Neurosyphilis masquerading as hemiparesis and Jacksonian epilepsy in an HIV positive patient: a case report

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Abstract

Background: Neurosyphilis is a common but often missed disease worldwide, mainly because it has many manifestations making its diagnosis difficult. It is often missed among HIV patients as the search for other co-infections such as toxoplasmosis often overshadows its consideration.

Objectives: To describe one of our cases of neurosyphilis in HIV, raise awareness about the reality of neurosyphilis in Africa and share our experiences in diagnosis and management of the disease.

Methods: A 40 year old, HIV positive female was admitted with a 2 month history of left sided facial and limb weakness followed by delirium, aphasia and Jacksonian epilepsy. She underwent clinical and laboratory evaluation.

Results: On examination she had a maculo-papular rash and left sided paresis. Rapid Plasma Reagin (RPR) was reactive (titre 1:16). Treponema Pallidum Haemagglutination Assay (TPHA) was also reactive. Cerebrospinal fluid (CSF) analysis revealed: protein 56 mg per dl, glucose 71 mg per dl, cells 14 per high power field (predominantly lymphocytes). The VDRL on the CSF was positive. The CD4 cell count was 320 per ml. She was treated with intravenous penicillin G, 4 mega-units 6 hourly for 14 days, with a very good response.

Conclusion: Neurosyphilis still occurs in Uganda. It should be considered in all patients with neurological/ophthalmic illness, including those with HIV. Most cases respond well to intravenous penicillin G.

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Introduction

Syphilis is still a major cause of morbidity in most developing countries and in some areas of North America and Europe. Syphilis and HIV infection are often closely related, with HIV accelerating progression of syphilis to neurosyphilis even after treatment with benzathine penicillin.

Neurosyphilis is still a common but often missed diagnosis in Africa, especially among HIV positive patients where it is overshadowed by consideration of more known co-infections such as cerebral toxoplasmosis. This could be due to inadequate knowledge of its protean manifestations by health workers coupled with the fallacy that syphilis is now a very rare problem. Reports from Africa and indeed worldwide have shown that neurosyphilis is still a significant cause of morbidity.

In this paper we share our experience in the diagnosis and treatment of neurosyphilis in HIV patients in resource limited settings in Africa. It illustrates that neurosyphilis still occurs and its diagnosis and treatment can be achieved without using advanced imaging systems such as Computed Tomogram (CT) scan or Magnetic Resonance Imaging (MRI).

Methods

Clinical findings

In November 2004, a 40 year old left-handed widow was admitted with a 2 month history of progressive left sided weakness involving the face, arm and leg. Two weeks earlier her condition had been complicated by mental confusion, inability to talk and jerky seizures. The seizures would start with the left side of the face spread to the left arm, left leg and then involve the entire body. There was attendant loss of consciousness and post-ictal sleep but no incontinence.

On examination she had a generalised healed maculo-papular rash, was conscious but delirious. There was left sided facial paresis but no meningeal signs, Argyll-Robertson pupils or retinopathy. There was left sided limb weakness (muscle power MRC scale grade 3 in both limbs). The tendon reflexes were brisk on that side but the plantar response was equivocal. Coordination, gait and sensation could not
be done owing to her state. The other systems were unremarkable.

Investigations
It was not possible to do neuro-imaging investigations such as CT scan, as these are not available in this hospital.

Laboratory results
Full blood count
Hb=10.1 grams/decilitre, ESR=106, WBC=2950 per ml, Neutrophils 79%, Lymphocytes 14%, Monocytes 7%. Red Blood Cell film revealed a moderate macrocytic hypochromic picture. The Platelet morphology and count was normal. No haemoparasites were seen.

Serological tests
HIV serology: Determine (Abbott, Japan) and Statpak (Chembio, USA) were both reactive. The screening Rapid Plasma Reagin (RPR) (Cypress, Belgium) was reactive with a titre of 1:16. The confirmatory Treponema Pallidum Haemoagglutination (TPHA) test (Abbott, Japan) was also positive. The Fluorescent Treponemal Antibodies Absorbed (FTA-ABS) test is not available in our setting. The antibody tests ‘Hexagon Toxoplasmosis’, ‘Hexagon Tuberculosis’ (both by Human, Germany) and Brucella Agglutination test (Cypress, Belgium) all were negative.

Cerebrospinal fluid (CSF) analysis results
Protein 56 milligrams per decilitre, glucose 71mg per decilitre, WBC 14 cells per high power field—predominantly lymphocytes. The VDRL test was positive (VDRL titration was not done). The Zielh-Neelsen, gram and Indian ink stains were all negative. 4. The CD4 cell count was 320 per ml. HIV viral load test was not done.

Treatment
The patient was treated with intravenous (IV) crystalline penicillin 4 mega units 6 hourly for 14 days, in accordance with 2002 guidelines. The delirium, Bell’s palsy, hemiparesis and seizures all cleared and the patient was able to walk out of the hospital fully recovered. She was discharged on oral doxycycline 200mg every twelve hours for 28 days according to the 2002 guidelines.

