Testicular myeloid sarcoma: a relapse of acute myeloid leukaemia after allogeneic peripheral blood stem cell transplantation- a rare presentation

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SUMMARY

Myeloid sarcoma is an uncommon pathological diagnosis of proliferation of blasts of one or more of the myeloid lineages in regions other than the blood and bone marrow. Myeloid sarcoma of the testis after allogeneic bone marrow stem cell transplantation is very rare and only few cases are reported in the literature. It is usually misdiagnosed as malignant lymphoma, particularly with large cell lymphoma, due to similar histological morphology. Due to difficulty in diagnosis, it is suggested that an appropriate panel of immunohistochemical marker studies be performed in conjunction with clinical correlation to avoid misleading diagnosis and improper treatment of patients. We report an interesting case of a 49-year-old man with a diagnosis of acute myelogenous leukaemia. He had undergone allogeneic peripheral blood stem cell transplantation, achieved complete molecular remission and later relapsed with myeloid sarcoma of the testis.

BACKGROUND

Myeloid sarcoma is also known as chloroma due to its green colour attributed to the presence of myeloperoxidase enzyme expression.[1] It has been reported in 2%–8% of patients with acute myeloid leukaemia (AML) and is commonly diagnosed simultaneously with AML.[2] Myeloid sarcoma may also be associated with myeloproliferative neoplasm or myelodysplastic syndrome.[3–5] Occasionally it may present as an initial manifestation of AML, precede by months or years, or as relapse of a previously treated AML in remission.[6] The most common sites of involvement of myeloid sarcoma include the skin, bone, lymph node and soft tissues.[7] The testicles are considered a rare site.[8–10] Lately, there has been an increase in reports of myeloid sarcoma presentation after allogeneic stem cell transplantation, manifesting as an isolated disease or accompanying bone marrow relapse.[11] A European bone marrow transplantation retrospective analysis reported myeloid sarcoma in less than 1% of transplanted patients occurring 4–56 months after stem cell transplantation.[12 13] The present study reports a patient presenting with myeloid sarcoma of the testis as the only sign of AML relapse after allogeneic peripheral blood stem cell transplantation.

CASE PRESENTATION

A 49-year-old male patient with a diagnosis of AML was classified as M2 using the French-American-British system. Cytogenetic analysis at that time showed t(8;21)(q22;q22) and deletions of the long arms of chromosomes 9 and 11. He received induction chemotherapy with cytarabine (ara-C) and daunorubicin with the 7+3 regimen, in which cytarabine was given continuously for 7 days, along with short infusions of an anthracycline on each of the first 3 days. After 6 months of diagnosis of AML, he received allogeneic peripheral stem cell transplantation from his brother 1 year before. He presented with progressively enlarged right testis with heaviness in the scrotum of 3 months' duration. He also had systemic symptoms of low-grade fever, general weakness, night sweating and weight loss. On physical examination, he had an enlarged right testis with a hard nodule felt along the anterior aspect. The left testis was felt normal.

INVESTIGATIONS

Alpha-fetoprotein of 11.3 ng/mL (10–20 ng/mL), lactate dehydrogenase of 162 U/L (140–280 U/L) and beta-human chorionic gonadotropin of 2 mIU (0–5 mIU/mL) were all within normal limits. Complete blood count revealed haemoglobin of 12 g/L, white cell count of 4.52×10^9/L and platelet count of 210×10^9/L . Bone marrow aspiration comprised normoblastic erythroid series, adequate megakaryocytes and adequate maturation of myeloid series. Bone marrow biopsy showed normocellular marrow with unremarkable lineages of haematopoietic cells (without any evidence of a relapse of leukaemia).

Ultrasonography of the right testis demonstrated an enlarged heterogeneous mass suspicious for malignancy (figure 1). On cross section, greenish mass lesion in the testicular parenchyma with a central infarcted area of 3.6×2.7×3.4 cm was seen (figure 2). Histopathological examination of the testis revealed testicular parenchyma replaced by tumour cells, with few residual seminiferous tubules (figure 3), and sheets of tumour cells with round to oval nuclei with fine chromatin and eosinophilic cytoplasm, with increased mitosis (figure 4). Immunohistochemical studies consistently manifested the expression of lysozyme, CD68, CD34, CD117 (c-Kit), vimentin and leucocyte common antigen, confirming myeloid sarcoma, but not of B cell-specific (CD20) or T cell-specific (CD3) antigens, cytokeratin, periodic acid–Schiff (PAS) and epithelial membrane antigen (figures 5 and 6).

