Myelodysplasia is reported frequently in HIV/AIDS patients throughout the spectrum of the disease and is thought to be partly responsible for bone marrow failure in these patients. However, the frequency and type of myelodysplasia appear to differ at different stages of the disease in different populations with mechanisms of its development not well understood.

Objective: To document the pattern of myelodysplasia in Ugandan patients with terminal HIV/AIDS disease.

Design: Prospective descriptive study.

Subjects: Bone marrow necropsies from patients who died with AIDS disease at Mulago teaching hospital in Kampala, Uganda during a one-year period.

Results: Eighty-four (84%) of the 50 cases studied had myelodysplasia with 39 cases having megakaryocytic myelodysplasia. Myelodysplasia involving erythroid cell series occurred in 23 and in 20 of these cases was in combination with megakaryocytic dysplasia. Granulocyte myelodysplastic features were observed in only two cases and these two cases did not have other cell lines involved.

Conclusion: Myelodysplastic features are common in HIV patients with megakaryocytic and erythroid cell lines being the most affected. This could be due to the direct HIV effect, or the combined effect of opportunistic infections, neoplasms, drugs and HIV itself affecting the haemopoietic stem cell and or its microenvironment.

MYELODYSPLASIA IN UGANDAN PATIENTS WITH HIV/AIDS: AN AUTOPSY STUDY

S. NABADDA, M. ODIDA and H. WABINGA

ABSTRACT

Background: Myelodysplasia has been reported to occur quite frequently in the spectrum of HIV/AIDS disease and is thought to be partly responsible for bone marrow failure in these patients. However, the frequency and type of myelodysplasia appear to differ at different stages of the disease in different populations with mechanisms of its development not well understood.

Objective: To document the pattern of myelodysplasia in Ugandan patients with terminal HIV/AIDS disease.

Design: Prospective descriptive study.

Setting: Department of Pathology, Faculty of Medicine, Makerere University College of Health Sciences

Subjects: Bone marrow necropsies from patients who died with AIDS disease at Mulago teaching hospital in Kampala, Uganda during a one-year period.

Results: Eighty-four (84%) of the 50 cases studied had myelodysplasia with 39 cases having megakaryocytic myelodysplasia. Myelodysplasia involving erythroid cell series occurred in 23 and in 20 of these cases was in combination with megakaryocytic dysplasia. Granulocyte myelodysplastic features were observed in only two cases and these two cases did not have other cell lines involved.

Conclusion: Myelodysplastic features are common in HIV patients with megakaryocytic and erythroid cell lines being the most affected. This could be due to the direct HIV effect, or the combined effect of opportunistic infections, neoplasms, drugs and HIV itself affecting the haemopoietic stem cell and or its microenvironment.
RESULTS

The 50 cases studied included 26 males and 24 females with age ranging from 17 to 57 and mean age of 32 (SD 8.3) years. All the 50 cases were severely wasted with 18 out 24 females weighing 50kg and below while in males, 20 out of 26 weighed below 50 kg. Forty-four (88%) had myelodysplasia and of these 21 were males while 23 were females. Eighteen out of the 44 cases had mycobacteria in their bone marrow while 15 had cryptococcus neoformans infection in the bone marrow. There was one case of histoplasmosis capsulatum infection and two cases with unidentifiable fungal elements.

Table 1 shows age and sex distribution of the three cell lineages of dysplasia and there was no statistical difference in sex of the various cell lines ($x^2 = 0.03$, $p$ value = 0.87). There was also no significant difference between the mean age of the three cell line. ($p$-value = 0.86).

Megakaryocytic dysplasia was the most common followed by erythroid dysplasia and myelodysplasia. Twenty cases had both erythroid myelodysplasia and megakaryocytic dysplasia, while only one cell lineage dysplasia occurred in 24 cases. Of these 24 cases with one cell lineage dysplasia, 19 had pure megakaryocytic dysplasia, three pure erythroid dysplasia and two myelodysplasia.

Hypercellularity was a major finding with very few cases being hypocellular(12%) and normocellular (14%).

