Journal of
AIDS & Clinical Research
ISSN: 2155-6113

Gupta et al., J AIDS Clinic Res 2012, 3:5
DOI: 10.4172/2155-6113.1000155

Case Report Open Access

HIV-1 Infection and Erythroleukemia: A Rare Association

Nikhil Gupta*, Srimanta Sahu, Neelam Wadhwa and Subhash Giri

University College of Medical Sciences, Delhi, National Capital Region India

Case Summary

A 40 year old transgender, from Delhi, was diagnosed with HIV-1 infection 2 years back and was started on anti-retroviral drugs in the following doses AZT-300 mg bd, 3TC-150 mg bd, NVP-200 mg bd, which she was taking regularly for the last 2 years. At diagnosis, her CD4 cell count was 26 × 10^6/l which gradually improved to 227 × 10^6/l over two years on ART. During one of her regular visits to the ART clinic, she complained of easy fatigability for 2 months. There was no history of fever, blood loss, malignancy or any history of exposure to ionizing radiation, toxins or chemotherapy. After she was detected having anemia, AZT was replaced by d4T in the dose of 30 mg bd and a detail clinical and laboratory workup was undertaken. Her clinical examination revealed severe degree of pallor, rest of the general and systemic examinations were normal. Her hemoglobin was 61 g/l, total leukocyte count was 41 × 10^9/l and platelet count was of 37 × 10^9/l. Peripheral smear revealed macrocytosis and myeloblasts (70%) with cytoplasmic granules in few cells (Figure 1). Positive Myeloperoxidase and Sudan black cytochemistry confirmed the myeloid nature of the blast cells. Bone marrow aspiration revealed marked erythroid hyperplasia with erythroid cells constituting >50% of total nucleated cells, and myeloblast comprising >20% of the non erythroid cells population (Figure 2). The maturing myeloid precursor and megakaryocytes were sparse. Blasts expressed CD 33, CD117 and HLA-DR (heterogeneously). Serum levels of vitamin B_{12} and folate were in the normal range. There was no obvious dysmaturation detected in any of the cell lines.

Discussion

Last two decades (1991-2010) showed a 4.7% increase in the incidence of hematological malignancies in AIDS [1]. While non-Hodgkin's lymphomas occur commonly enough to be labelled as an AIDS defining illness, acute myelogenous leukemia is occasionally been reported in association with HIV-1 infection and are predominantly

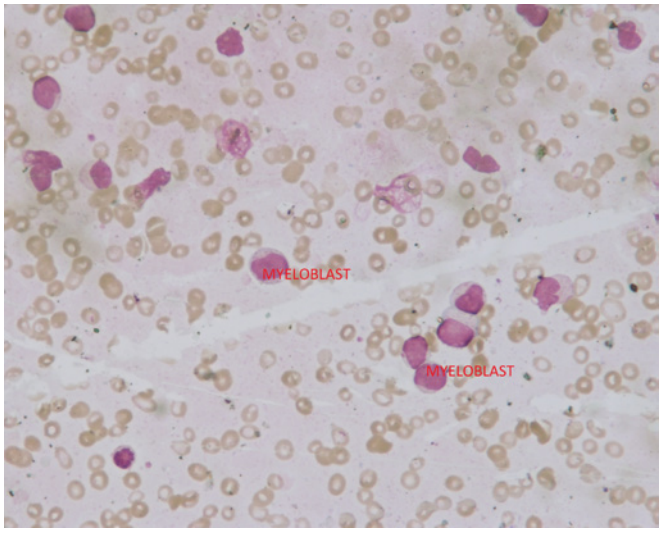

Figure 1: Peripheral smear showing myeloblasts.

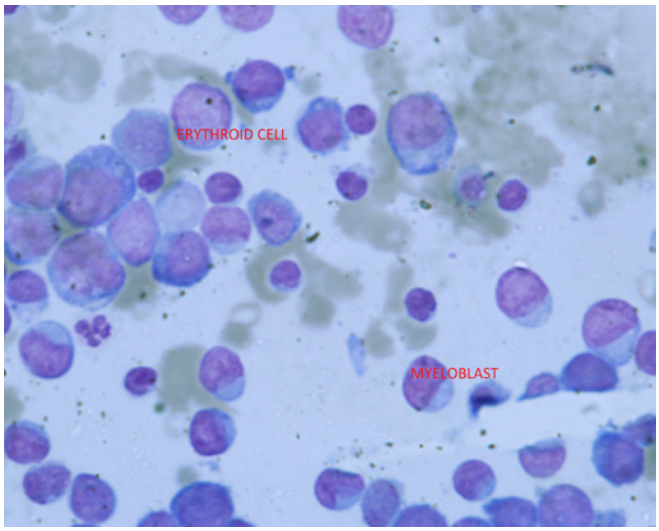

Figure 2: Bone marrow examination showing myeloblast and erythroid cells.