DIFFERENTIAL DIAGNOSIS

Myeloid sarcoma should be differentiated from other malignancies such as malignant lymphoma

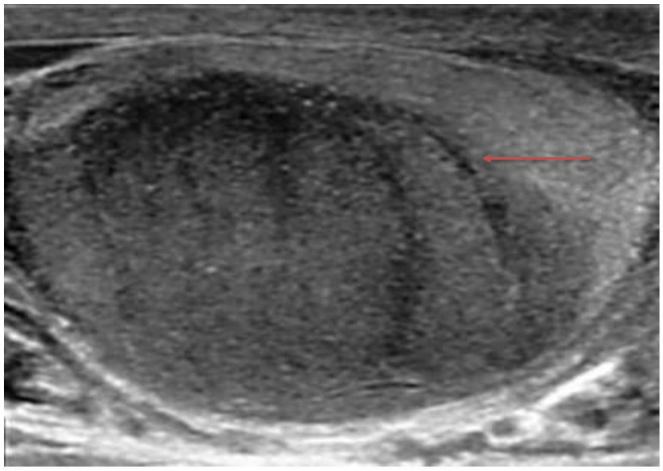

Figure 1 Ultrasonography of the scrotum showing enlarged heterogeneous mass in the right testis (arrow).

and other poorly differentiated carcinoma, predominantly due to the similar histopathological features on H&E sections. Immunohistochemical studies with a panel of antibodies were performed in this case and disclosed expression of lysozyme, CD68, CD34, CD117 (c-Kit), vimentin and leucocyte common antigen, but not of B cell-specific (CD20) or T cell-specific (CD3) antigens, cytokeratin, PAS and epithelial membrane antigen.

TREATMENT

The patient underwent right high inguinal orchidectomy and received palliative chemotherapy with three cycles of intermediate-dose cytosine arabinoside along with radiotherapy to the left testis.

OUTCOME AND FOLLOW-UP

The patient is on regular follow-up with the oncology department. He developed fungal infection on the abdominal and thigh regions of the body and received antifungal (tablet fluconazole 150 mg) treatment. At present, he is doing well and is under continuous follow-up with the oncology department.

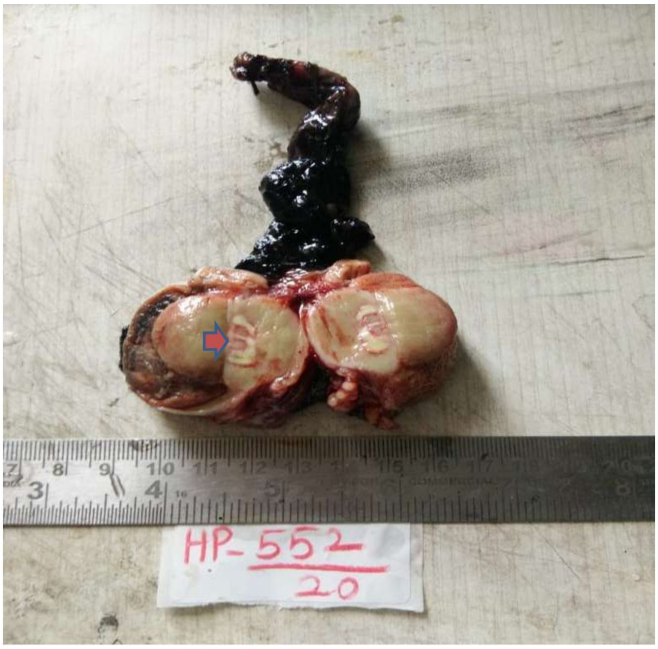

Figure 2 Greenish mass lesion in the testicular parenchyma with central infarcted area (arrow).

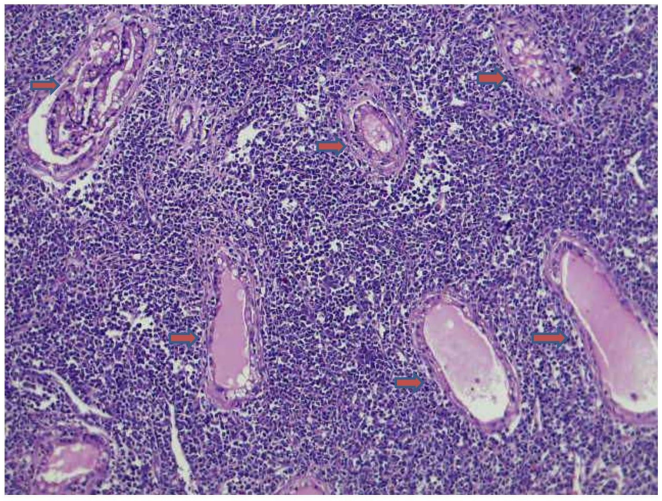

Figure 3 Testicular parenchyma replaced by tumour cells, with few residual seminiferous tubules (arrows). H&E stain, ×10.

