

Stroke in Human Immunodeficiency Virus (HIV) infected patients

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Introduction

- The association of stroke and HIV/AIDS has been studied since 1988 (1)
- Among stroke patients, the proportion found to be HIV+ is increasing over time:
 - *0.09% in 1997 vs. 0.15% in 2006* (2)
- The incidence of ischemic stroke is higher in HIV+ patients:
 - *5.27/1000 person-years in HIV + patients*
 - *3.75/1000 person-years in HIV - patients* (3)

Introduction

Many hypotheses have been proposed to explain the increased incidence of stroke in HIV patients:

- **Accelerated Atherosclerosis**
 - *HIV/HAART related dyslipidemia, metabolic syndrome (1)*
 - *Endothelial dysfunction due to HIV protein, HIV vasculopathy(2)*
 - *Lifestyle factors, e.g. smoking (3)*
- **Hypercoagulability**
 - *Immune activation due to infections*
 - *Protein S deficiency (4)*
 - *Anti-phospholipid antibodies(5)*
- **Opportunistic Infection**
 - *Increased systemic inflammation*
 - *CNS infections, e.g. meningitis due to tuberculosis or cryptococcus*
 - *Vasculitis due to syphilis, viruses (VZV, HSV) (6)*

(1)Grunfeld. et al, J Clin Endocrinol Metab 1992, (2)Tipping B. et al J Neurol Neurosug Psych 2007,
(3)Cockerham L. et al JAIDS, (4)Qureshi AI. et al Arch Neuro 1997,
(5)Hassoun A. et al AIDS Care and STDs, (6)Connor MD. et al Stroke 2000

Objective / Methods

- **The goal of our study:**
To compare clinical and epidemiological characteristics of stroke patients with and without HIV infection
- **Retrospective chart review**
- **Periods :** January /2005 to June/2011
- **Location:** Beth Israel Medical Center, NY
- **HIV+ group:** HIV+ patients hospitalized with Acute Stroke
(Only Patients with known HIV infection were included)
- **HIV- group:** Randomly selected pts w/o known HIV infection hospitalized with diagnosis of Acute Stroke
- **Acute Stroke:** Acute onset of neurological symptoms and confirmed by imaging
- **Transient Ischemic Attack (TIA)** excluded
- **Statistical analysis: Exploratory** Chi Square test for categorical variables, t-test for continuous variables, exploratory significance: $p < 0.05$

Methods

Characteristics, severity, and type of stroke:

- **National Institute of Health Stroke Scale (NIHSS):** a standardized, validated neurological examination that defines the severity of stroke
 - 0 = No Stroke
 - 1-4 = Minor Stroke
 - 5-15 = Moderate Stroke
 - 16-20 = Moderate/Severe Stroke
 - 21-42 = Severe Stroke
- **Stroke Types:** Ischemic, Hemorrhagic
- **Ischemic Stroke Sub-types:**
 - Large Vessel, Small Vessel, Cardioembolic, Cryptogenic
 - Defined by imaging and clinical findings

Results

Total: 1679 admissions : January 2005 - June 2011
 41 HIV+ patients were admitted with acute stroke

HIV positive Group

Characteristic	HM Positive Group(N=41)	
HAART – yes (%)	31/38 (81.6%)	
PIs	17/31 (54%)	LPV/r 7 NFV/r 1
		ATV/r 4 fos-AMP 1
		DRV/r 4
NRTIs	23/31 (74%)	TDF/FTC 7 AZT/3TC/TDF 1
		AZT/3TC 4 3TC/TDF 1
		ABC/AZT/3TC 4 TDF/d4T 1
		ABC/3TC 4 3TC/TDF/ABC 1
NNRTIs	7/31 (22%)	NVP 4
		EFV 2
		ETR 1
Integrase Inhibitors	2/31 (6.4%)	RAL 2
CCR 5 inhibitor	1/31 (3.2%)	MVC 1
Mean CD 4+ cell count	320.9 cells/mm ³ (Range: 8-1034 cells/mm ³)	

