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Role of CD4+ and CD8+ T Lymphocyte in the Onset of Stroke in People Living with HIV in Pointe-Noire

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Abstract

Objective: To determine the role of CD4+ and CD8+ T lymphocytes in the onset of stroke in people living with HIV. **Methodology:** This was a descriptive, cross-sectional study from January to July 2019, in the neurology department of loandjili general hospital, including any patient hospitalized for a first episode of stroke confirmed by brain scan. The study variables were: age, sex, CRP value, serum T cell CD4+, CD8+. The statistical analysis was carried out using the EPI info 7 software. **Results:** Twenty stroke patients were included. The relative frequency of HIV was 20%. The risk factors were potentiated by immunosuppression of CD4+ T cells. Sixty percent (60%) of the patients had a CD4+ count < 200/mm^3 and the mean CD4+ count was ±191/mm^3. Stroke was the predominant mechanism of injury with a frequency of 70%, the only injury mechanism of stroke in patients with CD8+ T cell count > 800/mm^3 (p = 0.04). **Conclusion:** Risk factors are potentiated by TCD4+ lymphocyte immunosupression, also CD8+ lymphocytes of immune system activation marker are a cardiovascular risk factor for living people with HIV.

Keywords

CD4+, CD8+ T Lymphocytes, HIV, Stroke, Pointe-Noire

1. Introduction

HIV infection and cardiovascular disease, including stroke, are two major global

public health problems. According to the 2014 UNAIDS report, in 2013, there were an estimated 35.3 million people living with HIV (PLHIV) worldwide; Sub-Saharan Africa had 24.7 million the number of PLHIV, 70% of new HIV infections worldwide [1].

The growing impact of stroke in HIV-positive patients is due to the fact that treatments have allowed patients to live longer, so reaching an age from which vascular diseases are developed; and on the other hand that some treatments can act on stroke. There is also an increase in the risk of stroke in HIV-positive patients [1].

Immunosuppression of CD4+ T cells in the onset of stroke in people living with HIV (PLHIV) has been reported in most studies examining stroke and HIV comorbidity [2] [3] [4]. Thus, while the risk of stroke in people with HIV infection is fairly well documented, in Congo there are no studies on stroke-HIV comorbidity. Thus, the profile of stroke risk factors in PLHIV is not known. HIV seroprevalence among stroke patients is high in Pointe-Noire. HIV via the immunosuppression of CD4+ T lymphocytes and the activation of CD8+ T lymphocytes is thought to potentiate the risk of stroke in Pointe-Noire.

It is with this in mind that we conducted this study, the aim of which is to determine the role of immunosuppression of CD4+ and CD8+ T lymphocytes in the onset of stroke in people living with HIV.

2. Methodology

This was a cross-sectional and comparative descriptive study carried out in the neurology department of Loandjili general hospital during the period from January 1 to July 31, 2019, *i.e.* a period of 7 months.

The study population concerned patients living with HIV for 1 year victim of a stroke confirmed by the brain scanner. Patients treated with antiretroviral drugs, statins and those who refused to participate in the study were excluded from the study. Likewise, subarachnoid hemorrhage cases were excluded.

The socio-demographic characteristics of the population taken into account were: age, sex following a clinical survey which sought notions of familial hypertension, diabetes, obesity. The biological and sero-immunological investigation consisted of looking for the CRP assay and CD4+ and CD8+ T lymphocyte typing

In all patients, a 4 ml blood sample was obtained from a median cubital vein phebotomy and kept in a tube with no additive, then analyzed using a multiparametric biochemistry auto-analyzer (HUMA Star 100), from two kits: a kit of CD4+ and CD8+ T cell counting and typing reagents (FACS Count REAGEN BDR, Facs Flow, Facs clean, FACS rinse, T cell binding solution), and a GeneXpert viral load kit (Xpert®HIV-1 Viral Load).

The database was made from the 2010 version of Microsoft Excel. Qualitative variables were expressed as frequency and quantitative variables as mean ± standard deviation. Fisher's Chi-Square Exact test was used for univariate analysis between two variables.

3. Results

During the study period, 20 patients were hospitalized in the Department of Neurology. The mean age of our study population was 44.6 ± 8.2 years with extremes of 27 to 67 years, of which 75% were males and 25%, with a sex ratio of 3.

Inflammation defined by serum CRP > 6 mg/L was common with a significant difference, moreover the majority of patients were in the AIDS stage (CD4+ < 200/mm^3). The mean CD4+ T cell count was 195.4 ± 114.42/mm^3. The mean CD8+ T cell count was 636.7 ± 354.16/mm^3. Table 1 represents the distribution of patients in functions of the sero-immunological parameters.

The frequency of inflammation in patients stratified by the number of T CD4+ lymphocytes is shown in Table 2.

Immunosuppression of CD4+ T cells (CD4+ < 200) was common regardless of the type of stroke. While the increase in the number of CD8+ T lymphocytes (CD8+ > 800/mm^3) was mainly noted in stroke patients with a significant difference.

The distribution of patients according to the type of strokes stratified by the number of T cells CD4+ and T CD8+ is shown in Table 3 and Table 4.

Table 1. Shows the distribution of patients according to the sero-immunological parameters.

Paramètres	HIV/Stroke		*P value*
	n	%	
CRP (mg/l)			
• High (>6)	13	76.5	
• Normal (<6)	14	25.5	
CD4+ (/mm³)			
• ≥200	12	60	0.006 *DS*
• <200	8	40	
CD8+ (/mm³)			
• >800	6	35	
•≤800	14	65	

Ischemic stroke was the predominant mechanism of injury in 70% of cases.

Table 2. Frequency of inflammation in patients stratified by CD4+ T cell count.

