

HIV-1 Infection in adults with haematological malignancies in Yaoundé, Cameroon

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Summary

To determine the association between haematological malignancies and the HIV-1 in Yaoundé, Cameroon, adult patients (>16 years) followed up in the Haematology Clinics of two major hospitals were screened for the HIV between 1994 and 1999. There were nine haematological malignancies diagnosed among the 172 patients including Non Hodgkin's lymphomas (31.9%); chronic lymphocytic leukaemia (21.5%); chronic myelogenous leukaemia (18.0%); acute myelogenous leukaemia (9.9%); acute lymphoblastic leukaemia (7.6%) and multiple myeloma (7.0%). Burkitt's lymphoma, Hodgkin's disease and myelodysplastic syndrome were less frequently diagnosed. Forty-five of all cases (26.2%) had antibodies to the HIV-1 virus, predominantly in patients with Non-Hodgkin's lymphomas ($p < 0.001$, OR=5.8, adjusted for age; CI=2.7 – 12.4). About 19.4% and 11.8% of cases with chronic and acute myelogenous leukaemia respectively were HIV-1 positive. Although B-lineage-derived malignancies are more often associated with the HIV infection, other malignant proliferations of the haematopoietic system may not be coincidental.

Key words: HIV, HIV-1, Haematological malignancies, Non-Hodgkin's lymphoma, Cameroon.

Résumé

Pour déterminer l'association entre les maladies hématologiques malignes et le VIH-1 à Yaoundé, Cameroun, les adultes âgés de plus de 16 ans dans deux services d'hématologie cliniques de Yaoundé ont subi les tests de dépistage du VIH entre 1994 et 1999. Neuf différents types de pathologies ont été diagnostiqués parmi 172 patients suivis. Les lymphomes malignes non-Hodgkiniens (LMNH) étaient retrouvés dans 31,9% des cas, la leucémie lymphocytaire chronique chez 21,5%; la leucémie myéloïde chronique chez 18% et la forme aiguë dans 9,9% des cas; la leucémie aiguë lymphoblastique dans 7,6% des cas et le myélome multiple chez 7,0%. Par ailleurs le lymphome de Burkitt, la maladie d'Hodgkin et le syndrome myélodysplastiques n'étaient pas fréquents. La prévalence du VIH-1 chez les 172 cas était de 26,2%. Les malades présentant le LMNH montraient une association significative avec la séropositivité VIH-1 ($p < 0.001$, OR=5.8, ajusté pour l'âge; IC=2.7 – 12.4). Environ 19,4% et 11,8% respectivement de cas de leucémie myéloïde chronique et aiguë étaient séropositifs pour le VIH-1. Quoique l'infection à VIH est souvent associée aux pathologies malignes de la lignée B, la prolifération des autres lignées du système hémopoïétique ne sont pas forcément une co-incidence.

Introduction

In 1995, available data in Cameroon indicated that the most frequent cancers were hepatomas and skin cancers, constituting about 20% and 15% respectively of all diagnosed cancers (Unpublished data, Cameroon Anti-Cancer Society). Lymphomas represent 8% of cancers and leukaemias represent another 5%. The main haematological malignancies diagnosed include both myeloproliferative and lymphoproliferative disorders such as acute and chronic myelogenous and lymphoid leukaemias respectively, lymphomas, paraproteinaemias and Kaposi's sarcomas (unpublished observations). Several reports suggest that there has been an increase in the incidence of cancers since the advent of HIV/AIDS^{1,2}. Haematological malignancies have also been observed more frequently in these patients^{3,4}. Furthermore, these

opportunistic cancers may result from direct and indirect action of regulatory Tat proteins of the HIV-1 causing cytokine and immunological dysregulation, resulting in diverse cancers. They may also result from interactions with other oncogenic viruses¹.