Results

Characteristic	HM Positive Group(N=41)	HM negative Group (N=101)	P Value
Age - Mean (Range)	57.2 (41 - 80)	72.4 (34 - 99)	0.001
Male sex - no (%)	30 (73.1%)	47 (46.5%)	0.004
Race			0.001
Caucasian	10 (24.4%)	74 (74.0%)	
African American	14 (34.2%)	14 (14%)	
Asian	0 (0%)	12 (12%)	
Conventional Risk Factors at Presentation			
Smoking			0.001
Never Smoker	15 (36.5%)	89 (88.1%)	
Former Smoker	6 (14.6%)	10 (9.9%)	
Current Smoker	15 (36.9%)	1 (0.9%)	
DM	12 (29.3%)	39 (38.6%)	0.293
HTN	28 (68.3%)	80 (79.2%)	0.167
Hyperlipidemia	11 (26.8%)	31 (30.7%)	0.709
Atrial Fibrillation	1 (2.4%)	17 (16.8%)	0.019
Previous Hx of Stroke	7 (16.7%)	13 (12.9%)	0.514

Results

Characteristic	HM Positive Group(N=41)	HM negative Group (N=101)	P Value
Medication at presentation			
DM Medication	10 (26.8%)	32 (32%)	0.414
HTN Medication	22 (56.1%)	71 (70.3%)	0.084
Lipid lowering Medication	10 (24.4%)	40 (39.6%)	0.102
Anti-Coagulation	4 (9.8%)	7 (6.9%)	0.54
Anti-Platelet	13 (34.1%)	29 (29%)	0.683
BMI	25.2	26.9	0.12
Systolic BP on Admission	139.97	154.5	0.033
Laboratory Data			
Coagulation			
PT-INR	1.122	1.17	0.43
PTT (sec)	29.8	30.5	0.49
Lipid Panel			
Total Cholesterol (mg/dl)	167	181	0.081
LDL (mg/dl)	98	104.4	0.45
HDL (mg/dl)	40.8	47.8	0.04
TG (mg/dl)	134.1	148.5	0.53
HgbA1c (%)	6.8	6.8	0.998

Results

Characteristic	HV Positive Group(N=41)	HV negative Group (N=101)	P Value
Stroke Related Data			
*NIHSS on admission	5.19	9.54	0.02
Outcome Mortality(%)	2 (4.8%)	11 (10.9%)	0.241
Stroke Type			
			0.044
Ischemic Stroke	39 (95.1%)	82 (82.2%)	
Intracranial Hemorrhage	2 (4.9%)	19 (17.8%)	
Ischemic Stroke Subtype			
Large vessel	21 (53.8%)	54 (65.8%)	0.808
Small vessel	15 (38.4%)	25 (30.4%)	0.155
Cardioembolic	2 (5.1%)	3 (3.6%)	0.576
Cryptogenic	1 (2.6%)	0 (0%)	0.115

*NIHSS – NIH stroke scale

Summary

Among hospitalized patients with acute stroke

- Traditional stroke risk factors (HTN, DM, hyperlipidemia) did not distinguish HIV+ from HIV- groups
- Mortality did not differ between the two groups
- Profile of HIV+ patients (HAART 82%, mean CD4+ cell count 321/mm³) compared to HIV- patients:
 - Younger, Male, African American, Current smoker
 - Lower systolic BP, Lower HDL concentrations
 - Milder stroke by *NIHSS
 - Ischemic stroke
 - History of atrial fibrillation less likely
- When the analysis was repeated with HIV- controls restricted to a subset that was age-matched to the HIV+ patients, similar results were observed.

*NIHSS – NIH stroke scale

Conclusions

- Stroke was different in HIV+ compared to HIV- patients
- The fact that HIV+ patients compared to HIV- patients were significantly younger and yet had greater likelihood of ischemic stroke, despite similar traditional risk factors, supports that HIV in some way promotes stroke
- Lower HDL concentrations in HIV+ stroke patients may be pro-atherosclerotic:
 - Low HDL is reported in untreated, uncontrolled HIV; related to ART, smoking, insulin resistance, metabolic syndrome (1-3)
 - Longitudinal studies will be needed to evaluate the independent contribution of these factors to stroke risk

Conclusions

- The higher rate of smoking in HIV+ patients underscores that smoking cessation could be an important modifier of stroke risk in this population
- HIV status should be determined as part of routine evaluation of stroke especially in younger stroke patients
- Limitations: retrospective study; missing data, e.g. viral load data unavailable; small sample size; no adjustment for multiple comparisons