

Case report

Cerebral venous thrombosis in an HIV infected patient

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History of present illness

- ◆ caucasian male, 31 yo
- ◆ previously documented HIV infection (last CD4 count : 320 cell/ μ L)
- ◆ time of HIV diagnosis and initiation of antiretroviral treatment : one year prior to current admission
- ◆ medication at time of admission :
 - ◆ Lamivudine/Zidovudine (Combivir) 1 tb x 2/day
 - ◆ Lopinavir/Ritonavir (Kaletra) 2 tb x 2/day

Chief complaint

- ◆ bilateral occipital headache
- ◆ progressive onset during the course of a week
- ◆ neurological examination upon admission was unremarkable with no focal neurological signs
- ◆ modified Rankin score (mRS) was 1 (no significant disability despite symptoms; able to carry out all usual duties and activities)
 - ◆ mRS measures functional independence on a seven grade scale – a score of 0 means asymptomatic, a score of 5 severe disability and 6 death

Differential diagnosis

- ◆ HIV and other immunosuppressed patients with headache are at significant risk for intracranial disease, including :
 - ◆ toxoplasmosis,
 - ◆ stroke (arterial or venous),
 - ◆ brain abscess,
 - ◆ meningitis,
 - ◆ malignancy of the central nervous system
- ◆ the most important factor is the degree of immunosuppression in the host :
 - ◆ CD4 cell counts $>500/\mu\text{L}$, benign and malignant brain tumors and metastases predominate, as in immunocompetent hosts.
 - ◆ CD4 cell counts from 200 to $500/\mu\text{L}$, HIV-associated cognitive and motor disorders are common
 - ◆ CNS mass lesions are most common in severely immunosuppressed patients with CD4 cell counts $<200/\mu\text{L}$

Work up

- ◆ routine blood tests : within normal range
- ◆ head MRI with venography: **partial thrombosis of the superior sagittal sinus**, without the appearance of parenchymal brain lesions
- ◆ screening panel for inherited thrombophilias : **PAI-1 homozygous mutation**, MTHFR C677T homozygous mutation and hyperhomocysteinemia



Treatment

- ◆ LMWH for 5 days
- ◆ acenocumarol titration : a challenge due to the fact the patient was constantly below the target range despite administration of high doses (up to 16 mg daily)
 - ◆ efficient oral anticoagulation in HIV patients is difficult, in spite of treatment adherence, probably due to interactions between antiretroviral medication and cytochrome P450 enzymes
 - ◆ a study performed by Andreson et al. on 73 HIV infected individuals with oral anticoagulant treatment, followed over 911 visits, found INR in therapeutic range in only 34.5 % of visits.
 - ◆ the group also found that 50 % more oral anticoagulant was required in patients treated with lopinavir/ritonavir versus efavirenz with NRTI

Drug interactions

Anti-coagulant, Anti-platelet and Fibrinolytic	Lopinavir	Ritonavir	Lamivudine (3TC)	Zidovudine (AZT/ZDV)
Acenocoumarol	■	■	◆	◆
Antiretrovirals (Nucleoside/tide Analogues)	Lopinavir	Ritonavir	Lamivudine (3TC)	Zidovudine (AZT/ZDV)
Lamivudine (3TC)	◆	◆	n/a	◆
Zidovudine (AZT/ZDV)	◆	◆	◆	n/a
Antiretrovirals (Protease Inhibitors)	Lopinavir	Ritonavir	Lamivudine (3TC)	Zidovudine (AZT/ZDV)
Lopinavir	n/a	■	◆	◆
Ritonavir	■	n/a	◆	◆

- ◆ Lopinavir/ritonavir and acenocoumarol : in vivo and in vitro data suggest that ritonavir is a modest inducer of CYP2C9. Lopinavir/ritonavir could potentially decrease acenocoumarol concentrations. INR monitoring is advised.

Follow up and prognosis

- ◆ disease progression : favourable outcome with complete remission of symptomatology
- ◆ MRI reevaluation: complete venous recanalization
- ◆ cerebral venous thromboses have a better prognosis than arterial strokes – 80% of patients have a good outcome – with complete recovery or minor residual symptoms or signs; less than 5 % of patients die either in the acute phase or within 30 days of symptom onset; poor outcome is usually associated with delay of diagnosis
- ◆ Long term complications : recurrence of thrombosis, either cerebral or at a different location; depression; vascular epilepsy; chronic headaches.
- ◆ Particular aspects of the case :
 - ◆ Rare form of stroke
 - ◆ HIV infection is rarely associated with cerebrovascular events
 - ◆ Association of mechanisms – inherited thrombophilia and HIV infection – leading to a hypercoagulable state
 - ◆ Oral anticoagulant resistance, probably related to antiretroviral treatment

THANK YOU !