Discussion
The symptoms of neurosyphilis8 include: ‘personality change 33%, ataxia 28%, stroke 23%, opthalmic symptoms e.g. blurred vision 17%, urinary symptoms incontinence 17%, lightning pains 10%, headache 10%, dizziness 10%, hearing loss 10%, seizures 7%. Signs of neuro-syphilis include:

- hyporeflexia 50%, sensory impairment 48%, pupillary changes 43%, craniopathy 36%, dementia, mania, paranoia 35%, Romberg sign 24%, Charcot joint 13%, hypotonia 10%, optic atrophy 7%.

There are 2 broad divisions:
1. early—which is usually limited to the meninges and vessels,
2. late—which involves the parenchyma (brain and spinal cord).

There are 6 recognised neurosyphilitic syndromes8.
1. Asymptomatic
2. Acute syphilitic meningitis
3. Meningovascular (arteritic) syphilis
4. Tabes dorsalis (parenchymal)
5. General paresis (of the insane)
6. Optic atrophy

These syndromes may overlap in the same patient. The mode of presentation of this patient and the laboratory findings suggested meningovascular syphilis (even though there were no meningeal signs clinically) or cerebral gumma. The CSF results were consistent with syphilitic meningitis (raised protein, pleocytosis and positive VDRL)9.

Cerebral syphilitic gummas are rare entities, consisting of masses of granulation tissue that result from an exacerbated cell-mediated inflammatory response to Treponema pallidum, usually arising from the meninges. They can involve the basal ganglia and cerebral artery territories and may thus present with stroke-like syndromes. Definitive diagnosis is made on the basis of neuroimaging, brain biopsy and positive syphilitic tests10,11.

Our case had a lesion in the territory of the internal capsule as evidenced by the equal involvement of both the upper and lower limbs and upper motor neuron facial paresis.

Meningeal neurosyphilis usually manifests with the clinical features of acute meningitis such as hydrocephalus, craniopathies and formation of gummas. Seizures due to irritative foci may occur as happened with our patient and noted by other authors8,9,11,12,13,14. A positive CSF VDRL is a specific but not very sensitive test for neurosyphilis, with a significant portion of patients having false-negative
CSF VDRL results, especially in HIV positive cases.

The term Neurosyphilis literally means syphilitic infection of the nervous system. Although neurosyphilis is traditionally termed as one of the tertiary stages of syphilis, evidence has shown that it can develop as early as in the primary stage, thus necessitating the search for its existence even in newly infected patients. The decision to do lumbar puncture in HIV patients with syphilis remains controversial. According to the Centers for Disease Control (CDC), a lumbar puncture is indicated in an HIV positive patient with syphilis, if (1) the patient has late latent syphilis or syphilis of an unknown duration, regardless of the CD4 cell count or rapid plasma reagin titer; (2) if the CD4 cell count is 350 cells/mL or less and/or the rapid plasma reagin titer is 1:32 or more, regardless of the syphilis stage; and (3) if there is no serologic response to syphilis therapy.

Our case had hemiparesis, delirium and Jacksonian epilepsy all of which cleared on getting appropriate treatment. This agrees with other workers that high dose IV penicillin is indeed effective treatment for neurosyphilis in HIV though some reports say there is varied response to IV penicillin.

This varied response to treatment may be related to the degree of immunosuppression, it could be that the higher the degree of immunosuppression the poorer the response. Our patient had a relatively high CD4 count of 320. Other authors have also stated that response to treatment in HIV patients with a CD4 count < 200 was poorer than in those with a CD4 count of > 200.

Successful use of other antimicrobials for neurosyphilis exists in the literature. These include daily intramuscular Procaine Penicillin Fortified 2.4 mega in combination with oral probenecid 500mg 6 hourly for 10-14 days and IV ceftriaxone 2grams OD for 14 days. Ceftriaxone, however, has been found to have a failure rate of 23%. Oral doxycycline 200 mg BD for 28 days, which have also successfully used in the past) following previous guidelines and case reports, although there are no large clinical trials supporting its effectiveness.

Erythromycin fell out of favour when it failed to cure fetuses of syphilis in utero. Azithromycin would have been a good alternative to penicillin but it has been bedevilled by treponemal resistance to it. Resistance to high dose IV penicillin has been reported with the patient eventually responding to IV chloramphenicol.

The serologic criteria of response to therapy is a four-fold or greater decrease in VDRL/RPR titre over 6 to 12 months. We were unable to do 6 month and 1 year reviews as our patient was lost to follow up but the initial clinical response was very compelling. Some authors have demonstrated that a four-fold fall in VDRL/RPR titre is a reliable indicator of neurophilis cure among HIV-negative patients and HIV-positive cases on antiretroviral therapy than HIV-positive cases not on antiretroviral therapy. Therefore for HIV positive neurosyphilis cases not on ART, serum RPR cannot be relied on to indicate response to therapy thus necessitating CSF examinations to be done during follow up.

Our case had a left sided hemiparesis implying a right cerebral hemisphere lesion, possibly a gumma. On CT imaging, a gumma usually reveals a hypodense lesion that enhances with contrast. Magnetic resonance imaging usually demonstrates hypointensity on T1, hyperintensity on T2, and enhancement with gadolinium.

Neurosyphilis has protean manifestations and should therefore be considered in the differential diagnosis of all neurological (and or ophthalmic) cases including those with HIV. High-dose intravenous penicillin G (12-24 megunits daily in divided doses) for 2-3 weeks is effective treatment.

References