Misdiagnosis of Treatable Stroke Mimic: The Case for HIV Screening in Practice Guidelines

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Abstract

Notably absent from current practice guidelines for common neurologic diseases as stroke and seizure is the revised Centers for Disease Control (CDC) recommendation for human immunodeficiency virus (HIV) testing of all clinical encounters. During a 9-month period 2 patients with treatable stroke mimics related to HIV type 1 infection were misdiagnosed resulting in delay in beginning antiretroviral therapy and increased cost and morbidity. This study was conducted to determine the frequency of HIV-I screening in our stroke center population and consider the implications of such testing on neurologic disease. We surveyed our stroke center database to determine the frequency of HIV screening in ischemic strokes from January 2005 through May 2011. Of 2806 ischemic strokes, 27 (0.96%) patients were HIV-tested during the 6.5-year study period. We suggest that incorporating the CDC recommendations for HIV screening into neurology practice guidelines can impact diagnosis and treatment of unsuspected HIV-related neurologic disease with reduction in cost of care and morbidity.

Keywords

HIV testing, progressive multifocal leukoencephalopathy, HIV encephalitis, stroke mimic, practice guidelines

Introduction

Studies have shown that changing physician behavior is challenging and failure to utilize all methods available including practice guidelines makes change in care practices all the more difficult. Despite Centers for Disease Control and Prevention (CDC) recommendations for human immunodeficiency virus (HIV) type 1 testing for all clinical encounters,¹ practice guidelines for 2 major neurologic conditions, that is stroke² and seizure,³ do not include routine screening for HIV infection. We describe 2 patients misdiagnosed with stroke mimics subsequently determined to be due to treatable complications of HIV infection. The HIV status was not determined until late in the illness with delay in institution of antiretroviral therapy (ART) with considerable cost and morbidity. To better appreciate the scope of the issue of routine HIV screening⁴ we reviewed the frequency of HIV testing in our stroke center population and highlighted the need to incorporate the CDC HIV testing recommendations in neurology practice guidelines.

Method/Results

Ischemic strokes seen at Hartford Hospital Stroke Center from January 2005 through May 2011 using ICD-9 diagnostic codes (436, 43301, 43311, 43321, 43331, 43401, 43411, 43491) were included in this study. It was determined which of these

patients were HIV tested and which had a positive result. The local institutional review board exempted this study from review. There were 2806 patients qualifying as ischemic stroke. A chart review of all HIV-tested patients of the 2806 was conducted. After excluding 11 patients; 2 for testing HIV positive on previous testing, 3 for test canceled or consent not obtained, 3 for test performed on subsequent admission, and 3 not verified by chart review, 27 unique patients remained. Each patient was tested by Enzyme Immunoassay-Reflex Western Blot. None of the 27 patients tested positive.

Case Histories

Case 1

A 42-year-old man was admitted to the hospital 10 months earlier with new-onset speech difficulty and right-sided weakness. He was diagnosed as having stroke and was treated with intravenous tissue plasminogen activator. Workup for stroke

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Figure 1. MR-FLAIR from initial hospitalization shows subtle T2 hyperintensity in the periventricular area (A; arrowheads). The MR-FLAIR 10 months after first MR shows diffuse increased signal in cerebellar and cerebral white matter (B, C; arrowheads).

was unrevealing as were routine laboratory studies except for an increased erythrocyte sedimentation rate (ESR) of 66 mm/h. A transesophageal echocardiogram showed a patent foramen ovale. Head computed tomography and magnetic resonance (MR) were reported normal and his symptoms resolved completely within 24 hours. It was felt that his neurologic deficits were likely due to either seizure or a transient ischemic attack. Over the next several months he developed depression and was treated with mirtazapine and fluoxetine. Eight months following initial hospitalization his wife noted cognitive and behavioral deterioration along with decreased appetite. Two months later he was readmitted following several generalized seizures witnessed by his wife.

