Chloroma of the Testis After Allogeneic Peripheral Blood Stem Cell Transplantation: A Case Report

Shih-Wen Hu, Shu-Pin Huang,[1] Sheau-Fang Yang, and Chee-Yin Chai
Departments of Pathology and [1]Urology, Kaohsiung Medical University
Chung-Ho Memorial Hospital, Kaohsiung, Taiwan.

Chloroma, or granulocytic sarcoma, is a rare extramedullary solid hematologic cancer that affects many sites, usually in concert with acute myeloid leukemia. It is infrequently associated with other myeloproliferative disorders or chronic myelogenous leukemia. Chloroma of the testis after allogeneic bone marrow transplantation is particularly sparsely represented in the literature. It is often incorrectly diagnosed as malignant lymphoma, especially large-cell lymphoma, owing to the similarity of the histologic morphology, scanty eosinophilic myelocytes, and no or overlooked history of leukemia. Although erroneous diagnosis is decreasing with the advent of ancillary studies, the diagnosis of chloroma continues to be a nightmare for pathologists. It is thus suggested that an appropriate panel of marker studies be performed in conjunction with clinical correlation and circumspection to avoid reaching a misleading conclusion and improper treatment of patients. We report an interesting case of a 35-year-old male with a clinical history of chronic myelogenous leukemia post allogeneic peripheral blood stem cell transplantation and complete molecular remission, who was found to have chloroma of the left testis.

Key Words: chloroma, granulocytic sarcoma, chronic myelogenous leukemia, testis
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Chloroma, or granulocytic sarcoma, is a rare extramedullary solid hematologic tumor composed of primitive myeloid cells and their granulocytic precursor cells [1–3]. It is found concomitant with any form of myelodysplastic syndrome, myeloproliferative disorder, or acute or chronic myeloid leukemia [4]. Several sites of the body may be affected, including head and neck, limbs, trunk, body cavities, sex glands, and mammary glands, among which bone, skin, soft tissue, periosteum, and lymph nodes are the most common locations involved [1–5]. Chloroma in the testis is a peculiar presenting site [3,6]. Its occurrence as relapse of chronic myelogenous leukemia (CML) after allogeneic bone marrow transplant is an extremely singular event and, to the best of our knowledge, there are only a few reports in the literature [7–10]. Here, we present the rare case of a 35-year-old man with reactivation of CML following allogeneic peripheral blood stem cell transplantation (PBSCT).

Case Presentation

A 35-year-old male patient with a history of CML presented with a progressively enlarged and tender left testis over approximately 3 months. Tracing his history, he had had initial symptoms and signs of fever, general weakness, night sweating, and weight loss of 5–6 kg in 2–3 months approximately 13 months previously. He had been admitted to hospital due to black stool and loss of consciousness. After serial examinations, he was diagnosed as having CML

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Address correspondence and reprint requests to: Dr. Chee-Yin Chai, Department of Pathology, Kaohsiung Medical University Chung-Ho Memorial Hospital, 100 Tzyou 1st Road, Kaohsiung 807, Taiwan.
E-mail: cychai@kmu.edu.tw

and received allogeneic PBSCT 7 months before the current presentation. He was in complete molecular remission without systemic relapse of CML thereafter. On physical examination, he had no fever or chills and only a progressively enlarged hard nodule with local heat and tenderness in the left testis. Alpha-fetoprotein, lactate dehydrogenase, and beta-human chorionic gonadotropin were all within normal limits. Aerobic and anaerobic bacterial cultures of aspiration fluid from the affected testis failed to demonstrate any infectious agents. Repeated cytogenetic analyses showed normal male karyotype without any chromosomal abnormalities. Repeated peripheral blood smear studies revealed normal white blood cell and platelet counts without any evidence of a relapse of leukemia. Bone marrow aspiration comprised normal erythroid series, adequate megakaryocytes, and adequate maturation of myeloid series. Bone marrow biopsy showed normocellular marrow with unremarkable lineages of hematopoietic cells. Serial ultrasonography of the left testis during follow-up demonstrated an increasingly enlarged heterogeneous mass (Figure 1). Malignancy or infectious disease were clinically suspected.