![Figure I](https://via.placeholder.com/150)

Clustering of hypolobulated micromegakarocyte x200

![Figure II](https://via.placeholder.com/150)

Bone marrow shows hypercellular marrow. Some of the normoblasts are binucleated x 400

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Megakaryocyte</th>
<th>Combined megakaryocytes and erythroids</th>
<th>Erythroid</th>
<th>Granulocyte</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of cases</td>
<td>19</td>
<td>20</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>M:F</td>
<td>9:10</td>
<td>10:10</td>
<td>2:1</td>
<td>0:2</td>
</tr>
<tr>
<td>Mean age</td>
<td>32 (SD 8.45)</td>
<td>31.7 (SD 9.96)</td>
<td>28.5(SD 5.65)</td>
<td>26.5 (SD 4.95)</td>
</tr>
</tbody>
</table>

DISCUSSION

The severe weight loss coupled with tuberculosis and fungal infections found in our cases qualified them to be in terminal stages of HIV/AIDS disease and this could probably explain the high prevalence of myelodysplasia (5). Similar findings have been reported by Diebold et al (6) who found 91% of patients with terminal stage of HIV/AIDS disease...
with myelodysplasia. In another study by Marche et al (7), myelodysplasia was found in 74.4% of the 125 patients studied at different stages of HIV infection and frequency was related to the severity of the infection. However Tripathi et al (8) did not show any correlation between HIV RNA load and the occurrence of myelodysplasia and this was thought to be due to the small numbers of cases studied.

Hypercellularity of bone marrow was a frequent finding. Previous reports indicate that most cases with HIV have hypercellular bone marrow (9). This was also observed in the study of Spivak et al (3) in which it was found five out twelve patients with severe HIV disease had hypercellular marrow. The hypercellularity observed in this study was mainly associated with increasing number of abnormal megakaryocyte and to large extent erythroid cell lines. Khalil et al (10) also reported similar findings when they studied 18 patients with HIV infection and found 72% had hypercellularity mainly due to megakaryocytic hyperplasia. Similarly Delacrelaz et al (11) reported dysmegakaryocytopoiesis and dyserythropoiesis in 88% and 83% of the 18 patients studied. Bello et al (12) found abnormal maturation more prominent in megakaryocyte but unlike in the present study, abnormal granulocyte maturation was also prominent. On the other hand in the study of Tripath et al (8) the most commonly affected cell line was granulocytic followed by erythroid. Schneider and Picker (1) also found granulocytic myelodysplasia more frequent although the degree of dysplasia was more severe in the megakaryocytic series.

In addition to the quantitative changes observed in this study, morphological cellular changes were also noted. The megakaryocytic series had the most striking changes including clustering of the megakaryocytes, a tendency often associated with myeloproliferative disorders. Other qualitative changes observed in the megakaryocyte series were micromegakaryocyte, hypolobulation of nuclei and abnormal localisation of megakaryocytes, features similar to those reported in pre-leukemic syndrome. In the erythroid series the binucleated erythroblasts observed mainly in this study also were suggestive of hypoproliferative disease and would rule out the possibility of nutrition and drugs as causative factors. This was exemplified by the study of Karcher and Frost (13) who did not find any association between myelodysplasia and anti-retroviral drugs. Cytoplasmic vacuolation found in the only two granulocytic cell series has been reported by Tripathi et al (8) as the most important dysplastic change and accounted for 60% of the dysplastic changes in the granulocytes in their study. The pattern of involvement of different cell lines with megakaryocyte and erythrocyte being more frequently involved as observed in the present study would suggest a hypothesis similar to that brought forward by Linman and Bagby (14) concerning the evolution of pre-leukemic syndrome in which myelodysplastic changes affected erythrocytes initially, followed by platelets and lastly granulocytic series. This same argument had earlier been reported by Koeffler and Golde (15) who also found that there was erythroid hyperplasia and megablastoid features which were accompanied by micromegakaryocytes in pre-leukemic syndrome. However Katsarou et al (16) were able to differentiate between myelodysplastic syndrome and HIV related myelodysplasia by finding abnormal karyotype in the latter. It has also been observed that CD34 + human haematopoietic progenitor are substantially not susceptible to HIV infection in either vitro or vivo and therefore their defects seem rather related to the alteration of bone marrow and peripheral blood microenvironments probably due to the presence of soluble HIV specific products rather than direct effect of the virus on the stem cell (17).

More studies have demonstrated reduced colony growth factors for the haematopoietic progenitor cells in most patients with AIDS and the cause of the reduction of these factors need to be investigated (18) (Leiderman et al 1987). In support of the above theories in our study population, acute leukemia was not observed and there is no evidence that HIV / AIDS patients in this African population are at a high risk of developing acute leukemia (19).

In conclusion, myelodysplastic features are common in HIV patients with megakaryocytic and erythroid cell lines being the most affected. This could be due to the direct HIV effect, or the combined effect of opportunistic infections, neoplasms, drugs and HIV itself affecting the haemopoietic stem cell and or its microenvironment, but this needs to be elucidated in further studies.

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REFERENCES

5. Ledru, E., Daigbouga, S., Meda, N., Sanou, P. T., Dahourou,. et al. A proposal for basic management of HIV disease in West Africa: use of clinical staging


