Case Report
Assessment of PET/CT in multifocal myeloid sarcomas with loss of TET2: a case report and literature review

Yu Pan1,2, Yongguang Tao1,3,6,7,8, Chunyan Fu1,2, Jiantao Jia3,4, Shuang Liu5, Desheng Xiao1,2

1Department of Pathology, Xiangya Hospital, Central South University, Changsha 410078, Hunan, China; 2Department of Pathology, School of Basic Medicine, Central South University, Changsha 410078, Hunan, China; 3Cancer Research Institute, Central South University, Changsha 410078, Hunan, China; 4Department of Pathophysiology, Changzhi Medical College, Changzhi 046000, Shanxi, China; 5Center for Medicine Research, Xiangya Hospital, Central South University, Changsha 410008, Hunan, China; 6Key Laboratory of Carcinogenesis and Cancer Invasion, Ministry of Education 410078, Hunan, China; 7Key Laboratory of Carcinogenesis, National Health and Family Planning Commission 410078, Hunan, China; 8Center for Molecular Imaging, Central South University, Changsha 410078, Hunan, China

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Abstract: Myeloid sarcoma is a rare solid tumor consisting of leukemic myeloblasts and/or myeloid precursors occurring outside the blood or bone marrow. The unique site with myeloid sarcoma has been reported, the multiple sites of myeloid sarcoma have rarely been cited in the medical literature. Here we report that the unusual clinical presentation and management of myeloid sarcoma in multiple sites with PET-CT, highlighting the utility of PET-CT was useful in detecting and monitoring myeloid sarcoma. We also found that loss of TET2 and gain of 5hmC in the case of myeloid sarcoma, indicating the mechanism for myeloid sarcoma is totally different with other hematopoietic malignancies.

Keywords: Myeloid sarcoma, PET-CT, TET2, 5hmC, MPO, CD117

Introduction

Myeloid sarcoma is a rare solid tumor consisting of leukemic myeloblasts and/or myeloid precursors occurring outside the blood or bone marrow [1]. The tumor is also regarded as chloroma or granulocytic sarcoma in extramedullary sites. Myeloid sarcoma can occur throughout the body with or without concurrent neutropenia, and they most commonly involve in the skin and soft tissue, lymph nodes, and gastrointestinal tract [2, 3]. Position emission tomography-computed tomography (PET-CT) is more effective in the detection of myeloid sarcoma than other diagnostic tools such as computed tomography (CT) or magnetic resonance imaging (MRI) [4]. The unique site with myeloid sarcoma has been reported, the multiple sites of myeloid sarcoma have rarely been cited in the medical literature. Here we report that the unusual clinical presentation and management of myeloid sarcoma in multiple sites with PET-CT.

Case report

A 12-year-old girl was admitted to our hospital due to severe pain in both lower limbs, unable to walk, and fever three days ago. She felt pain in the neck and post aurem, mild pain of four limbs half of the month ago. Five days later, the pain gradually worsened especially in the lower limb and resulted in immobility. She lost body weight of 9.5 kg within half month. On examination, an enlarged lymph node of 6 mm × 8 mm could be palpated in her right groin and there was tender pain in her sternum and bilateral iliac region. CBC showed a WBC of 12.0 × 10⁹/L, hemoglobin of 111 g/L, platelet count of 456 × 10⁹/L, neutrophils 83.3%, lymphocytes 12.4%.

Bone marrow biopsy of the patient indicated abnormal increasing of type-I cells and metastatic carcinoma. There was a diffused infiltration of immature cells with oval nuclei (Figure 1A, hematoxylin and eosin staining). Immunohistochemistry was positive for MPO (Figure 1B, CD117, Figure 1C, TET2, Figure 1D, 5hmC). The case was diagnosed as myeloid sarcoma with loss of TET2. PET-CT showed fluorodeoxyglucose uptake in the region of the lymph nodes, sternum, and iliac region. The patient was treated with chemotherapy and response was observed. Her pain gradually decreased and she was able to walk again.
1B), CD117 (Figure 1C), Ki67 (Figure 1D) and 5-hmC (Figure 1F), and negative for CD20, CD3, CD34, CD68, LCA, TdT and TET2 (Figure 1E). These findings were diagnostic for myeloid sarcoma (MS) with blastic subtype.