The patient underwent left radical orchiectomy. On cross-section, a firm and heterogeneous tumor with a light-yellow, grayish-white to cream-colored appearance effaced the whole normal architecture of the testis, and measured 3.8 × 2.5 × 3.6 cm (Figure 2). Histopathologic examination of the testis revealed diffuse infiltration of immature monotonous large hyperchromatic neoplastic cells with scanty cytoplasm and round-to-oval nuclei, effacing the normal testicular architecture and spermatic cord with areas of necrosis (Figure 3). Interspersed within these neoplastic cells were eosinophilic myelocytes, which were extremely scarce and only haphazardly found if carefully sought, and were therefore easily missed (Figure 4). Repeated immunohistochemical studies consistently manifested the expression of lysozyme, CD68, CD34, CD117 (c-Kit), vimentin, and leukocyte common antigen, but not of B-cell-specific (CD20) or T-cell-specific antigens (CD3), cytokeratin, periodic acid Schiff (PAS), and epithelial membrane antigen. The patient received regular follow-up and chemotherapy in the outpatient department for 3 months.

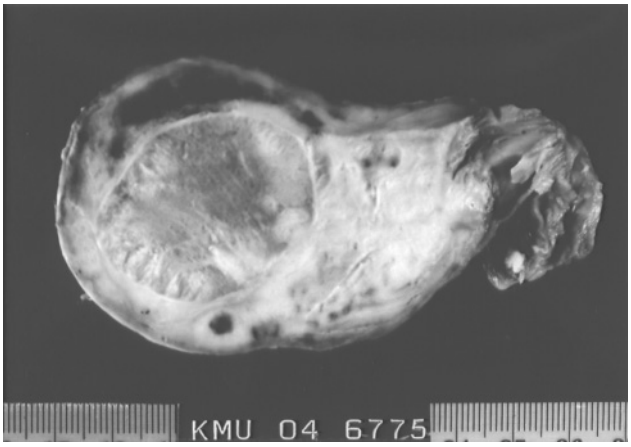

Figure 2. *Light yellow to cream-colored, heterogeneous, firm tumor on cross-section of the testis.*

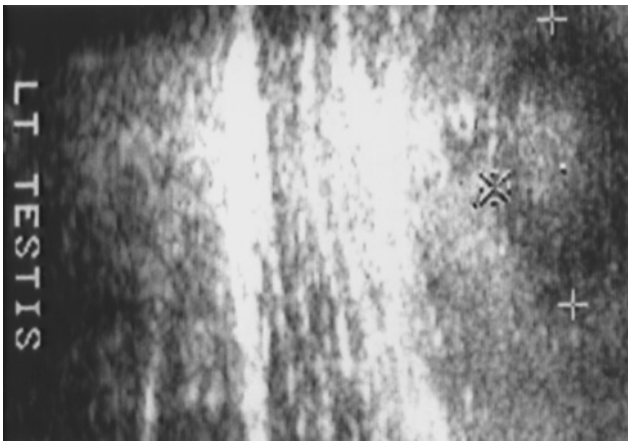

Figure 1. *Ultrasonography demonstrates a heterogeneous hypoechoic mass in the left testis.*

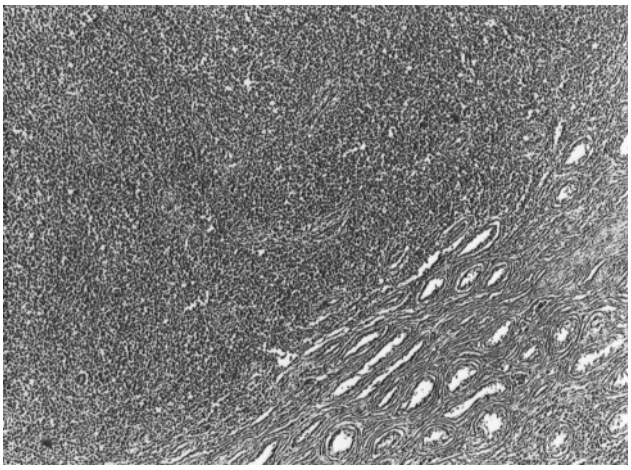

Figure 3. *Diffuse monotonous large hyperchromatic neoplastic cells with scanty cytoplasm effacing normal testicular architecture (hematoxylin & eosin, original magnification ×40).*

