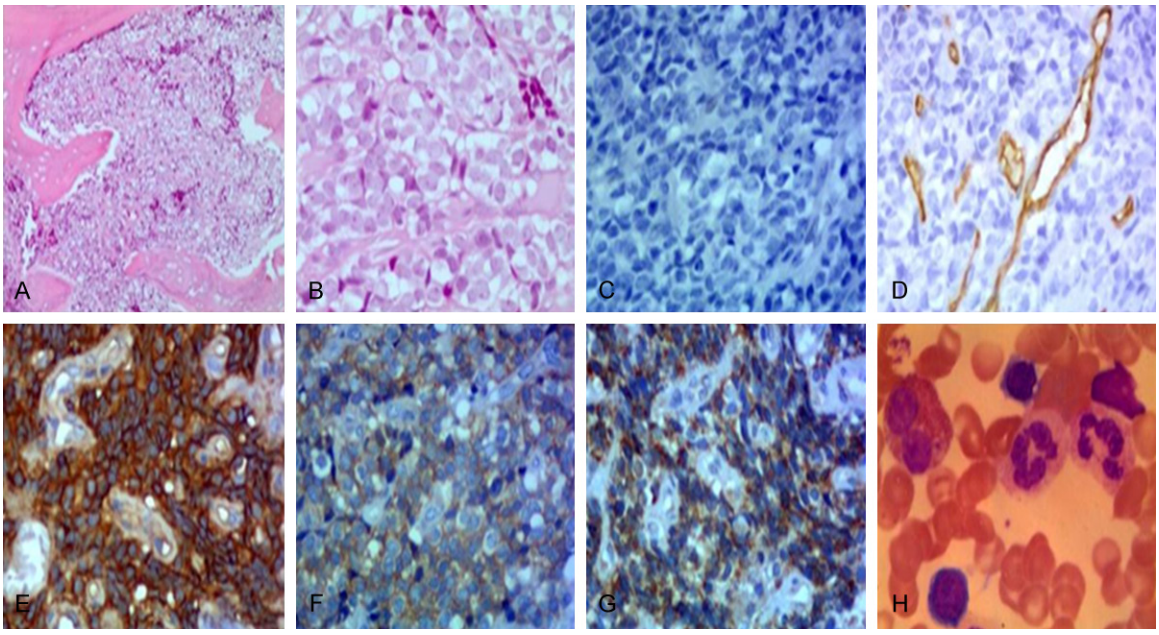

Figure 2. H&E and immunohistochemical analyses of the MS (A-G) and the bone marrow aspirate examination (panel H) of the patient. The neoplastic cells were small primitive cells, which diffused among the trabecular bone (A, original magnification ×10). The cells had larger nuclei, delicate chromatin, and small nucleoli. Only a small number of the cells underwent mitosis (B, original magnification ×40). Immunohistochemical staining revealed that the cells were negative for CD20 (C) and CD34 (D), but positive for CD99 (E), CD117 (F), and MPO (G) (original magnification ×40, respectively). The bone marrow aspirate examination revealed no evidence of AML, MDS, and MPN (H, original magnification ×100). H&E, hematoxylin and eosin; CD, cluster of differentiation; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasms; MPO, myeloperoxidase.

On the 10th day after admission, the patient received induction chemotherapy with an idarubicin and cytarabine induction regimen (10 mg/m^2/day of idarubicin on day 1-3 and 100 mg q12h of cytarabine on day 1-7). During chemotherapy, the symptoms gradually disappeared, and the patient was able to walk with assistance. One month later, she received another cycle of chemotherapy with the same regimen. The repeated MRI scan revealed that the tumor was shrunk remarkably (arrowheads, **Figure 1D-F**). The repeated bone marrow aspirate still showed no evidence of AML, CML, MPN, or MDS (data not shown). About 2 months later, the patient received one cycle of consolidation chemotherapy with high-dose cytarabine regimen (2 g/m^2 q12h on days 1, 3, and 5). She was scheduled for a second cycle of consolidation chemotherapy with the same regimen, followed by local radiation therapy. However, the patient voluntarily stopped both treatments due to financial constraints. Seven weeks later, she was readmitted due to pain on the left lower extremity for 5 days. MRI scan showed a greater extent of the lesion on the sacral vertebrae as compared with the previous result. The repeated bone marrow aspirate still revealed no evidence of AML, CML, MPN, or MDS. Therefore, the progress of isolated MS was considered, and the patient received one cycle of chemotherapy with mitoxantrone (10 mg/d, on days 1-3), cytarabine (100 mg q12h, on days 1-7) and etoposide (0.1 g/d, on days 1-5) regimen. The patient was discharged after the pain was significantly relieved. Although the patient was advised to receive local radiotherapy as soon as possible, she did not receive any further treatment due to financial constraints. The patient died 13 months after first symptom.

Discussion

Isolated MS involving the spine is extremely rare. Movassaghian et al. have analyzed 345 cases of isolated MS in the Survival, Epidemiology, and End Results (SEER) database, and demonstrated that there are only 4 cases of isolated MS involving vertebral column (1.17%, 4/339) and 2 cases involving spinal

cord (0.59%, 2/339) [3]. Our comprehensive literature search found that only 8 cases of isolated MS involving the spine have been reported thus far (**Table 1**) [6-11].

