Background:

Holmes tremor is a rare symptomatic movement disorder [1]. It has a predominantly proximal distribution in the limb and is characterized by its large amplitude, low frequency (less than 4 Hz), and postural and action patterns that worsens during movement and markedly increases in goal directed movements. [2, 3]. We report on a case of Holmes tremor in an acquired immune-deficiency syndrome (AIDS) patient with cerebral toxoplasmosis. Because of the location of the lesion in the postero-lateral thalamus, the extension of surrounding edema to the brain stem and the short delay from initial neurological deficit to tremor onset, this case may strengthen the currently suggested pathophysiological mechanisms of the disease. Although a few cases of Holmes tremor in acquired immune-deficiency syndrome (AIDS) patients with cerebral toxoplasmic abscess have been reported, they can potentially strengthen the currently suggested pathophysiological mechanisms of the disease.

Case report

A 35-year old heterosexual man consulted for fatigue and speech disturbances on the 17th January 2009 at the Yaounde University Hospital Center. One week before, he started complaining of head dullness and slurred speech. His weight had dropped by 22%, from 72 to 56 kg over the past few months during which he also had persisting fever.

On neurological examination, he was confused and had cerebellar dysarthria. His pupils were symmetric with neither ophtalmoplegia nor ptosis. Facial sensation, swallowing and gag reflexes were normal. There was a left-sided hemiparesis with reduced sensation to pain and touch. There was a left Babinski sign. Reflexes were brisk on both sides, and no abnormal movement was present. A brain scan showed a ring-enhanced lesion in the right thalamus
with edema extending downward to the upper midbrain (figure1). Human Immunodeficiency Virus 1 (HIV-1) serology was positive with a CD4 count of 14 cells/mm3. Viral load was not available. Full blood count showed moderate anemia (Hemoglobin 10.4g/dl) and lymphopenia (1075 cells/mm3). Serum glutamate pyruvate transaminase and serum glutamate oxalate transaminase were respectively 61 and 62 IU/l. Hepatitis C and Hepatitis B viruses’ serologies were negative. Immunoglobulin G anti-toxoplasmic antibodies were positive (1/1012).

Sulfadiazine 4g/ pyrimethamine 25mg daily and Methyl-prednisone 80mg daily were started 3 days after admission. He was prescribed Lamivudine 30mg/ Zidovudine 300mg 12 hourly, Efavirenz 600mg daily and Fluconazole 200mg daily for cryptococcal meningitis prophylaxis. On day-8 of admission, the patient was less confused, but developed a low frequency tremor of the upper and lower left limbs with jerky-like patterns. It was a postural and intention tremor with a more discreet resting component. No dystonic posture was noted (Video1). No tremor was observed in the paretic limbs. Electroencephalography was normal. Clonazepam 1mg 12 hourly and trihexyphenidyl 5mg 12 hourly were added to his treatment, with a reduction in the tremor 24 hours after and a complete resolution 8 days later (video2). On discharge, 3 weeks after admission, his speech was fluent and motor power was normal on all limbs.