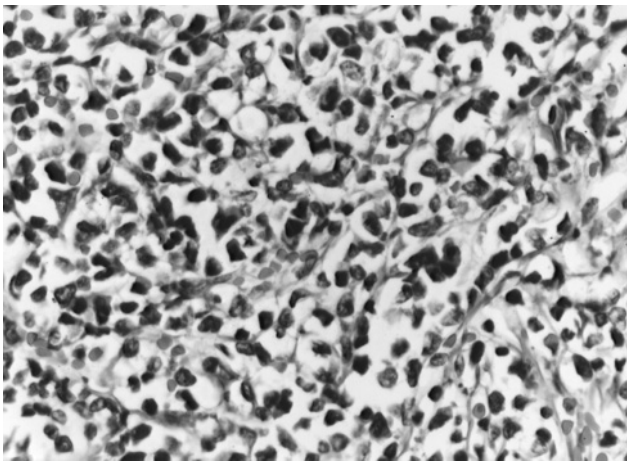

Figure 4. *High-power magnification of monotonous cancer cells scattered with a few eosinophilic myelocytes (hematoxylin & eosin, original magnification × 400).*

Discussion

Chloroma is also known as granulocytic sarcoma or myeloblastoma. It is a rarely encountered variant of myeloid malignancy defined as extramedullary myeloblasts and their granulocytic precursor cells at various levels of granulocytic differentiation [11–14]. Several sites of the body have been affected, and erratic sites such as the brain, mediastinum, gastrointestinal tract, and testis are also described in the literature. The original name, chloroma, was first used by King in 1853 because of the characteristic greenish facade produced by the enzyme myeloperoxidase [11]. The epidemiology of these tumors is uncertain and quite difficult to study. A prevalence of 4% was reported in patients with CML in one autopsy series, while other retrospective studies have reported an incidence of between 3% and 5% [11]. Translocation t(8:21)(q22:q22) is the most common cytogenetic abnormality in leukemia patients with chloroma [11]. In this case, repeated chromosomal studies at different time intervals showed a normal karyotype.

Chloroma mostly occurs with acute myeloid leukemia (AML), but has also been documented in CML patients [4,10,15]. It may occur without other hematologic disorders, during the course of, or preceding the onset of other hematologic disorders such as AML [4]. When it occurs without preceding leukemia history, no evidence of any abnormality in the bone marrow or peripheral blood, or is not suspected by the clinician, the diagnosis of chloroma always requires much effort and circumspection. Thus, it is frequently missed from the pathologist's list of differential diagnoses [16].

A combination of histopathologic findings, clinical history, and a panel of antibodies in immunohistochemistry is mandatory for a correct diagnosis of chloroma [15,17–21]. Differential diagnoses include infectious process, poorly differentiated carcinoma, malignant lymphoma, and seminoma. Without identification of any microorganism by laboratory data or aerobic and anaerobic cultures, an infectious process was less favored over malignancy in this case. However, it is still challenging to distinguish chloroma from malignant lymphoma and other poorly differentiated carcinoma or malignancy, chiefly because of the similar histopathologic features on hematoxylin and eosin sections, without other ancillary studies. Repeated immunohistochemical studies with a panel of antibodies were performed in this case and disclosed expression of lysozyme, CD68, CD34, CD117, vimentin, and leukocyte common antigen, but not of B-cell-specific (CD20) or T-cell-specific antigens (CD3), cytokeratin, PAS, and epithelial membrane antigen. Poorly differentiated carcinoma is unlikely because of the negative cytokeratin result. Neoplasia is quite often misdiagnosed as malignant lymphoma, especially non-Hodgkin's lymphoma and large-cell lymphoma, solely based on morphologic features because of the similar histopathologic picture [1,4,15,17,22]. The expression of leukocyte common antigen without expression of B-cell-specific (CD20) and T-cell-specific antigens (CD3) made malignant lymphoma less likely. Seminoma must also be considered here because it is the most commonly encountered cancer in the testis [23]. However, the lack of PAS immunoreactivity and no clear and vacuolated cytoplasm excluded the possibility of seminoma [24,25]. Lysozyme and CD117 are among the most sensitive immunohistochemical markers for extramedullary myeloid cells, while myeloperoxidase stains a smaller proportion of poorly differentiated and blastic subtypes with varied focal staining, depending on the type of chloroma or individual cases [17,19,26]. In this case, histopathologic 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, chloroma was the final diagnosis from the histopathologic findings, clinical history, and immunohistochemistry.

