Leukemia – Lymphoma and Myeloma

Spine Myeloid Sarcoma: A Case Series with Review of Literature

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Abstract

Myeloid sarcoma (MS) is a malignant extramedullary tumor consisting of immature cells of myeloid origin. It may precede, present concurrently or follow acute myeloid leukemia (AML) in de novo case or may also be present and might be the only manifestation of recurrent AML, myelodysplastic syndrome, or chronic myeloid leukemia. It frequently involves skin, orbit, bone, peristeme, lymph nodes, and gastrointestinal tract, soft tissue, central nervous system, and testes. Because of its different localization and symptoms, and the lack of diagnostic algorithm, MS is a real diagnostic challenge particularly in patients without initial bone marrow involvement. The correct diagnosis of MS is important for optimum therapy, which is often delayed because of a high misdiagnosis rate. We reported three cases of MS derived from spine presented with back pain, paraplegia, paraparesis, respectively, and reviewed the relevant literature.

Keywords

► acute myeloid leukemia
► chronic myeloid leukemia
► granulocytic sarcoma
► myelodysplastic syndrome
► myeloid sarcoma

Introduction

In 1811, myeloid sarcoma (MS) was described for the first time by Burns. Afterward, in 1853, King called the disease chloroma due to its greenish appearance.¹ MS, also known as granulocytic sarcoma, is an extramedullary tumor composed of mature or immature myeloid blast cells.² According to the World Health Organization, MS is categorized as a subtype of acute myeloid leukemia (AML).³ 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 nonleukemic MS.⁴ The isolated MS is a rare disease with an incidence of 2 in 1,000,000 adults,⁵ accounting for only 0.7% of all AML cases.⁶ According to a large study of 746 patients in a national dataset,⁷ isolated MS may develop at any anatomical site, and the most common site is the soft tissues (31.3%). By contrast, only 4.9 to 6.6% of isolated MS are derived from the bone.⁸ Especially, isolated MS involving the spine is extremely rare. Here, we report three cases of MS from spine presented with back pain, paraplegia, paraparesis, respectively, and review the relevant literature. This study was approved by the institutional review board.

Case 1

A 47-year-old male presented with back pain radiating to right lower limb for the last 6 months. He also complained of anorexia and weight loss of ~5 kg. Physical examinations revealed that mild-to-moderate tenderness on sacral region and pelvis showed presence of ill-defined lytic lesion with soft tissue component measures 112 × 86 × 155 mm, which involves adjacent paraspinal muscles from L4 to S5 vertebrae on left side (– Fig. 1A–C). Biopsy of lesion revealed MS on immunohistochemistry. Bone marrow was normocellular
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for only 0.7% of all AML cases. 4 According to a large study of acute myeloid leukemia (AML). 3 The MS can arise before the diagnosis of intramedullary AML without evidence of blood or bone marrow disease, which is defined as isolated, blood or bone marrow disease, which is defined as isolated, the diagnosis of intramedullary AML without evidence of tissues (31.3%). By contrast, only 4.9 to 6.6% of isolated MS cases are misdiagnosed. 9 Movassaghian et al have analyzed 345 cases of isolated MS involving vertebral column (1.17%, 4/339) and two cases involving spinal cord (0.59%, 2/339). 9 Our comprehensive literature search found that

with no high-risk cytogenetic (¬ Fig. 2A–D). The patient received induction chemotherapy with cytarabine and an anthracycline. The combination is a 5-day continuous infusion of cytarabine at the dosage of 100 mg/m² per day on days 1 to 5 and daunorubicin at 60 mg/m² per day on days 1 and 2 due to poor performance status of patient (significant weight loss). During chemotherapy, the symptoms gradually disappeared, and the patient was able to walk without support. Magnetic resonance imaging (MRI) scan revealed that residual shrunken lesion. Later, the patient received four cycles of consolidation chemotherapy with high-dose cytarabine regimen (2 g/m² q12h on days 1, 3, and 5) followed by local radiation therapy.