Isolated MS involving the spine are associated with or without bone involvement or bone destruction [6]. Isolated MS can be manifested with various symptoms depending on the tumor size and primary tissue/organ, which makes the diagnosis challenging. It has been reported that up to 47% of MS cases are misdiagnosed [12]. The differential diagnosis for MS includes, but not limited to, blastic plasmacytoid dendritic cell neoplasm, extramedullary hematopoiesis, medulloblastoma, melanoma, undifferentiated carcinoma, non-Hodgin's lymphoma, neuroblastoma, small undifferentiated round cell tumors, lymphoblastic leukemia, primitive neuroectodermal tumor, Ewing's sarcoma, and rhabdomyosarcoma [13, 14]. Histological examination is crucial for MS diagnosis. The histological characteristics can vary for MS diagnosis according to the degree of myeloid differentiation. Typically, MS consists of myeloblasts and granulocytic cells, and the enlarged neoplastic cells [14]. If developed concurrently with AML, the cell lineage of MS would be similar to leukemia.

In addition to H&E staining, immunohistochemical analysis is the most important method for the diagnosis of MS. The markers of MS include CD4, CD30, CD34, CD56, CD61, CD68, CD99, CD117, MPO, lysozyme, CD68-KP1, TdT, and glycophorin A [15, 16]. Intracellular staining of MPO is an effective method for the diagnosis of MS and differential diagnosis from other tumors [17]. Notably, MPO maybe not expressed in some monocytic or poorly differentiated MS [18]. The markers MPO, CD3, CD20, and CD79A should be used for differential diagnosis. In our patient, the MS cells expressed MPO, CD99, and CD117 but did not express CD34, CD3, and CD20, making the diagnosis straightforward without evidence of leukemia or clinical history.

It has been shown that patients with MS involving the bone or nerve system have a short 6-month overall survival as compared with those involving other sites [3]. As shown in **Table 1**, 4 cases of isolated MS involving the spine died within one year after disease onset. Currently, there is no consensus on the optimal treatment for isolated MS [19]. Nearly half of isolated MS will develop into medullary AML within approximately 5-11 months after the diagnosis of MS [20]. Thereby, the remission induction chemotherapy regimen is usually the same as that of medullary AML [21]. Alternatively, surgical resection or local radiotherapy could be used for induction. Nevertheless, these treatments cannot delay disease progression [22]. The systemic cytarabine-based chemotherapy can retard disease progression and improve the overall survival as compared with local therapy [23]. As shown in **Table 1**, chemotherapy is the most common treatment for isolated MS involving the spine. In our patient, an AML-type regimen was used for induction chemotherapy, and the patient responded well. After two cycles of treatment, all the symptoms disappeared and the mass size was significantly reduced. In addition, the patient tolerated well the high-dose cytarabine consolidation, thus was scheduled for a second cycle of the same regimen. Unfortunately, the patient could not continue therapy due to financial constraints. These findings suggested that the prognosis of isolated MS involving the spine is poor. Without standardized chemotherapy and radiotherapy, the patient is likely to die within a couple of months after the disease onset, even without evidence of progression to AML.

In addition to chemotherapy and radiotherapy, allogeneic hematopoietic cell transplantation (HCT) is also used to treat isolated MS. It has been shown that patients with isolated or leukemic MS receiving allogeneic HCT had longer median survival time [24]. Widhalm *et al*. have reported that in an isolated MS case involving brain and spinal cord, the patient receiving combined treatment of radiotherapy, chemotherapy and allogeneic bone marrow transplant had a disease-free survival of 7 years [10].

In conclusion, the prognosis of isolated MS involving the spine is poor. Our patient responded well to the cytarabine and anthracycline-based induction regimen and tolerated the high-dose cytarabine-based consolidation regimen, which could provide a reference for standardized chemotherapy for isolated MS.

Acknowledgements

This study was supported by the grants from the Ministry of Education, the People's republic of China, and from the Science and Information Bureau of Tianhe District, Guangzhou, Guangdong, China (grant number 201404KW003).

Table 1. Literature review of isolated myeloid sarcoma involving the spine

Organ involved	Age (years)	Gender	Treatment	Outcome after diagnosis	Published date	Reference
Cervical, thoracic and lumbar spine	22	M	Radiotherapy, chemotherapy	Died	2010	[6]
Cervical spine	43	F	Radiotherapy, chemotherapy	Died, 2 months	2010	[6]
Thoracic spinal canal	33	F	Operation	Died, 6 days	2016	[7]
Multiple sites: orbit, ear, brain, and spinal cord	15	M	Chemotherapy	AML, 6 months	2018	[8]
Multiple masses in the thoracic sacral spinal canal	27	M	Chemotherapy	Alive, 9 months	2017	[11]
Multiple masses in the lumbar and sacral spinal canal	54	M	Surgical resection, chemotherapy	Alive, 22 months after the second surgery	2017	[11]
Brain, lumbar spinal canal	27	M	Surgical resection, radiotherapy, Chemotherapy	Alive well, 2 years	2015	[9]
Brain, spinal cord	35	F	Chemotherapy, radiotherapy, Allo-BMT	Disease-free survival, 7 years	2006	[10]

M, male; F, Female. Allo-BMT, allogeneic bone marrow transplantation.

Disclosure of conflict of interest

None.

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