**Discussion:**

Holmes tremor was originally described by Benedikt and Souquesso and then by Holmes in 1904 who reported a patient with midbrain lesion and a 3-5 Hz tremor that was present at rest and increased markedly during intentional movement or with certain sustained postures [2,3]. There have been several terms used in the literature to designate this unique tremor. Using the terms “Holmes tremor”, “midbrain tremor”, “myorhythmia”, “thalamic tremor”,...
“mesencephalic tremor” and searching through Medline, we found only 5 cases of Holmes tremor complicating cerebral toxoplasmosis in AIDS patients. Mattos et al reported one case of midbrain toxoplasmosis and one case of midbrain and cerebellar toxoplasmosis [4] while Koppel (5) described a case with midbrain lesion. Strecker and al [6] reported on a case of mesencephalic toxoplasmic abscess involving the red nucleus and extending to the cerebellar peduncle. In the case reported by Pezzini [7], multiple nodular lesions were found in the post-central gyrus, in the right frontal superior gyrus, in the inferior parietal lobule and more importantly in the thalamus extending to the midbrain. There is one report of a patient with Holmes’ tremor and toxoplasmic abscess in the left posterior thalamic region and in the posterior arm of the internal capsule [7]. Our patient had a ring-enhanced lesion in the thalamus with edema extending to the midbrain and diencephalic white matter. Our case has two specific features: there was an abscess in the thalamus and the internal capsule with extensive edema involving the midbrain and the very short delay from initial neurological deficit to tremor onset. Because in our patients, the postero-lateral thalamus was involved, the cortico-thalamic tracts may have therefore been damaged. In addition to the abscess, surrounding edema could have damaged neural structures including the dento-rubro-olivary tract as it extended downwards to the brain stem. Thus, in all cases of Holmes tremor in AIDS patients with cerebral toxoplasmic abscess reported in the literature these cases, various anatomical locations of brain abscesses were associated with Holmes tremor (Table 1). The unifying feature of all these observations is the involvement of either the cerebello-thalamo-cortical and/or the dentato-rubro-olivary pathways. Involvement of the same tracts, which have often also been involved reported in Holmes tremor due to other causes, especially those secondary to vascular or brain traumatic lesions [3]. In our patient, the role of a superimposed dysfunction of the nigrostriatal system either by the abscess in the internal capsule or surrounding edema may account for the rest component, although it
remains hypothetical as in the case reported by Micheli F in our patient ([2, 3]). The nigrostriatal system was not involved in all reported cases of toxoplasmic-related Holmes tremor. There is one report of Strecker K and al performed a [123I]-FP-CIT: Ioflupane Single Photon Emission Computerized Tomography (DaTSCAN SPECT study -scan) in AIDS and Holmes tremor related to a toxoplasmic abscess [6]. The author showed that there were in their patient and showed a left-sided reduction in of dopamine transporter 4 months following a treatment of cerebral toxoplasmosis. Recently, in a retrospective DaTSCAN SPECT study of six patients with Holmes tremor, there was no remarkable visual difference in presynaptic dopaminergic nigrostriatal system involvement. The authors concluded that nigrostriatal pathway damage may not be crucial for the development of Holmes tremor [8]. Finally, it is also possible that direct HIV- infections of neural cells in these pathways play a modulatory pathophysiological role thus explaining why not all patients with cerebral toxoplasmosis (which predominantly involves basal ganglia) develop Holmes tremor.

In our patient, the delay from initial neurological deficit to the onset of tremor-onset was only eighteen days. In previous reports, this delay from onset of neurological deficit related to initial toxoplasmic lesion to the onset of tremor (when available) ranged from 1 month to 5 months [4-7]. The role of a secondary degeneration in the mechanisms of tremor has been advocated as it usually arises as a delayed manifestation of the initial lesion ([3]). In our observation and in that of Mattos JP ([REF4]), tremor occurred within one month of initial neurological deficit. Unlike other cases of Holmes tremor including those related to toxoplasmic abscess, in these two cases, there was a dramatic improvement of the tremor while on antitoxoplasmic/steroid treatment. It is likely that in our case, neuronal integrity was restored before degeneration could be initiated and very unlikely that the improvement could have occurred spontaneously as reported cases of spontaneous relief occurred within one year of tremor onset [9].
Conclusion:

Our case further illustrate the role of neural pathways namely the cerebello-thalamo-cortical and/or the dentato-rubro-olivary and not strict anatomical locations along with the few other available cases in the literature provides additional arguments for the role of the thalamo-cortical and/or the dentato-rubro-olivary pathways dysfunction in the pathogenesis of Holmes tremor. Put together, reported cases of Holmes tremor in the setting of AIDS and toxoplastic abscess suggest that involvement of the nigro-striatal pathway may not be crucial in the development of this syndrome. Our case also brings additional indirect arguments for the role of secondary neuronal degeneration in the mechanism of Holmes tremor.

Consent:

Written informed consent was obtained from the patient for publication of this case report and any accompanying images/video. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interest:

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Clinical work-up and literature search were performed by AL, RD and APK. All authors made critical contributions to the paper and approved the final manuscript.

References:


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Figure 1: Brain computerized tomography showing ring-enhancing lesion in the right thalamus and internal capsule with edema extending downward to the upper mesencephalum.
Additional files provided with this submission:

Additional file 1: video1.mpg, 10210K
http://www.biomedcentral.com/imedia/5662789853426995/supp1.mpg
Additional file 2: video2.mpg, 5778K
http://www.biomedcentral.com/imedia/6121498603426995/supp2.mpg