Case 2

A 24-year-old male presented with inability to move both lower limbs for the last 15 days. Physical examination revealed paraplegia with loss of sensation in both lower limbs. Blood reports showed hemoglobin of 7.8 g/dL, white blood cell of 102.4 x 10³ cells/µL, platelet of 540 x 10³ cells/µL. MR DL spine showed altered marrow signal intensity lesion involving D4-D7 vertebral body. Bone marrow was hypercellular marrow consistent with chronic myeloid leukemia chronic phase (CML-CP). The Philadelphia chromosome (translocation 9; 22) was present on karyotype and fish (9, 22) positive for BCR-ABL fusion. The patient treated with D4-D7 laminectomy surgery followed by radiation of 15 fractions with total dose of 30GY. Imatinib 400 mg was started and patient was monitored regularly on outpatient department basis.

Case 3

A 32-year-old female presented with bilateral lower limb weakness for the last 2 months. Physical examinations revealed paraparesis. Blood reports including complete blood count, renal function test, and liver function test were normal. MR DL spine showed altered narrow signal intensity lesion involving D6-D8 vertebral body. Bone marrow was normocellular with no high-risk cytogenetic. Patient treated with 7 + 3 induction chemotherapy combination is a 7-day continuous infusion of cytarabine at the dosage of 100 mg/m² per day on days 1 to 7 and daunorubicin at 60 mg/m² per day on days 1 to 3. Then patient operated with D6-D8 laminectomy followed by local radiation therapy 15 fractions with total dose of 30GY and achieved positron emission tomography-computed tomography complete remission. The patient received four cycles of consolidation chemotherapy with high-dose cytarabine regimen (2 g/m² q12h on days 1, 3, and 5) (¬ Tables 1 and 2).

At the 24-month follow-up, three patients reported complete relief of back pain and lower limb weakness. X-rays showed that the overall spine alignment was intact and there was no evidence of a recurrent lesion. MRI showed no evidence of compressive or remnant lesion.

Discussion

MS is classified according to the predominant cell type (blastic, monoblastic, and myelomonocytic). MS can have different clinical presentations. MS can appear simultaneously with AML. Isolated MS involving the spine is extremely rare. Isolated MS involving the spine is associated with or without bone involvement or bone destruction. 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. Movassaghian et al have analyzed 345 cases of isolated MS in the survival, epidemiology, and end results database, and demonstrated that there are only four cases of isolated MS involving vertebral column (1.17%, 4/339) and two cases involving spinal cord (0.59%, 2/339). Our comprehensive literature search found that

Fig. 1 (A–C) Computed tomographic scan of thorax, abdomen, and pelvis showed presence of ill-defined lytic lesion with soft tissue component measures 112 × 86 × 155 mm, which involves adjacent paraspinal muscles from L4 to S5 vertebrae on left side.

Fig. 2 (A and B) High-power view shows round cells with vesicular nuclei, small nuclei, and scanty cytoplasm; few eosinophilic precursors are also seen and lower-power view showing diffuse infiltration by small-to-medium round cells. (C, D) MPO immunohistochemistry stain positive and CD 13 stain positive.
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 of myeloid origin. It may precede, present concurrently or follow acute myeloid leukemia. It frequently involves skin, orbit, bone, periosteum, lymph nodes, and gastrointestinal tract. The markers of MS include CD4, CD30, CD34, CD56, CD61, CD68, MIB1-, desmin, vimentin, LCA, and CD13 (MPO), CD30, CD43, and CD99.

There is no consensus on the optimal treatment for isolated MS. The isolated MS is a rare disease with an incidence of 2 in 1,000,000 adults, accounting for only 0.7% of all AML cases. According to a large study of 746 patients in a national dataset, isolated MS may develop as a result of progression to AML. In addition to chemotherapy and radiation therapy, surgery could be used for induction. Nevertheless, these treatments cannot delay disease progression. The systemic cytarabine-based chemotherapy can retard disease progression and improve the overall survival as compared with local radiation. It has been shown that patients with MS involving the bone or nerve system have a short 6 months overall survival as compared with those involving other sites. Currently, there is no consensus on the optimal treatment for isolated MS. Nearly half of isolated MS will develop into medullary AML within ~5 to 11 months after the diagnosis of MS. The induction chemotherapy regimen is usually the same as that of medullary AML. Alternatively, surgical resection or local radiotherapy could be used for induction. Nevertheless, these treatments cannot delay disease progression. The systemic cytarabine-based chemotherapy can retard disease progression and improve the overall survival as compared with local therapy.

