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Granulocytic/myeloid sarcoma with trisomy 21 presented as an epididymal tumor: A case report and review of the literature

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Abstract

Myeloid sarcoma is an extramedullary tumor composed of immature myeloid cells and occurs in various extramedullary sites. We report a 48-year-old man diagnosed with myeloid sarcoma in the epididymis. He was admitted to our hospital due to a painless right intrascrotal mass. Magnetic resonance imaging showed a 30 mm tumor in the right epididymis, and we subsequently performed right high orchiectomy. The pathological diagnosis was myeloid sarcoma. Bone marrow aspiration and biopsy revealed no hematological disease, and cytogenetic analysis in the bone marrow showed normal karyotype. He was diagnosed with isolated myeloid sarcoma in the epididymis. Six months after the operation, myeloid sarcoma recurred in the para aorta and left sub-diaphragm. Bone marrow examination revealed myelodysplastic syndrome, and cytogenetic analysis showed 46, XY. We performed surgical resection of the recurrent mass, and cytogenetic analysis showed 47, XY, +21. He was diagnosed with recurrent MS with adult-onset trisomy 21. Although the effect of trisomy 21 on prognosis is unknown, the patient is currently undergoing systemic chemotherapy with maintained remission.

Keywords

Granulocytic/myeloid sarcoma, epididymal tumor, trisomy 21

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Introduction

Myeloid sarcoma (MS), also known as granulocytic sarcoma or chloroma, is a rare extramedullary tumor composed of immature myeloid cells.[1] MS occurs in all extramedullary sites of the body, and patients may present with various symptoms depending on tumor location and size. However, the optimal treatment of MS is not clear. Although MS may be treated by surgery, radiotherapy, and systemic treatments, such as chemotherapy or hematopoietic stem cell transplantation, the prognosis remains poor.[1] A variety of cytogenetic abnormalities have been reported in patients with MS; however, there are few reports of MS with trisomy 21.[2–4] Here, we present a case of MS occurring in the epididymis with trisomy 21 as the only acquired karyotypic abnormality.

Case report

A 48-year-old man with a painless right intrascrotal mass was admitted to our hospital. He had no past medical history of malignancy or hematologic disease. By physical examination, the mass was approximately 30 mm, hard, movable, and painless. The blood counts were within normal ranges (white blood cell, 5600 /μL; hemoglobin, 14.5 g/dL; platelet, 23.1×10^4/μL), and testicular tumor markers were all negative (lactate dehydrogenase, 164 IU/L; human chorionic gonadotropin β, <0.10 ng/mL; and alpha-fetoprotein, 2.3 ng/mL). Ultrasound examination showed a 30 mm hypervascular solid tumor in the right epididymis. By magnetic resonance imaging (MRI), the mass was observed as a faint high-signal intensity on T2-weighted

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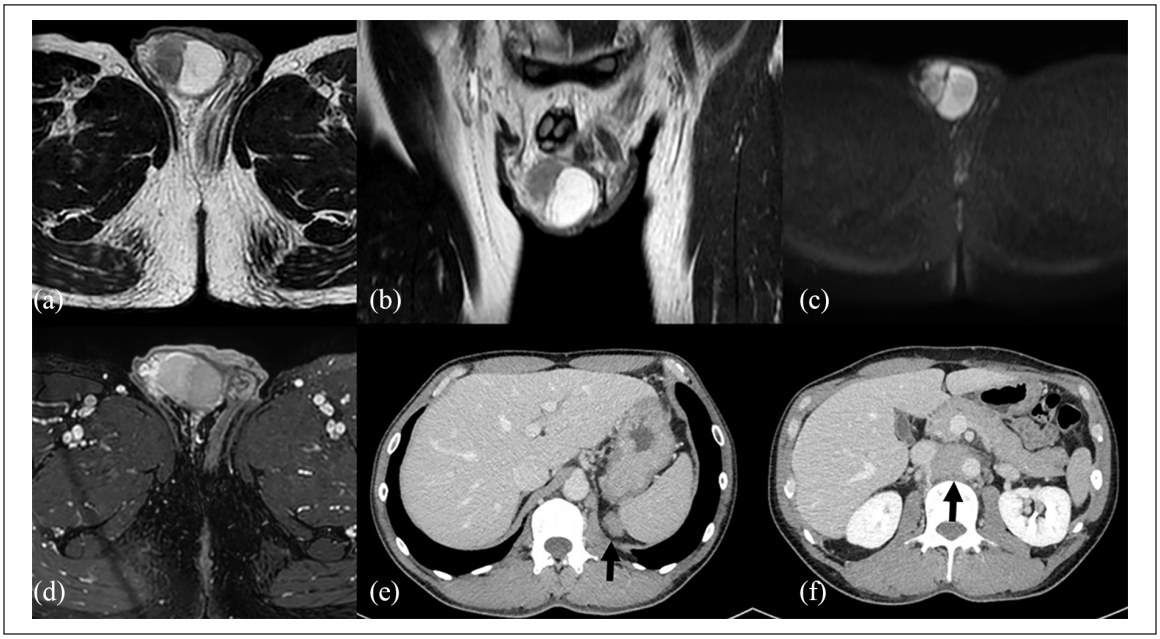