DISCUSSION

Isolated extramedullary relapse is defined as occurrence of new-onset leukaemic lesion in extramedullary sites during bone marrow remission in the absence of bone marrow relapse within a month.[14] The possible mechanism of extramedullary relapse is due to the ineffectiveness of antileukaemic effector cells at the extramedullary site (presence of barrier or microenvironmental condition). Isolated extramyeloid relapse after allogeneic stem cell transplantation is a rare event, with incidence rates of between 0.65% and 30%.[15–19]

The correct histological diagnosis is based on identification of granulocytic characteristics in the neoplastic cells. Due to non-identification of myeloid differentiation and high morphological variability, misdiagnosis may occur when the neoplasia presents minimal myeloid differentiation.[20 21]

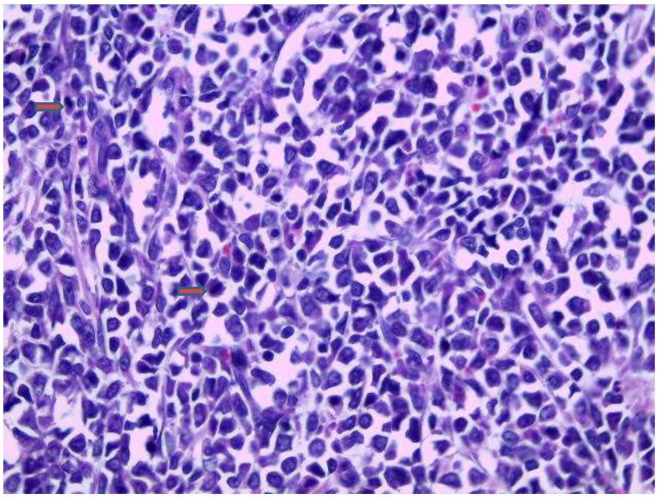

Figure 4 Sheets of tumour cells with round to oval nuclei with fine chromatin and eosinophilic cytoplasm, with increased mitosis (arrows). H&E stain, ×40.

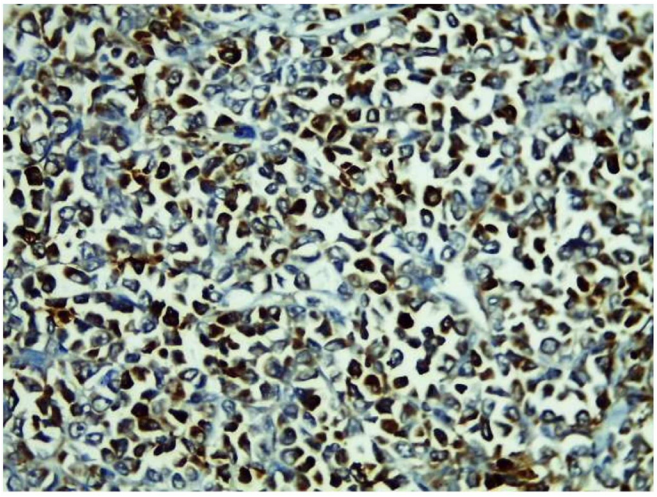

Figure 5 Tumour cells are positive for CD68 immunohistochemistry, ×40.

A combination of clinical history, histopathological findings and a panel of antibodies in immunohistochemistry is mandatory for a correct diagnosis of myeloid sarcoma.[22 23] However, it is still challenging to distinguish myeloid sarcoma from other malignancies such as malignant lymphoma and other poorly differentiated carcinoma, predominantly due to the similar histopathological features on H&E sections. Immunohistochemical studies with a panel of antibodies were performed in this case and disclosed expression of lysozyme, CD68, CD34, CD117 (c-Kit), vimentin and leucocyte common antigen, but not of B cell-specific (CD20) or T cell-specific (CD3) antigens, cytokeratin, PAS and epithelial membrane antigen.