### Table 1 Demographic and clinical features

<table>
<thead>
<tr>
<th>Sl. no</th>
<th>Age (year)</th>
<th>Sex</th>
<th>Presentation</th>
<th>Physical examination</th>
<th>Systemic examination</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>M</td>
<td>Back pain radiating to right lower limb, anorexia and weight loss of ~5 kg for the last 6 months</td>
<td>Tenderness on sacral region with a very mild bulging with firm consistency</td>
<td>No hepatosplenomegaly</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>M</td>
<td>Bilateral lower limb weakness and low-grade fever for the last 15 days</td>
<td>Paraplegia</td>
<td>Hepatosplenomegaly</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>F</td>
<td>Bilateral lower limb weakness for the last 2 months</td>
<td>Paraparesis</td>
<td>No hepatosplenomegaly</td>
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### Table 2 Histopathology, immunohistochemistry, imaging, and treatment

<table>
<thead>
<tr>
<th>Sl. no</th>
<th>Bone marrow aspirate biopsy</th>
<th>Biopsy with immunohistochemistry</th>
<th>CD marker positive</th>
<th>Imaging</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>1</td>
<td>Normocellular bone marrow</td>
<td>L4 to S5 vertebral bone lesion s/o diffuse infiltration of small primitive cells among the trabecular bone. Sections show high-grade malignant neoplasm comprising of sheets of rounded malignant cells with moderate eosinophilic cytoplasm, central to eccentric nuclear with prominent nucleoli, background eosinophilic, extensive necrosis and apoptosis</td>
<td>Myeloperoxidase (MPO), CD30, CD34, LCA) and CD13</td>
<td>Computed tomographic (CT) scan of thorax, abdomen and pelvis showed presence of ill-defined lytic lesion and soft tissue component measures 112x86x155 mm, which involves L4 to S5 vertebrae on left side</td>
<td>Cytarabine 100 mg/m²/day for 5 days and daunorubicin at 60 mg/m²/day for 2 days f/b consolidation chemotherapy and radiation</td>
</tr>
<tr>
<td>2</td>
<td>Hypercellular marrow consistent with chronic myeloid leukemia chronic phase (CML-CP)</td>
<td>D4-D7 vertebral bone lesion s/o malignant round cell tumor infiltrating bone and soft tissue</td>
<td>LCA, CD43, CKit (CD 117), CD68, MIB1-60–70 %</td>
<td>MR DL spine altered marrow signal intensity lesion involving D4–7 vertebral body</td>
<td>D4-D7 laminectomy followed by radiation with imatinib 400 mg daily</td>
</tr>
<tr>
<td>3</td>
<td>Normocellular bone marrow</td>
<td>D6-D8 vertebral bone lesion s/o malignant round cell tumor infiltrating bone and soft tissue</td>
<td>LCA, MPO, vimentin, CD99, desmin, CD68</td>
<td>MR DL spine altered marrow signal intensity lesion involving D6–8 vertebral body</td>
<td>7+3 induction chemotherapy D6-D8 laminectomy followed by radiation followed by consolidation chemotherapy</td>
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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 allageneic HCT had longer median survival time.26 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.13 MS as the initial presentation of CML-CP may be a unique subset of CML and the prognosis is unclear due to the rarity of the disease. However, considering that the treatment of MS is based on chemotherapy protocols of underlying leukemia, the prognosis of our case is expected to be better since the CML-CP is well controlled with only imatinib treatment. Further, in the tyrosine kinase inhibitors era, the overall survival of CML in the medullary blast phase, as well as CML patients with MS, has improved.25 Despite the rarity of the disease and diagnostic difficulty for clinician, MS can be correctly diagnosed with strong clinical suspicion and adequate panels of immunohistochemical stains. The bone marrow aspiration, cytogenetic study, and molecular analysis are also mandatory for the synchronous AML or CML. Systemic chemotherapy should be administrated shortly once the diagnosis confirmed. A local treatment for MS such as radiation therapy or surgical resection has been found less effective than chemotherapy at improving the disease-free interval. Since its pathogenesis and genomic landscape are not well understood, the prognosis remains dismal, even in the novel agent era.

Conclusion

In conclusion, isolated MS is a rare and unique entity of myeloid neoplasm. Therefore, each case description is fundamental to provide a better knowledge about this rare malignancy. Further prospective studies are necessary for stratification of the role of chromosome and genetic abnormality and the treatment outcomes. To fully understand the characteristics of isolated MS, a larger number of patients in a multinstitutional study are necessary to identify novel and selected treatments.

Conflicts of Interest

The authors declare that they have no conflicts of interest

References