Color Doppler ultrasound scan of body surface and joints showed multiple lymph nodes in the right inguinal and bilateral neck. Chest Computed Tomography (CT) scan showed bone destruction of multiple thoracic vertebral body and sternum, shadows of enlarged lymph nodes in the bilateral armpits. Magnetic resonance imaging (MRI) showed abnormal signals from T1-2, T4-S2 centums and partial appendixes, collapse of T8 vertebra and marginal bone sclerosis. Position Emission Tomography-Computed Tomography (PET-CT) in Figure 2

Figure 1. Hematoxylin-eosin staining (HE staining) and immunohistochemical staining. A. HE staining; B. MPO staining; C. CD117 staining; D. Ki67 staining; E. TET2 staining; F. 5 hmC staining; × 400.
showed obvious mal-distribution of developer: evident higher location of the right seventh anterior rib than that of the left, extremely uneven distribution in the vertebrae, sparse distribution in the T6, T12 thoracic vertebra, concentrated distribution in the T8, T11 thoracic vertebra, higher density in the right iliac crest and trochanter than that of left, uneven distribution in the left ala of ilium and right femur with local abnormal increase, all indicated multiple site of myeloid sarcoma in the patient.

Discussion

Myeloid sarcoma is an uncommon neoplasm of immature myeloid cells that arises at an extramedullary site. A review of 154 reported cases of extramedullary leukemia revealed that the skin was the most common site of involvement, followed by lymph nodes, spine, small intestine, orbit, bone, breast, cervix, and nasal sinuses [2]. Although head and neck involvement such as nasal cavities, orbits, and oral cavity is common for myeloid sarcoma [3, 5, 6, 14]. The diagnostic modalities such as CT, $^{18}$F-fluorodeoxyglucose-positron-emission tomography (FDG-PET) or magnetic resonance imaging (MRI) could be helpful for detecting myeloid sarcoma [4]. PET-CT imaging is now widely used for staging and restaging of many tumor types including lymphoma, Non-small-cell lung, esophageal, colorectal, breast, head and neck cancers, and melanoma [7]. Here we firstly presented multi-extramedullary sites of bone and lymph nodes with PET-CT. In recent years, only a few cases reported using PET-CT in the assessment for the patients [4, 8], which may enable clinicians to intensify or modify the therapy.

The ten-eleven translocation (TET) gene family initially found as a chromosomal translocation partner in leukemia, turned out to be a key
enzyme for DNA demethylation [9]. TET2 is a member of the TET family of proteins that can convert 5-hydroxymethylcytosine (5 mC) to 5-methylcytosine (5 hmC) and promotes site-specific DNA demethylation. Interestingly, TET2 is a critical regulator for hematopoietic stem cell homeostasis whose functional impairment leads to hematological malignancies such as acute myeloid leukemia (AML) and myeloproliferative disorder (MPD) or myelodysplastic syndrome (MDS) [10, 15]. This patient’s tumor cells were detected and the loss of TET2 was indicated. However, we found that the level of 5hmC gained in this patient tissue, while 5hmC is always lost in these cancers, indicating the mechanism for myeloid sarcoma is totally different with other hematopoietic malignancies.

As with all myeloid sarcomas, conjunctival cases can be either present before detection of systemic leukemia or may be the first sign of a relapse. No consensus can be reached on the optimal intensity and duration of treatment of MS. Most cases favor systemic antileukemic chemotherapy despite the location of the disease. Early antileukemic induction chemotherapy might delay the progression to AML and prolong survival [11]. However, remission could not be reached for a majority of patients ultimately experience a relapse after several round of chemotherapy. Interestingly, more aggressive treatment options, such as allogeneic hematopoietic stem cell transplantation, have been shown of benefit to the overall survival and disease-free survival rates [12], but the gastric myeloid sarcoma after the allergenic stem cell transplantation usually recur and transform to acute myeloid leukemia [13].

This report illustrates that PET-CT can be useful adjunct in detecting and monitoring myeloid sarcoma. Molecular markers and cytogenetics should be obtained from these tumors, given that they may guide therapy. Moreover, other diagnostic modalities such as CT or MRI cannot be skipped, and we must utilize these diagnostic tools that complement each other.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Desheng Xiao, Department of Pathology, Xiangya Hospital, Central South University, Changsha 410078, Hunan, China; Department of Pathology, School of Basic Medicine, Central South University, Changsha 410078, Hunan, China. Tel: +(86) 731-84805448; Fax: +(86) 731-84470589; E-mail: xdsh96@21cn.com

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