Figure 1. MRI shows the tumor in the right epididymis. The tumor is shown as a faint high-signal intensity on T2-weighted images ((a) axial image), ((b) coronal image), a high-signal intensity on diffusion-weighted images (c), and was also enhanced homogeneously (d). Abdominal CT at the time of recurrence shows the tumor located in the left sub-diaphragm (e) and para aorta (f).

images, high-signal intensity on diffusion-weighted images, and was also enhanced homogeneously (Figure 1(a)–(d)). Computed tomography (CT) scan showed no metastases or other abnormalities. For excisional biopsy and treatment, we performed right high orchiectomy. The tumor was located in the epididymis, measured approximately $30 \times 30 \times 25$ mm, and infiltrated the testis and spermatic cord. The surgical margin was positive. Histopathologic examination showed malignant cells proliferating invasively toward the seminiferous tubules. The malignant cells had monotonous structures, high nuclear-to-chromatin ratios, prominent nucleoli, scant cytoplasm, and fine chromatin. By immunohistochemistry, neoplastic cells were strongly positive for c-kit, CD43, CD34, CD45, CD7, and bcl-2. Furthermore, the cells were weakly positive for TdT, CD71, and CD68. MPO and markers for T-cells (CD3, CD4, CD5, and CD8) and B-cells (CD10, CD20, PAX5, and MUM1) were negative (Figure 2). Based on these findings, we diagnosed the tumor as MS despite few and no markers of CD68 and MPO, respectively. Bone marrow aspiration and biopsy showed normal maturation and no dysplasia. Cytogenetic analysis on the bone marrow aspiration specimen showed normal karyotype of 46, XY in all 20 cells. Therefore, the patient was diagnosed with isolated MS occurring in the epididymis.

Although there was no metastasis or residual tumor by whole-body MRI, we continued to monitor his condition.

Six months after the operation, CT showed masses in the para-aortic and left sub-diaphragm (Figure 1(e) and (f)). We suspected a recurrence of MS and performed re-biopsy of the bone marrow to determine whether it progressed to leukemia. The specimens showed a slight increase in atypical myeloid and erythroid cells as well as dysmorphic megakaryocytes. Furthermore, the myeloblast population was 2%. These findings are consistent with the characteristics of myelodysplastic syndrome (MDS). Cytogenetic analysis of the bone marrow aspiration specimen showed normal karyotype of 46, XY. We performed laparoscopic resection of the left sub-diaphragm masses. The specimen had similar histopathological characteristics as those in the epididymal tumor (Figure 2). However, cytogenetic analysis showed abnormal karyotype, 47XY, add(2)(p13), del(6)(q21q25), add(8)(p11.2), +21, in 13 of 20 metaphases examined (Supplemental Figure 1). Therefore, the patient was diagnosed with recurrent MS with adult-onset trisomy 21.

