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Case Report

When infections collide—gummatous syphilis in an HIV-infected individual

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ABSTRACT

Syphilis and HIV are both transmitted sexually and have emerged as important co-pathogens with reciprocal augmentation in transmission and disease progression. HIV-positive patients tend to experience more aggressive symptomatology due to syphilis and are at greater risk of developing neurological disease. Similarly, standard therapy for syphilis may be inadequate in HIV-positive individual suggesting intensified treatment regimens may be required along with close follow-up. We report here the case of a 50-year-old HIV-positive male presenting with an unusual constellation of neurological findings. Although he had been treated appropriately 10 years previously for primary syphilis, investigations revealed multiple current intracranial gummas. Treatment with high-dose intravenous penicillin G resulted in clinical and radiographic resolution. Given the broad differential for HIV-positive patients presenting with neurological symptoms, the clinician must maintain a high index of suspicion for syphilis known for its varied and at times unusual manifestations. Further, prior treatment of syphilis does not ensure cure and so syphilis must be considered irrespective of treatment history.

1. Introduction

Although syphilis had its origins in the New World,[1,2] this sexually transmitted disease now has a global distribution. In many industrialized nations, rates of infectious syphilis remained low through the 1980's,[3] but began to rise around the turn of the century.[4–7] In Canada, the rate increased nearly 10-fold from 0.4 cases per 100 000 in 1997 to 3.5 per 100 000 in 2004.[4] The majority of recent outbreaks of infectious syphilis in industrialized countries, as well as one report from China, have been among men who have sex with men (MSM).[8,9] In the developing countries of sub-Saharan Africa and Asia, syphilis appears prevalent in the general population ranging from 1.6% to 19%.[10–14]

HIV and syphilis are both transmitted sexually and have emerged as important co-pathogens. In several developed countries, the prevalence of HIV among patients with syphilis has ranged from 15.7% to 43%,[15–17] and as high as 64–90%.[15] These high rates of co-infection are not surprising given the reciprocal effects of the two pathogens on transmission and disease progression. Primary syphilis results in genital ulcers (chancres), which facilitate transmission of HIV.[18] Syphilis has also been shown to increase HIV viral loads in both blood and genital fluids, which may further increase the risk of HIV transmission as well as the rate of progression to immune deficiency.[19,20] Similarly, HIV facilitates the spread of syphilis. Multiple and persistent syphilitic chancres have been reported in patients with HIV infection.[21,22] Those with HIV also tend to experience more aggressive disease due to syphilis, particularly as CD4 counts decline,[22] and are more likely to have visceral involvement including neurosyphilis.[16,21,23,24] Indeed, those with a CD4 count less than 350 cells/μl and a rapid plasma reagin (RPR) titer greater than 1:32 are nearly 20-times more likely to have neurosyphilis compared to HIV-negative individuals.[24] Neurosyphilis may present in any of a number of forms depending on disease stage, including meningitis, meningovascular disease, parenchymal disease including general paresis and tabes dorsalis, as well as gummatous lesions.

We report here the case of a 50-year-old HIV-positive male treated for primary syphilis 10 years previously, who presented with multiple intracranial syphilitic gummas causing in an unusual constellation of neurological symptoms.

2. Case report

A 50-year-old HIV-infected man presented to a tertiary care center with a 1-month history of progressive right facial anesthesia, right facial droop, decreased hearing in the right ear, and pain in the right knee. There was a 6-month history of fatigue but no other constitutional symptoms. The patient reported new onset headaches within the last 2 weeks. Otherwise a review of systems yielded no other findings.

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The patient was diagnosed with HIV infection in 1997, and had declined antiretroviral therapy for personal reasons. At the time of presentation, he had a CD4 count of 296 cells/μl and a viral load of 120 664 copies/ml. The patient had been treated for primary syphilis in 1997 with one intramuscular injection of 2.4×10^6 units of benzathine penicillin G. At presentation, serologic testing for syphilis revealed a reactive enzyme-linked immunoassay (EIA) and a positive *Treponema pallidum* particle agglutination assay (TP-PA) with an RPR titer of 1:2, findings not inconsistent with previously treated disease. Serology for Toxoplasma was negative, while Epstein–Barr virus IgG was positive. The patient had recently been diagnosed with stage III anal intraepithelial neoplasia with plans for resection.

On examination the patient was alert, oriented and appropriate, and vital signs were within normal limits. Head and neck exam revealed seborrheic dermatitis over the brow. Pupils were equal and reactive to light with no evidence of Argyll–Robertson pupils. Fundi were normal with no papilledema. Cranial nerves II–IV, VI, and IX–XII were normal and symmetric bilaterally. Cranial nerve V on the right showed decreased sensation in all three distributions. Cranial nerve VII on the right showed an upper motor neuron lesion with facial droop and sparing of the forehead. There was also subjective decreased hearing in the right ear. Neurological exam showed decreased motor strength on right hip flexion, while sensation, coordination, and patellar and brachial reflexes were all normal. Gait revealed a limp secondary to pain in the right knee and decreased strength in the right hip.

Chest and cardiovascular examinations were unremarkable. The abdominal exam was normal. A digital rectal exam showed no evidence of prostate hypertrophy and no blood.