of the FAB M-2, M-4 and M-5 types [2]. Compared with the general population the incidence of AML in HIV infected patients is increased approximately two folds [3]. Myelodysplastic changes in the marrow are frequently observed in HIV infection; however their AML transformation is very unusual. Acute erythroleukemia (AEL) is a distinctively rare entity comprising only <5% of all acute myelogenous leukemia (AML) in adults in the general population. To the best of our knowledge, AEL has not been reported earlier in association with HIV infection. Erythroleukemia has a male preponderance and age distribution appears to be bimodal with a smaller peak below 20 years of age and a more definite and broader peak in the 7th decade of life [4]. In half of the cases, AEL appears secondary to chemotherapy, immunosuppressive therapy, may develop as blast crisis of myeloproliferative disease or as a final evolution of MDS [5-7]. AML with myelodysplasia related changes (AML-MRC), a new category has been proposed by the 2008 WHO classification of AML.

The differential diagnosis of AEL includes AML-MRC, MDS with erythroid predominance and other types of AML with increased erythroid precursors [8]. To differentiate these, a bone marrow examination with a differential count of all nucleated cells should be performed. If bone marrow shows blast cells which are more than 20% of all nucleated marrow cells with either multilineage dysplasia in more

***Corresponding author:** Nikhil Gupta, University College of Medical Sciences, Delhi, National Capital Region India, Tel: 91-9873098719; E-mail: nik.gupta4u@gmail.com

Received May 22, 2012; **Accepted** June 19, 2012; **Published** June 22, 2012

Citation: Gupta N, Sahu S, Wadhwa N, Giri S (2012) HIV-1 Infection and Erythroleukemia: A Rare Association. J AIDS Clinic Res 3:155. doi:10.4172/2155-6113.1000155

than 50% of the cells in atleast 2 lineages or a history of MDS or with MDS related cytogenetic abnormalities, a diagnosis of AML-MRC should be made [9]. If there are <20% total blasts and the erythroid precursors are >50% of all cells, the differential count of non-erythroid cells should be calculated, if blasts are >20% of non-erythroid cells the diagnosis is Erythroleukemia (Erythroid/Myeloid); but if they are <20% the diagnosis is usually MDS. In the WHO classification, the degree of dysplasia is considered a surrogate for cytogenetic abnormalities associated with MDS. Other common differential diagnoses are reactive erythroid hyperplasia following erythropoietin therapy or megaloblastic anemia due to vitamin B_{12} deficiency. Our patient had erythroid hyperplasia of bone marrow with >50% erythroid cells and blast cells were >20% of the non-erythroid cells. There was no evidence of any dysplastic cells in the bone marrow; neither had she any history of MDS. Her serum vitamin B_{12} and folate levels were normal and there was no history of erythropoietin therapy in the recent past. In the absence of history of radio-chemotherapy, toxin exposure or any other predisposing factor we assume the occurrence of AEL in our case as de novo.

Due to very few reported cases of AML among HIV infected patients the exact mechanism of leukemogenesis is not clear, few mechanisms have been proposed though. During acute infection of CD4 cells by HIV-1 the potent transactivator protein (Tat) is released extracellularly [10]. This Tat protein plays a vital role in the process of angiogenesis. Transgenic mice develop angioproliferative Kaposi's sarcoma-like lesions when the HIV tat is introduced into their germ line. Angiogenesis also plays a vital role in the pathogenesis of acute leukaemias. The potential role of Tat in the pathogenesis of leukemia is underscored by the ability of the basic domain of Tat to displace preformed basic fibroblast growth factor (bFGF) bound to heparan sulphate proteoglycans into a soluble form [11]. This bFGF has been demonstrated by several groups to augment myelopoiesis directly via FGF receptors on myeloid progenitors. HIV may also alter the bone marrow microenvironment, making it more permissive to the growth of leukemic cells. HIV-1 is capable of infecting monocytes and macrophages, leading to their activation and cytokine production, which could activate the genes of cytokines putatively involved in leukemogenesis (e.g., G-CSF, GM-CSF, and IL-6) [12,13]. Finally, a potential mechanism of leukemic evolution is reduced immune tumor surveillance, secondary to HIV immunosuppression. Our review of literature did not show a clear pathogenetic link between antiretroviral therapy and AML, however an earlier case report has shown an HIV infected patient developing a high risk MDS with progression to AML after 13 years of continuous ART [14]. Our patient was on ART for the past two years only, moreover she did not show any features suggestive of MDS at any stage.