He is currently undergoing systemic chemotherapy in accordance with acute myeloid leukemia (AML) remission induction treatment with cytosine-arabinoside (100 mg/m^2 on days 1–7) and idarubicin (12 mg/m^2 on days 1–3) with maintained remission.

Discussion

MS was first described in 1811,[5] and the term MS was accepted by the World Health Organization in 2002.[6] MS occurs in 2.5%–9.1% of patients with AML[7] and may be detected simultaneously and during the course of the disease. In addition to recurrences after definitive treatment for AML, MS may also occur in the accelerated phase of chronic myeloid leukemia (CML) or MDS. Although less common, MS that does not show any signs for AML, CML, or MDS in the bone marrow, called isolated MS, has also been observed.[1] MS occurs in a variety of extramedullary sites. The most

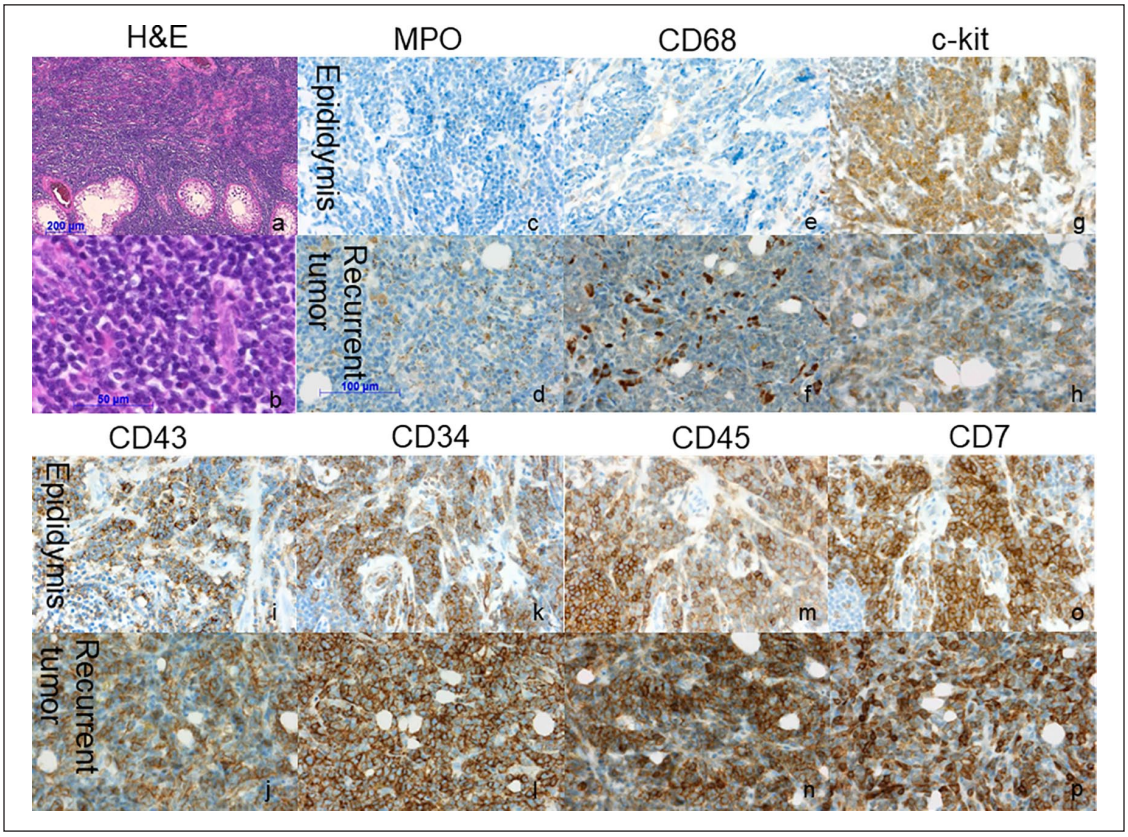

Figure 2. Pathological findings. Malignant cells proliferated invasively toward seminiferous tubules. They were shown to have monotonous structures, high nuclear-to-chromatin ratios, prominent nucleoli, scant cytoplasm, and fine chromatin. (Haematoxylin & eosin sections: (a) ×5; (b) ×20). By immunohistochemistry, the epididymis specimen was strongly positive for c-kit, CD43, CD34, CD45, and CD7l; however, it was weakly positive for CD68 and negative for MPO. The specimen from the epididymis and recurrent tumor showed similar characteristics except for MPO and CD68 stainings ((c)–(p) ×10).

