



# Isolated Myeloid Sarcoma of Femur in an Aleukemic Child: Case Report

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## Abstract

Myeloid Sarcoma (MS) is a tumour mass consisting of myeloid blasts, with or without maturation, occurring at an anatomical site other than the bone marrow. It can develop de novo, as well as occurs following a hematologic disorder such as acute myeloid leukemia, myeloproliferative disorder or myelodysplastic syndrome. In this report, we present the radiologic and pathologic findings of a case diagnosed as isolated MS of femur. According to our literature research, this is the first case of isolated MS of femur in an aleukemic patient. MS is a rare neoplasm with diagnostic difficulty owing to its similarity to many other tumors and by the lack of clinical suspicion in patients without any hematological disorder. Histopathological and a detailed immunohistochemical work-up is mandatory for accurate diagnosis of MS to avoid delay in treatment.

**Keywords:** Myeloid sarcoma; Aleukemic; Femur; Child

## Introduction

Myeloid Sarcoma (MS) is a rare neoplasm composed of proliferation of myeloid precursors at extramedullary sites such as skin, lymph node, bone and soft tissue, although it can arise at every site of the body [1-3]. It may develop spontaneously or can be seen simultaneously with hematopoietic disorders such as Acute Myeloid Leukemia (AML), Myeloproliferative Disorder (MPD) or Myelodysplastic Syndrome (MDS). MS can also be the first evidence of AML or progress to AML over months to years. It may even present as the first manifestation of a recurrence of previously treated AML in remission [2]. MS is defined as non-leukemic or isolated when Bone Marrow (BM) biopsy shows no evidence of hematological malignancy [1,4].

Because MS can develop in different regions of the body, the clinical manifestations of MS vary with signs and symptoms specific to the site of occurrence. Symptoms are generally secondary to the mass effect of the tumor [1]. In patients without pre-existing hematological disorders, the patients with MS is often misdiagnosed or generally delayed due to a lack of suspicion. Morphologically, it can mimic small round cell tumors, thus adding to the diagnostic challenge [1,2,5].

Herein, we aimed to present a case of MS diagnosed in a 15-year-old girl with a distal femur mass. On extensive clinical work-up, no accompanying hematological malignancy was put forward. So, the patient was accepted as isolated MS of femur without leukemic involvement. To the best of our knowledge, this is the first case determined as isolated MS of femur.

## Case Presentation

A 15-year-old girl was admitted to orthopedics clinic of our hospital with complaint of swelling and pain on her left knee. On physical examination, there was swelling and tenderness on palpation. The patient had no history of recent trauma.

An X-Ray was advised, which revealed a mass lesion in left knee region. On plain radiography, an intramedullary radiolucent lesion that extends from the femur distal diaphyseal to the metaphyseal section with no cortical destruction was detected (Figure 1a). On Magnetic Resonance Imaging (MRI), the lesion was measured 47 mm × 43 mm × 40 mm and observed as hyperintense in T2-weighted sequences (Figure 1b, 1c) and hypointense in T1-weighted sequences (Figure 1d) with marked contrast enhancement in the lesion in contrast-enhanced MRI and subtracted images (Figure 1e, 1f). There was diffusion restriction in the lesion and it was observed as hyperintense in diffusion-weighted imaging (Figure 2a) and hypointense in Apparent Diffusion Coefficient (ADC)