The number of HIV-infected persons living in the world have escalated dramatically since the initial discovery in 1981, to a total of about 33 million by the end of December 1999⁵. Sub-Saharan Africa is most affected with about 66% of all cases living in this continent. Cameroon with its 14 million inhabitants has an estimated prevalence of about 7.2% (Sentinel Surveillance of the Ministry of Public Health, 1999). This prevalence tends to vary in different groups within the population. For example, a prevalence of 0.43% was described in blood donors by Zekeng and Kaptue⁶ and among patients with tuberculosis, an HIV seroprevalence of about 23% has been described⁷.

With the increase in the number of haematologists in Cameroon from one in the eighties to three in the nineties, more cases with haematological malignancies are being diagnosed during the last few years. However, there is a paucity of data in most African countries and no data has been published on the prevalence of the HIV among these patients in Cameroon. Thus, this was undertaken to determine the predominant haematological malignancies seen and the prevalence of HIV-1 infection among them in this setting.

Materials and methods

This hospital-based cross-sectional study was carried out between 1994-1999 in the haematology clinic of Hôpital Central and the University Teaching Hospital, Yaoundé, Cameroon (major teaching hospitals of the country) were included. Participants consisted of patients seen routinely or as referrals to the clinic who verbally consented.

Haematological malignancies were diagnosed by routine procedures including clinical examinations, full blood counts, bone marrow aspirates, trephine biopsies and lymph node histology among others. The HIV screening test was requested in adult patients (>16 years) diagnosed with haematological malignancies, as part of the routine investigations into the aetiology of the malignancies. After a standard pre-test counselling, a clotted sample was collected from each patient and sent to the Centre Pasteur laboratory (Reference Laboratory of the country) where screening and confirmation tests for HIV antibodies were performed using enzyme-linked immunosorbent assays (ELISA) and Western Blot techniques. A post-test counselling was done for all cases during which the results were explained to the patients.

The statistical package for Social Sciences (SPSS) version 7.5 for windows was used for statistical analysis. Where appropriate, Odds Ratio was calculated (95% Confidence Interval) to establish statistical association between the HIV and haematological malignancies. Values of $p < 0.05$ were considered statistically significant.

Results

Of 195 cases, a total of 172 patients diagnosed with haematological malignancies were willing to be included in the study, a response rate of 88.2%. Their median age was 41 years (range 16 – 74 years). There were 94 males (54.7%) and 73 females (45.3%). The main haematological malignancies diagnosed among the study sample included Non Hodgkin's lymphomas (31.9%); chronic lymphocytic leukaemia (21.5%); chronic myelogenous leukaemia (18.0%); acute myelogenous leukaemia (9.9%); acute

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lymphoblastic leukaemia (7.6%) and multiple myeloma (7.0%). Burkitt's lymphoma, Hodgkin's disease and a myelodysplastic syndrome were diagnosed respectively in 1.7%, 1.2% and 1.2% of cases. None of the 12 cases with multiple myeloma diagnosed in this study were HIV-positive and no cases of Kaposi's sarcoma were noted in the study sample. There were 45 HIV-positive cases, a prevalence of 26.2% in the study population. About 62% of all the HIV-positive cases had NHL, an association that showed statistical significance (OR=5.8, adjusted for age; CI=2.7 - 12.4; $p<0.001$) - Table 1.