CRP (mg/l)	CD4+ < 200		CD4+ ≥ 200		Total	
	n	%	n	%	n	%
>6 mg/l	9	90	4	57.1	13	76.5
≤6 mg/l	1	10	3	42.9	4	23.5
Total	10	100	7	100	17	100

Inflammation was more common in patients with CD4+ count < 200/mm^3 than in patients with CD4+ count ≥ 200, however the observed difference was not significant.

Table 3. Distribution of patients according to the type of stroke stratified by the number of CD4+ T lymphocytes.

CD4+ number	Ischemic stroke		Hemorrhagic stroke		Total	
	n	%	n	%	n	%
<200	8	57.1	4	66.7	12	60
≥200	6	42.9	2	33.3	8	40
Total	14	100	6	100	20	100

The mean CD4+ T cell count was 192.07 ± 100.13/mm^3 for patients with ischemic stroke. In patients who had an hemorrhagic stroke, it was 203.17 ± 153.54/mm^3.

Table 4. Distribution of sick patients according to the type of stroke stratified by the number of CD8+ T lymphocytes.

CD8+ number	Ischemic stroke		Hemorrhagic stroke		Total	
	n	%	n	%	n	%
>800	7	50	0	0	7	35
≤800	7	50	6	100	13	65
Total	14	100	6	100	20	100

Ischemic stroke: the mean CD8+ T cell count was 736.86 ± 368.87/mm^3; Hemorrhagic stroke: the mean CD8+ T lymphocyte count was 403 ± 170.97/mm^3.

4. Discussion

The relative frequency of HIV infection in stroke patients in our study was 20%. Qureshi *et al.* in their series of 113 patients found a prevalence of 22% [5]. Gnonlonfoun D *et al.*, in Benin, in a larger series, reported an HIV seroprevalence of 26.1% [6]. In Malawi where the prevalence of HIV in the general population is high (12%), Heikinheimo *et al.* reported a higher prevalence than ours, at 34% in hospitalized patients for stroke [7]. The data from these different studies appeared to be higher than what we obtained during our study. The differences observed could be explained by the number of patients included, as well as by the duration of the different studies. Added to this difference in number of patients and duration, the inequality of national prevalence of HIV infection in the countries cited, the difference in sensitivity and specificity of the tests used for the serological diagnosis of HIV, and finally, care according to the geographical location of the patients as well as health and therapeutic education of the populations.

The HIV seroprevalence in our study was superimposable to that reported by Qureshi *et al.* [5]. However, the HIV seroprevalence in stroke patients in our study was about four (4) times higher than that of the general population in Pointe-Noire which is 4.6%.

In our study, we noted a predominance of the male sex. Although the female predominance in the occurrence of stroke was noted in a study conducted in Senegal [8] with a sex ratio of 0.68; most studies on stroke in PLWHA have

found a predominance of men [6] [7] [9]. In fact, Longo-mbénza *et al.*, reported a male predominance with a frequency of 94.1% in PLHIV victims of stroke [9]. This frequency was higher than ours. Gnonlonfoun D *et al.* [6], who reported a male sex frequency of 51.3%.

Raised CRP defines inflammatory syndrome. Our study reported a significant increase in CRP. This result corroborates that reported by Longo-mbénza *et al.* [9] who noted a significant increase in CRP in stroke/HIV + patients compared to stroke/HIV-patients. In our study, the increase in CRP was more frequent in patients with CD4+ T lymphocyte count < 200/mm^3. This implies the hypothesis of inflammation in the process of atherosclerosis, as pointed out by Marcus *et al.* [10]. Krikke *et al.* [11] have highlighted the role of inflammation and activation of T cells in the development of atherosclerosis in PLHIV. Assallun H *et al.* [12] reported elevations of fibrinogen and CRP as a cardiovascular risk factor associated with HIV.

The mean CD4+ T cell count was 195.4 ± 114.4/mm^3. Sixty percent (60%) of patients had a CD4+ T cell count less than 200/mm^3. Low CD4 counts during stroke in HIV positive patients have been reported by Gnonlonfoun D *et al.* [6] who reported a CD4+ count of 119 ± 36/mm^3; Longo-mbénza *et al.* [9] reported an average CD4+ count of 107.7/mm^3, Ortiz *et al.* [13] reported an average CD4 count of 113/mm^3, and 85% of these patients had a CD4+ < 200/mm^3. Tipping *et al.* in South Africa reported 46% of patients with a CD4+ count < 200/mm^3 [14]. All of these results corroborated our own.

The number of CD8+ T lymphocytes > 800/mm^3, a marker of activation of the immune system, is a cardiovascular risk factor according to the AFSSAPS recommendations on cardiovascular risk factors suitable for PLWHIV [15].

The mean CD8+ T cell count was 636.70 ± 354.16/mm^3. Thirty-five percent (35%) of our patients had CD8+ T cell counts > 800/mm^3. The increase in serum T lymphocyte level (CD8+ > 800/mm^3) mainly affected patients with stroke with a statistically significant difference (p value = 0.04).

Chronic inflammation, decrease in HDL-cholesterolemia, increase in LDL-cholesterolemia, immunosuppression of CD4+ T lymphocytes and activation of the immune system marked by elevation of CD8 T lymphocytes, contributes to the acceleration of process of atherosclerosis [10] [11] [12], which may explain the young age of onset of ischemic stroke.

5. Conclusion

Risk factors are potentiated by TCD4+ lymphocyte immunosupression, also CD8+ lymphocytes tagging immune system activation are a cardiovascular risk factor for living people with HIV. Thus the immunodepression of T CD4+ lymphocytes would it be risk marker rather than stroke risk factor? This shows the existence of a significant association between the activation of the immune system characterized by the elevation of CD8+ T cells and the AVCI which was the main lesion mechanism in positive AVC/HIV patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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