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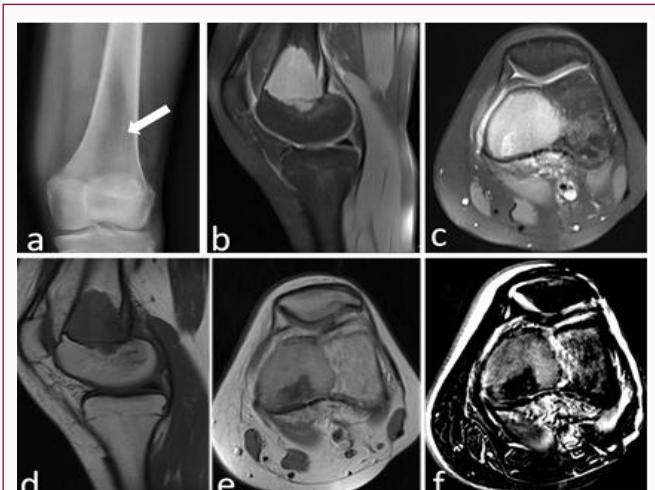
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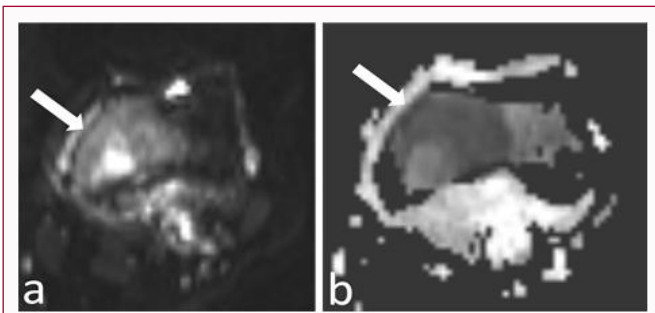
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**Figure 1:** A-P plain radiography (a) shows an intramedullary radiolucent lesion (arrow) that extends from the femur distal diaphyseal to the metaphyseal section, whose borders cannot be clearly identified, has a wide transition zone and does not cause cortical destruction. The lesion is observed as hyperintense in T2-weighted sequences (b, c) and hypointense in T1-weighted sequences (d) on magnetic resonance imaging. In contrast-enhanced magnetic resonance imaging (e) and subtracted images (f), there is a marked contrast enhancement in the lesion.



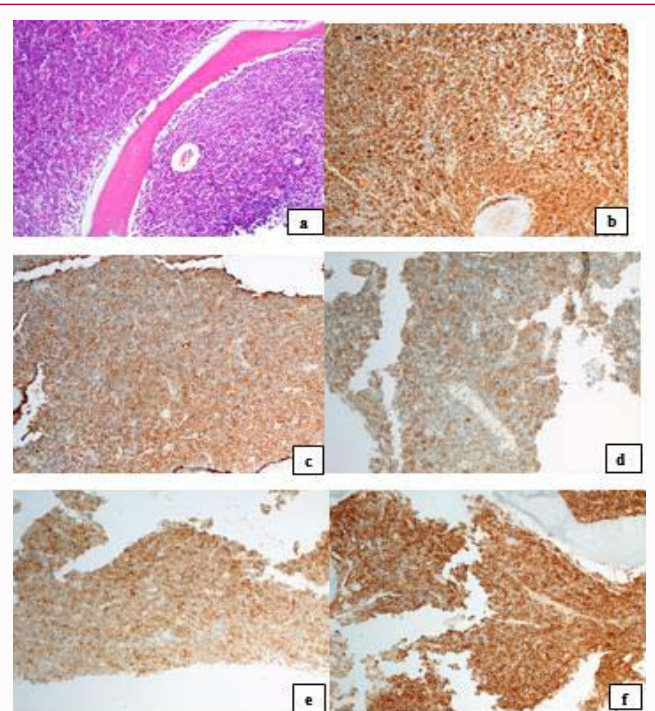
**Figure 2:** There is diffusion restriction in the lesion (arrow), the lesion is observed as hyperintense in diffusion-weighted imaging (a) and hypointense in apparent diffusion coefficient (ADC) mapping (b).

mapping imaging (Figure 2b).

Following these findings, a core needle biopsy was performed. On pathologic examination; a tumor diffusely infiltrating bone composed of cells with round to oval, pale staining nuclei and scant cytoplasm was observed (Figure 3a). Differential diagnosis included many entities such as Ewing sarcoma, rhabdomyosarcoma, lymphoma, leukemia, plasmacytoma and neuroblastoma.

An immunohistochemical panel was applied for differential diagnoses. Tumor cells were diffuse positive with Myeloperoxidase (MPO), CD68 (KP-1), CD117, CD43 and CD99, (Figure 3b-3f) and negative with CD3, CD20, CD79a, Friend Leukemia Antigen-1 (FLI-1), glycophorin-A, CD10, NKX2.2, terminal deoxynucleotidyl Transferase (Tdt), CD34, CD56, CD138, Lambda, Kappa, synaptophysin and myogenin. Depending on these results, the pathology report indicating the malignant cells could be a leukemic infiltration and suggesting a clinical work-up was established.

