Granulocytic sarcoma and HIV

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Hematopoietic neoplasms are known to occur in the setting of HIV. Excluding Kaposi's sarcoma, the neoplasms are generally high-grade lymphoproliferative disorders. Granulocytic sarcoma, an extramedullary hematopoietic malignancy that may precede or occur during the course of acute myeloid leukemia, has rarely been described in the HIV population. We present the fourth documented case, to our knowledge, of a granulocytic sarcoma occurring in an HIV-positive individual. This has been associated with a very poor prognostic outcome.

Granulocytic sarcoma (chloroma) is a tumor composed of immature myeloid/monocytic precursors occurring in an extramedullary site (1). These tumors often develop during the course of, or as a presenting sign of, acute myeloid leukemia (AML) (2). Whereas hematopoietic lesions are well known to occur in the setting of HIV/AIDS, these are predominantly lymphomas, including Hodgkin lymphoma and multiple myeloma (3–5). Granulocytic sarcomas are exceedingly rare in the HIV population, with only a few documented cases (6–8). We report another unusual case of granulocytic sarcoma occurring in an HIV-positive individual.

CASE REPORT

A 59-year-old man with a >5-year history of HIV had developed a nodule in his right thigh several months prior to admission. About 1 month before admission, he noted that the nodule seemed to be growing, and he sought consultation. Magnetic resonance imaging of the right thigh demonstrated several nodules within the soft tissue, the largest measuring $3.8 \times 2.7 \times 2.8$ cm. A presumptive diagnosis of lymphoma was considered. A biopsy of this lesion revealed an immature cellular infiltrate (*Figure 1*). Further workup with immunohistochemical stains revealed that the lesion was CD45 positive (hematopoietic); it also stained with CD15, CD68, and CD168 (*Figure 2*). Lymphoid markers including CD3, CD20, CD79a, and CD30 were negative. Based upon the morphology and immunohistochemistry results, a diagnosis of granulocytic sarcoma with a monoblastic morphology was rendered.

A bone marrow examination was then done. At that time, the patient's white blood cell count was $5.9 \times 10^9/L$; hemoglobin, 13.9 g/dL; hematocrit, 38.7%; and platelet count,

$144 \times 10^9/L$. The peripheral blood differential count was within normal limits, and no blasts or atypical monocytes were noted. The bone marrow examination revealed a myeloid to erythroid precursor ratio of 3.5 to 1 (normal). There was trilineage maturation with 2% blasts counted. After starting an AML regimen with cytarabine and idarubicin, he suffered a number of complications, including septic shock, acute renal failure, and respiratory failure. He survived a prolonged stay in the intensive care unit. However, he was unable to receive further chemotherapy because of the multiple comorbidities.

Over the next several weeks, his disease recurred at several extramedullary sites. A repeat biopsy of a chest wall mass again revealed granulocytic sarcoma with morphology similar to that of the first biopsy. He was given radiation therapy to sites of

Figure 1. Granulocytic sarcoma, immature infiltrate. Hematoxylin and eosin, $\times 500$.

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Figure 2. Granulocytic sarcoma. (a) Positive CD163 stain indicating a monoblastic origin, $\times 400$. (b) Positive CD68 stain indicating a monoblastic origin, $\times 400$.

his disease. However, his disease continued to rapidly progress, and he developed epidural masses with involvement of the cranial nerves. After extensive discussions with the patient and his family, all agreed that hospice was the best approach. He died about 3½ months following the first biopsy diagnosis of granulocytic sarcoma.

DISCUSSION

Immunodeficiency is associated with an increased risk of malignancy in the setting of multiple etiologies (*Table 1*) (9). The spectrum of tumors in the context of HIV infection varies on the basis of risk group and has been substantially affected

Table 1. Tumor types with increased incidence in HIV disease*

Definite increase	Possible increase
Kaposi's sarcoma	Seminoma
Non-Hodgkin lymphoma	
Squamous cell neoplasias	
Hodgkin lymphoma	
Plasmacytoma	

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by the use of highly active antiretroviral therapy (HAART) (10, 11). There has been a widespread decline—estimated to be as much as 80-fold—in Kaposi's sarcoma. The incidence of systemic AIDS-related lymphomas appears to be more modestly affected by HAART (12–14). The picture emerging is that the incidence of systemic lymphoma is diminished, but the extent of reduction is not nearly as dramatic as that of Kaposi's sarcoma.

Our reported case of granulocytic sarcoma arising in an HIV-positive individual adds to the very few cases reported. Interestingly, in one of the reported cases, the granulocytic sarcoma also arose in the thigh, while the other two cases arose in the mandible. All cases experienced a relatively short survival period of days in two cases and 4 months in the other. Our patient also had a short survival period.

AML is also reported to be uncommon in the AIDS population. A report by Aboulafia et al described five HIV-infected individuals who developed AML and also included a literature review describing 42 additional cases between 1981 and 2001 (15). Most of the leukemias were FAB M2 (myeloid leukemia with maturation), M4 (myelomonocytic leukemia), and M5 (monoblastic leukemia), with a rare case of M3 (promyelocytic leukemia). The median survival of the chemotherapy-treated group was 7.5 months compared with 1 month in patients who did not receive induction chemotherapy.

Several investigators have sought to determine whether there is more than a coincidental association between HIV infection and the subsequent development of AML. Farber and associates cocultured peripheral donor lymphocytes with leukemic monocytes from an HIV-seropositive man with AML M4 but were unable to identify the presence of viral particles (16). Costello and colleagues also failed to detect HIV hybrid fragments in monoblast DNA from an HIV-seropositive patient with AML M5 (17). Assumptions regarding an etiopathological link between AML and HIV infection must be viewed in the context of the limited number of cases identified.

In the HAART era, the overall survival of patients with AIDS is improving dramatically and, as a result, perhaps the occurrence of malignancies not typically associated with HIV infection, especially those malignancies such as AML in which the incidence increases with age, may become more prevalent as the HIV-infected population ages. Our patient

was 59 years old. Therefore, it is possible that in the future we may see more cases of granulocytic sarcoma, a precursor of AML, and this lesion needs to be considered among the neoplastic entities occurring in the HIV individual. Granulocytic sarcoma may mimic a large-cell lymphoma, and the correct diagnosis needs to be established since the therapeutic modalities will differ.

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