common locations are the soft tissues, bone, periosteum, lymph nodes, and skin.[8–10] In a few cases, there were occurrences in the genitourinary system of both males and females such as the testis, epididymis, spermatic cord, vagina, and cervix.[4,11–13] In our case, MS occurred in the epididymis. Epididymal tumors are rare and often misdiagnosed as testicular tumors. They commonly originate from the soft tissue or mesothelial neoplasm. Cystadenomas, papillary tumors, and adenomatoid tumors are the most common; however, preoperative diagnosis is difficult.[14]

In immunohistochemistry, some key markers, such as MPO, c-kit, and CD68PG-M1, have been used in the diagnosis of MS.[2] In this case, we were able to diagnose MS based on the presence of other markers for immature myeloid cells despite the few or no markers of CD68 and MPO in the epididymal specimen. Although most markers for the recurrent tumor had similar characteristics to the primary tumor, markers of MPO and CD68 were positive in the recurrent tumor specimens. Therefore, the tumor characteristics may have changed during recurrence.

A previous report found several chromosomal aberrations, such as monosomy 7, trisomy 8, trisomy 4, trisomy 11, and monosomy 16, in 54% of patients.[2] Furthermore, cytogenetic abnormalities t(8;21) or inv(16) were often detected.[2] There are few studies regarding MS complicated with Down syndrome,[3,4] and their relevance is unclear. In our case, trisomy 21 was detected in the recurrent tumor; however, the patient had no features of Down syndrome and his bone marrow showed normal karyotype. Although discrepancies in karyotype between the bone marrow and tissue have been reported, the degree of similarity and clinical significance are still unknown and require further studies.[7]

Although the optimal treatment strategy for isolated MS has not yet been established, delayed or inadequate treatment will result in a relapse or fast progression of AML. The median time to the development of AML ranges between 5 and 12 months.[7]

A study focusing only on patients with isolated MS suggested that the incidence of AML and extramedullary relapse was significantly higher in patients initially treated by surgical resection only.[15] In addition, patients who underwent systemic therapy, chemotherapy, or hematopoietic stem cell transplantation had longer event-free survival time compared to those who did not.[15] There was no significant difference in overall survival (OS) between patients undergoing chemotherapy or surgery alone with median OS of

13 and 14 months, respectively.[15] We performed right high orchiectomy for diagnostic purposes, and 6 months after the operation, MS recurred at the para aorta and left sub-diaphragm. Furthermore, trisomy 21 was present with the recurrent tumor. Although the effect of trisomy 21 on prognosis is unknown, the patient is currently undergoing systemic chemotherapy with maintained remission.

We report a case of MS occurring in the epididymis. Although MS in this case occurred in the epididymis without any hematological disorders, MS is highly associated with hematological malignancy. MS recurred in the para aorta and left sub-diaphragm with MDS 6 months after the operation. Based on the high rate of recurrence or progression to AML, adjuvant chemotherapy should have been administered immediately. The patient is undergoing systemic chemotherapy, in accordance with AML remission induction treatment, with maintained remission.

Author contributions

M.M. and T.N. were the major contributors to the writing of the manuscript, and T.N. is the corresponding author. M.M., O.N., Y.I., Y.N., Y.S., and T.N. were involved in the care and therapy of the patient. G.H. performed histopathological examination of the specimen. T.N. reviewed and approved the final version of the manuscript. All authors read and approved the final manuscript.

Data availability

Data sharing is not applicable to this article since no data were generated or analyzed during this study.

Declaration of conflicting interests

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Informed consent

Written informed consent was obtained from the patient to publish this case report and all accompanying images.

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Supplemental Material

Supplemental material for this article is available online.

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