Thereafter, a peripheral blood film and BM biopsy were performed. No blasts were detected in peripheral blood film and there was not a leukemic infiltration on BM biopsy. In the light of these findings, the final diagnosis was ‘Myeloid sarcoma’.



**Figure 3:** Tumor cells with round to oval, pale staining nuclei and scant cytoplasm diffusely infiltrating bone (a, Hematoxylin-Eosin x200). Immunohistochemical staining of the tumor cells with MPO (b), CD68 (c), CD117 (d), CD43 (e) and CD99 (f). (x200).

The patient then admitted to child oncology department and chemotherapy with daunorubicin and cytarabine was began.

### Discussion

Myeloid sarcoma, also known as chloroma or granulocytic sarcoma is a rare solid tumor composed of primitive precursors of the granulocytic series of white blood cells that include myeloblasts, promyelocytes, and myelocytes. It was first described by Burns in 1811. Due to the green color of typical forms caused by high levels of myeloperoxidase in these immature cells, King called it chloroma [1,6].

Isolated MS is a rare manifestation known as non-leukemic MS and is defined as the infiltration of myeloblastic tumor cells in one or more extramedullary organs. In these patients, there is no evidence of leukemia in the peripheral blood or BM [7]. Infiltration of any site of the body by myeloid blasts in a patient with leukemia is not classified as myeloid sarcoma unless it presents with tumour masses in which the tissue architecture is effaced [8].

MS can also be the first evidence of AML or progress to AML over months to years [2]. The period between initial diagnosis of isolated MS and development of AML varies from 0.5 to 24 months (median 3 to 9 mo) [7,9].

In our literature research, we encountered many different sites of involvement by MS including ovary [3], small intestine [9], brain [10], orbita [11], gastric [12], lymph node [13], mediastinum [14], larynx and nasopharynx [15] and epidural region [16]. Additionally, some reports determined bone involvement by MS including finger [17], temporal bone [1,18], pelvic bones [19], spine [5,20] and knee [21]. To the best of our knowledge, this is the first case determined as isolated MS of femur.

The diagnosis of MS may sometimes be challenging, particularly in the absence of known hematological disorder [1]. About 46% to 75% of MS cases are initially misdiagnosed, most commonly as a malignant lymphoma or even as non-hematopoietic tumors [7]. Because of the limitation of diagnosis by conventional light microscopy, immunohistochemical analysis is important to make differential diagnosis and establish accurate final diagnosis [1,7,16]. In differential diagnosis; small round blue cell tumors such as lymphoma, poorly differentiated carcinoma, rhabdomyosarcoma and metastatic neuroblastoma have to be included.

CD68 (KP1) is the most frequently expressed marker in MS, followed by MPO, CD117, CD99, CD68 (PGM1), lysozyme, CD34, Tdt, CD56, CD61/linker of activated T lymphocyte/factorVIII related antigen, CD30, glycophorin A, and CD4. CD99 positivity in MS can cause diagnostic confusion with small round blue cell tumors [1]. In our case, tumor cells were positive with CD99, CD117, CD43, MPO and CD68 (KP-1).

Our differential diagnosis included Ewing sarcoma, lymphoma, rhabdomyosarcoma and metastatic neuroblastoma. We ruled out Ewing sarcoma depending on negativity of NKX2.2 and FLI-1, lymphoma with negativity of CD3, CD20 and CD79a, rhabdomyosarcoma with negativity of myogenin and neuroblastoma with negativity of synaptophysin. Although it is extremely rare in pediatric population, a plasmacytoma was also a possible differential and ruled out depending on CD138, Lambda and Kappa negativity.

From a prognostic point of view, *de novo* MS is sensitive to radiotherapy or chemotherapy and survival is longer. In contrast, the prognosis is worse in the presence of MPD, MDS or AML accompanying MS. However, recent studies suggest that highly specific medications or aggressive treatment regimens should be used to achieve stable remission and cure in MS. To date, no definitive conclusion has been made regarding the optimal treatment of MS [2]. After two months of the initial diagnosis, our patient is still under chemotherapy treatment with daunorubicin and cytarabine and doing well.

In conclusion; MS is a rare neoplasm with diagnostic difficulty owing to its similarity to many other tumors and by the lack of clinical suspicion in patients without any hematological disorder. Histopathological and a detailed immunohistochemical work-up is mandatory for accurate diagnosis of MS to avoid delay in treatment.

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