In terms of medications, the patient was taking co-trimoxazole and bupropion daily, and olanzapine at night.

Neurological findings progressed over the next 2 weeks with increased weakness on right hip flexion and the development of reduced motor strength on right knee extension. The right facial droop also became more prominent.

A computed tomography (CT) scan of the brain done immediately on presentation revealed no evidence of stroke. Subsequent magnetic resonance imaging (MRI) revealed the presence of multiple space occupying lesions (Figures 1 and 2). One lesion (28 mm diameter) was identified at the emergence of cranial nerve V from the right brain stem and extended into and obliterated Meckel's cave (Figure 2A). A 16 mm dural-based mass at the junction of the high left anterior convexity and falx cerebri was noted (Figures 1A and 2B), along with three dural-based masses at the cerebral vertex (16, 17, and 17 mm) (Figures 1B and 2C–E). These lesions were immediately adjacent to, but did not invade, the superior sagittal sinus.

The differential diagnosis at this point included meningiomas as suggested by the MRI images, and Schwannoma given the lesion extending into Meckel's cave. Also high on the differential was metastatic cancer in view of the known anal intraepithelial neoplasm. There was also a high degree of suspicion for syphilitic gummas. Imaging was not consistent with lymphoma, while brain abscesses, Toxoplasma and progressive multifocal leukoencephalopathy were considered unlikely.

Lumbar puncture and analysis of the cerebrospinal fluid (CSF) revealed a lymphocytic pleocytosis with a white blood count of 143×10^6 cells/l (92% lymphocytes). CSF glucose was low at 1.9 mmol/l (30% serum glucose) and total protein elevated at 1.19 g/l. The venereal disease reference laboratory test (VDRL) in the CSF was non-reactive, but fluorescent treponemal antibody absorption (FTA-ABS) was reactive. Cultures of the CSF for bacteria, mycobacteria, and fungi were all negative. Pathological analysis of the CSF revealed no malignant cells.

Biopsies of the skull and underlying dura revealed ill-defined granulomas consisting of lymphocytes, plasma cells and macrophages, with no evidence of necrosis. Stains for acid-fast bacteria and fungi were negative. Steinert and Warthin–Starry stains for spirochetes demonstrated the presence of appropriately sized corkscrew-shaped organisms consistent with *T. pallidum*.

The diagnosis of intracerebral syphilitic gummas was thus confirmed and therapy consisting of intravenous penicillin G 24 million units daily divided into six doses was given for a total of 21 days.

Within 1 week of initiating treatment, the patient began to show improvement with increased sensation on the right side of his face, partial resolution in the right facial droop, complete resolution of his right knee pain, and increased motor strength in both right hip flexion and knee extension. Within 4 weeks of treatment, there was complete resolution of all symptoms with the exception of some mild persistent numbness on the right side of his face.

Follow-up MRI images 9 months later showed dramatic improvement, with no enhancing intracranial lesions (Figure 2F–J). Serum syphilis serology 6 months post-treatment showed, as expected, a persistently reactive EIA and TP-PA. The RPR had converted to non-reactive. Repeat lumbar puncture at 1 year post-treatment revealed no white cells and normal glucose and protein levels (glucose 3.0 mmol/l, 54% of serum glucose;

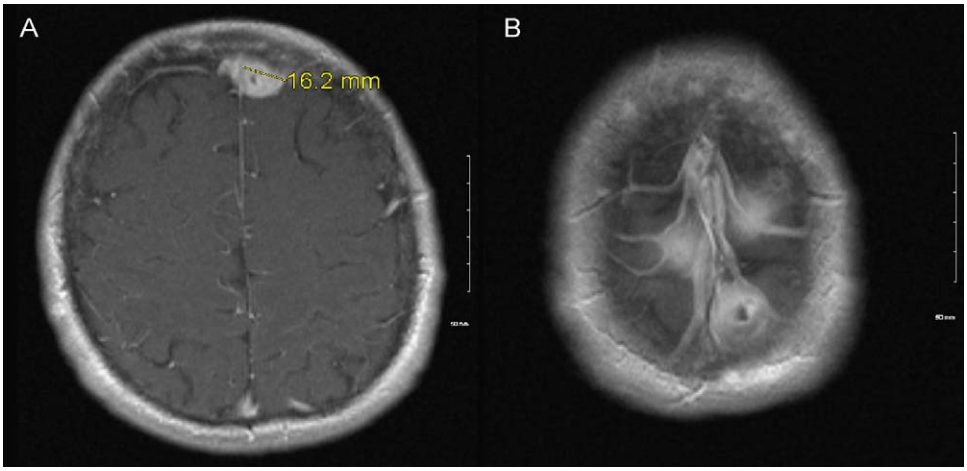

Figure 1. MRI post-contrast coronal spin-echo, inversion recovery and diffusion-weighted images obtained through the brain. (A) A 16.2 mm diameter dural-based mass at the junction of the high left anterior convexity and falx cerebri. (B) Three dural-based masses at the cerebral vertex: 17 mm (right-sided), 16 mm (left-sided anterior), and 17 mm (left-side posterior). These three lesions were immediately adjacent to the superior sagittal sinus but did not appear to invade the sinus.