Table 1 Frequency of haematological malignancies and HIV status

| Type of malignancy | Frequency % | No. HIV Positive (%) | % Positive of all HIV-positives | OR (95% CI, adjusted for age) | P value |
|---------------------------|-------------|----------------------|---------------------------------|-------------------------------|---------|
| Non-Hodgkins | | | | | |
| Lymphoma | 55(31.9) | 28(50.9) | 62.2 | 5.8(2.7-12.4) | 0.001 |
| CLL | 37(21.5) | 5(14.3) | 11.1 | 0.9(0.3-2.9) | 0.85 |
| CML | 31(18.0) | 6(19.3) | 13.3 | 0.5(0.2-1.3) | 0.16 |
| AML | 17(9.9) | 2(11.8) | 4.4 | 0.3(0.1-1.2) | 0.08 |
| ALL | 13(7.6) | 1(7.7) | 2.2 | 0.1(0.02-1.0) | 0.05 |
| Multiple Myeloma | | | | | |
| Myeloma | 12(7.0) | 9(0.0) | 0 | - | NS |
| Burkitt's Lymphoma | | | | | |
| Lymphoma | 3(1.7) | 1(33.3) | 2.2 | 1.0(0.1-13.5) | 0.97 |
| Hodgkin's disease | | | | | |
| disease | 2(1.2) | 1(50.0) | 2.2 | 1.9(0.1-32.9) | 0.46 |
| MDS | 1(1.2) | 1(50.0) | 2.2 | 6.5(0.3-130.4) | 0.22 |

CLL = chronic lymphocytic leukaemia, ALL = Acute lymphoblastic leukaemia,

CML = Chronic myelogenous leukaemia

AML - Acute myeloid leukaemia

MDS = Myelodysplastic syndrome

CI = Confidence Interval

OR = Odds Ratio

The main histological types of NHL observed in association with the HIV infection were the diffuse lymphoblastic sub-type (observed in 64.3% of all the HIV-1 positive cases with the diagnosis of NHL), the follicular centroblastic types (noted in 17.9% cases) and the diffuse centroblastic sub-type in 14.3% cases.

Discussions

The Non-Hodgkin's lymphomas, the chronic lymphocytic and the myelogenous leukaemias were the predominant haematological malignancies diagnosed in this series, but a significant prevalence of HIV-1 infection was only established in the NHL group, suggesting an association with lymphoid malignancies. As far back as 1975, Penn⁸ recognised the association between abnormal cellular immunity and the increased incidence of NHL, implying that the profound defect of cell-mediated immunity in HIV-positive patients will allow a high prevalence of the disorder. Furthermore, in their analysis of patients with lymphoid malignancies in Nigeria, Analo et al⁹ noted a high HIV-1 prevalence among NHL.

The histological subtypes of NHL mainly associated with HIV-1 infection in our study were diffuse lymphoblastic and diffuse centroblastic (both high grade malignancies with poor prognosis) as well as follicular centroblastic type (low grade). Diffuse large cell tumours of either the intermediate or high-grade immunoblastic type was mostly observed in previous studies in HIV-positive patients^{10,11}. These lymphomas may result from spontaneous genetic mutations or viral transformations. Perhaps racial or environmental factors would determine histological differences in different populations. Although there was no statistical association between the HIV-1 antibodies detected in patients with myelogenous leukaemias in this study, many cases were noted, and some authors have suggested that the monocytotropism of the HIV, the chronic cytokine-mediated activation of the monocytes and macrophages and the immunodeficiency may explain the occurrence of these disorders in HIV infection³.

No significant association was established in this study between the HIV-1 and Burkitt's lymphoma, but this being a B-cell malignancy, has shown an increased incidence in AIDS patients, due to B-cell hyper activation in these patients¹². The small numbers in this study would not establish such an association.

None of the cases of multiple myeloma were HIV-positive and no cases of Kaposi's sarcoma were recorded in this series. However, an increasing incidence of Kaposi's sarcoma has been associated with HIV infection^{13,14} and a close association has been established between Kaposi's sarcoma, multiple myeloma and the human herpes virus 8^{15,16}. The role of the human herpes virus I in the pathogenesis of multiple myeloma is cumulating but this virus was not screened for in this study.

A high prevalence of the HIV infection occurs among patients with haematological malignancies in Cameroon. Non-hodgkin's lymphoma is a common opportunistic malignancy in these patients, predominantly the diffuse lymphoblastic sub-type. Although B-lineage-derived malignancies are more often associated with the HIV infection, other malignant proliferations of the haematopoietic system may not be coincidental.

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