Disease aggressiveness and overall survival in AEL is strongly related to cytogenetic risk group and not related to the blast count or morphologic dysplasia. In a recent study of a small series of HIV-AML patients, CD4 cell count $\leq 200 \times 10^6$/l is found to be a strong predictor of short survival regardless of karyotype [15]..

References

1. Evans MW, Sung AD, Gojo I, Tidwell M, Greer J, et al. (2012) Risk assessment in human immunodeficiency virus-associated acute myeloid leukaemia. Leuk Lymphoma 53: 660-664.
2. Aboulafia DM, Meneses M, Ginsberg S, Siegel MS, Howard WW, et al. (2002) Acute myeloid leukemia in patients infected with HIV-1. AIDS 16: 865-876.
3. Sutton L, Guenel P, Tanguy ML, Rio B, Dhedin N, et al. (2001) Acute myeloid leukaemia in human immunodeficiency virus-infected adults: epidemiology, treatment feasibility and outcome. Br J Haematol 112: 900–908.
4. Park S, Picard F, Dreyfus F (2002) Erythroleukemia: a need for a new definition. Leukemia 16: 1399–1401.
5. Goldberg SL, Noel P, Lumpp TR, Dewald GW (1998) The erythroid leukemias: a comparative study of erythroleukemia (FABM6) and Di Guglielmo disease. Am J Clin Oncol 21: 42-47.
6. Wheatley K, Burnett AK, Goldstone AH, Gray RG, Hann IM, et al. (1999) A simple, robust, validated and highly predictive index for the determination of risk directed therapy in acute myeloid leukemia derived from the MRC AML10 trial. United Kingdom Medical Research Council's Adult and Childhood Leukaemia Working Parties. Br J Haematol 107: 69-79.
7. Davey FR, Abraham N, Brunetto VL, MacCallum JM, Nelson DA, et al. (1995) Morphologic characteristics of erythroleukemia (acute myeloid leukemia; FAB-M6): a CALGB study. Am J Hematol 49: 29-38.
8. Zuo Z, Polski JM, Kasyan A, Medeiros LJ (2010) Acute Erythroid Leukemia. Arch Pathol Lab Med 134: 1261-1270.
9. Arber A, Brunning RD, Orazi AI (2008) Acute myeloid leukaemia with myelodysplasia-related changes. In: Swerdlow SH, Campo E, Harris NL, et al, eds. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Lyon, France: International Agency for Research on Cancer 124-126.
10. Ensoli B, Buanoguro L, Barillari G, Fiorelli V, Gendelman R, et al. (1993) Release, uptake and effects of extracellular human immunodeficiency virus type 1 Tat protein on cell growth and viral transactivation. J Virol 67: 277-287.
11. Barillari G, Sgadari C, Fiorelli V, Samaniego F, Colombini S, et al.(1999) The Tat protein of human immunodeficiency virus type-1 promotes vascular cell growth and locomotion by engaging the α5β1 and αvβ3 integrins and by mobilizing sequestered basic fibroblast growth factor. Blood 94: 663-672.
12. Guillemain C, George F, Courcoul M, Dhiver C, Brunet C, et al. (1996) Monoblastic leukemia in an HIV infected patient: absence of viral expression in RNA blasts. Am J Hematol 52: 47-52.
13. Kane D, Keating S, McCann S, Mulcahy F (1997) The management of acute myeloid leukemia (AML) in human immunodeficiency virus (HIV) infection: a case report and review. Int J STD AIDS 8: 272-274.
14. Rieg S, Lubbert M, Kern W, Timme S, Gartner F, et al. (2009) Myelodysplastic syndrome with complex karyotype associated with long-term highly active antiretroviral therapy. Br J Haematol 145: 670-673.
15. Hagiwara S, Yotsumoto M, Okada S (2011) 'Non-AIDS-Defining Hematologic Malignancies in HIV- Infected Patients', A Nationwide Epidemiologic Study in Japan. 53rd ASH Annual Meeting and Exposition, Hall GH (San Diego Convention Center), December 10-13, 2011, American Society of Hematology 2021 L Street NW, Suite 900, Washington, DC 20036.