Ultrasonography is now a helpful tool for detecting the size, morphology, vascularity, extension, and texture of testicular lesions. However, the ultrasonographic features of testicular chloroma and other testicular lesions such as

metastasis, seminoma, lymphoma, and other tumors are similar and indistinguishable. To our knowledge, sonographic features of testicular chloroma have rarely been reported, with only one reported case found in the literature [27]. The ultrasonographic findings of testicular lymphoma and leukemia in the literature were hypoechoic texture, solitary, multifocal, or hypervascular lesions regardless of size. A basket-like appearance with a low resistive index was also reported in the ultrasonographic findings of testicular lymphoma. Chiou et al reported a smooth border and homogeneous echo texture in testicular chloroma [27]. However, in our case, the sonographic features were heterogeneous and not similar to those reported in the literature. Hence, the sonographic features in this case were not helpful in the differential diagnosis.

Our patient achieved hematologic remission, but the disease was reactivated as a chloroma after allogeneic PBSCT. Its occurrence exhibits a worse outcome, especially after allogeneic PBSCT [5,13,28–30]. Chloroma is very clever at imitating other diseases [26]. Optimal treatment needs to be worked out [5]. Some patients have chemotherapy [2,3,29], while others have combined chemotherapy and radiotherapy [13,30]. Our patient received chemotherapy and had regular follow-up in the outpatient department for 3 months. We present the case not only for its rarity but also to alert physicians to the importance of a high index of suspicion for chloroma in the differential diagnosis of other diseases, such as extramedullary hematopoiesis, infectious diseases, poorly differentiated carcinoma, melanoma, T-cell lymphoma, lymphoblastic lymphoma, Hodgkin's disease, and non-Hodgkin's large-cell lymphoma, to render a correct diagnosis and proper treatment [2,16,26].

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同種組織周邊血液幹細胞移植後發生的睪丸綠色瘤 — 病例報告

胡士文[1] 黃書彬[2] 楊曉芳[1] 蔡志仁[1]

高雄醫學大學 [1]病理科 [2]泌尿科

綠色瘤又叫做粒性細胞肉瘤，是個少見的腫瘤，它可以發生於身體的任何部位，最常與急性骨髓性白血病有關。骨髓移植後以綠色瘤再發於睪丸的呈現方式在文獻上更是少見。在無臨床血癌或忽略血癌的病史時，缺乏嗜伊紅性骨髓細胞，或常因為病理上的型態類似淋巴瘤而經常被誤診。雖然近年來有一些輔助診斷工具，診斷上還是相當困難的，診斷綠色瘤或粒性細胞肉瘤仍舊需要一些足夠的免疫組織化學染色並加臨床資料來達到正確診斷，才能給予正確的治療。我們報告一個 35 歲的慢性骨髓性白血病的病人，在緩解期後，以發生於睪丸的綠色瘤為疾病再發的罕見病例。在此我們將討論他的病理變化，並回顧一下文獻中的記載。

關鍵詞：綠色瘤，粒性細胞肉瘤，慢性骨髓性白血病，睪丸

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通訊作者：蔡志仁醫師

高雄醫學大學附設中和紀念醫院病理科

台灣高雄市三民區自由一路 **100** 號