Seminoma may also be considered as it is the most commonly encountered tumour in the testis.[24] However, the lack of PAS immunoreactivity and the absence of clear and vacuolated cytoplasm excluded the possibility of seminoma.[25 26]

In the present case, histopathological findings comprised overwhelming monotonous hyperchromatic cells with scanty cytoplasm and sparse eosinophilic myelocytes, a helpful diagnostic clue but not always found in other cases. Hence, myeloid sarcoma was the final diagnosis based on the histopathological findings, clinical history and immunohistochemistry.

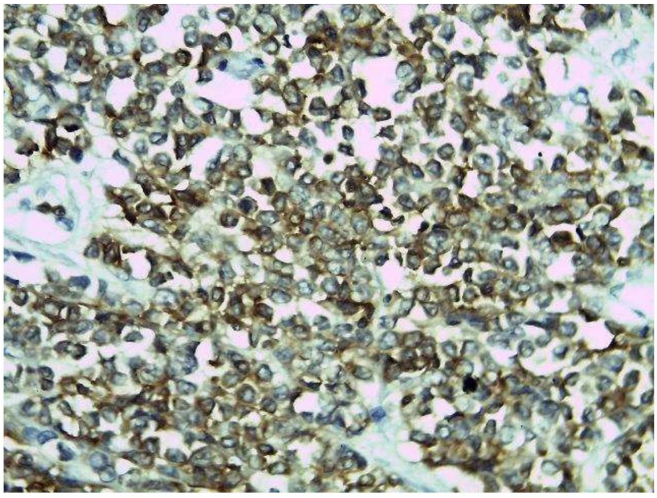

Figure 6 Tumour cells are positive for CD34 immunohistochemistry, ×40.

In the present study, the patient achieved haematological remission, but the disease reactivated as a testicular myeloid sarcoma after allogeneic stem cell transplantation. Relapse after allogeneic stem cell transplantation exhibits a worse outcome.[27 28] Optimal treatment needs to be individualised. There are no standard strategies for the treatment of these patients. However, various reports emphasised the use of combined local treatments (radiation therapy and surgery) along with systemic therapy.[29] After a single extramedullary relapse, progression at other sites and bone marrow occurs within a year.[30] Chemotherapy helps in preventing systemic relapse. The role of donor lymphocyte infusion and second allogenic stem cell transplantation is yet to be elucidated.[31]

We present the case not only due to its rarity, but also to guide physicians on the importance of a high index of suspicion for

Patient's perspective

I consulted doctor after having increased in size of right testis in recent time. I was little concern because one year back had undergone allogenic peripheral blood stem cell transplantation for AML. In past also had low grade fever, generalised weakness, night sweating, and weight loss. During consultation doctor asked me about personal life, relationship with wife and kids. After examination doctor asked me to go for further investigations. I undergo blood test which showed normal haemoglobin level, total leucocyte count and platelet count. Meanwhile ultrasound of scrotum also done and after seeing the report, doctor told me that there is some mass in right testis. So he advise me to undergo operation which is right high inguinal radical orchidectomy. We discussed at home and I came after about 3 days for admission. Before operation hospital stay was smooth and I underwent operation in the next day morning. After recovering from anesthesia, my wife met me first and in front of her my team of doctors came to see me. They explained that they had removed the right testis through right inguinal approach. Our team of doctors slowly explained to us about my condition, possible causes, complications, similar cases in the world, prognosis and future implications. I recovered well after operation and was discharged after 2 days of hospital stay. After reviewing the biopsy report doctor advice me to follow up with department of oncology. I consider this whole experience a bit shocking, but had good support of my wife throughout and doctors helped we with counselling, post-operative care and helped us understanding facts and about the condition we were going through.

Learning points

- Testicular myeloid sarcoma is a rare haematological malignancy that is difficult to diagnose, but should be taken into consideration in the differential diagnoses of undifferentiated neoplasia after acute myeloid leukaemia treatment.
- Immunohistochemical techniques help in differentiation of other pathologies, as well as in making rapid diagnosis and starting appropriate treatment.
- Management of relapsing myeloid sarcoma involves combined modality approach, localised (surgical and radiotherapy) and systemic (chemotherapy or immunotherapy).

myeloid sarcoma in the differential diagnosis of other diseases, such as extramedullary haematopoiesis, poorly differentiated carcinoma, melanoma, T cell lymphoma, Hodgkin's disease and non-Hodgkin's large cell lymphoma, to render correct diagnosis and proper treatment.[32 33]

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