Neurologic examination showed stable vital signs but the patient did not follow any commands. He was awake with spontaneous eye opening. Motor power was 0/5 in the right upper extremity and 4/5 elsewhere. Routine blood chemistries, complete blood count, and electrolytes were normal. The ESR was 88 (0-15mm/h) and cerebrospinal fluid showed pleocytosis of 98 white blood cells (WBCs)/ μ L, predominately lymphocytes, protein of 164 mg/dL, and glucose of 49 mm/dL. Electroencephalogram showed left-sided periodic lateralizing epleptiform discharges consistent with severe encephalopathy. The HIV Western blot was positive, CD4 cell count was 205/mm³, viral load was 93 100 (<20 copies/mL), and the patient was started on ART as well as levetiracetam. The MR showed diffuse, increased signal in white matter in the cerebral and cerebellar hemispheres and no enhancement with gadolinium (Figure 1B and C). Review of an MR 1 year earlier showed subtle changes in the white matter of both cerebral hemispheres (Figure 1A). The patient remained confused and disoriented with a fluctuating level of consciousness and required intensive care unit (ICU) care for 1.5 months. He was subsequently transferred to a rehabilitation facility.

Case 2

A 25-year-old immigrant from El Salvador was seen in the neurology clinic on referral from the hand clinic for

right-hand weakness to rule out of a peripheral nerve problem. The neurology consultant suspected a central process, and a subsequent MR of the head showed a left thalamic and left parietal lesion felt to represent chronic cerebral infarction (Figure 2A, B, and C). Routine chemistries were normal, WBC was 2300/ μ L, and the ESR was 45 mm/h. The patient was referred to the stroke clinic, where his examination showed 2/5 right-hand weakness in flexion and extension. A transesophageal echocardiogram was normal and the patient was diagnosed with stroke of cryptogenic origin. One month later, he was rehospitalized with worsening right-sided symptoms. The ESR was 47 mm/h, WBC was 2700/ μ L, lymphocyte count was 0.83 (N = 1.5-4.5 thou/ μ L) and HIV Western blot was positive. Repeat MR showed progression of the left hemisphere lesions; however, this was not appreciated at the time. On follow-up stroke clinic evaluation after 6 weeks, there was increased spastic right hemiparesis and he was referred to the HIV clinic for further management. Three weeks later, prior to being seen in the HIV clinic, the patient was readmitted to the neurology service with new left-sided weakness. Repeat MR showed further progression of left hemisphere lesions and a new right hemisphere lesion (Figure 2D, E, and F). The CD4 cell count was 47/ μ L. The MR changes suggested progressive multifocal leukoencephalopathy (PML) and cerebrospinal fluid polymerase chain reaction for JC virus was positive confirming the diagnosis of PML. The patient was transferred to the HIV service to begin ART. His clinical status deteriorated and, because of the risk of aspiration, no oral medications including ART were given. The patient expired 4.5 months after symptom onset less than 1 month after transfer to the HIV service.

Discussion

In the United States, some 250 000 individuals are unaware of their HIV infection. Often they are not tested as neither they nor their health care provider recognize they are at risk of HIV infection.⁵ Within a 9-month period 2 young patients with

Figure 2. Initial MR-FLAIR shows increased signal in left thalamus and posterior left frontal lobe (A, C; arrowheads). Last MR-FLAIR 4 months later shows marked extension of lesion with new posterior right frontal lesion (D, E, F; arrowheads).

undiagnosed HIV infection presented as stroke mimics to our stroke center. Contributing to misdiagnosis were failure to recognize suggestive signs and to consider a broader differential diagnosis in the clinical circumstance that would have included HIV testing.

Retrospective studies of HIV-infected patients have suggested a benefit from early ART. Recently, it has been clearly demonstrated that early initiation of combination ART not only reduces the rate of HIV transmission to uninfected partners, but also reduces clinical events in infected persons.⁶ In this study involving 1763 serodiscordant couples in which HIV-infected participants had a CD4 count of 350 to 500 cells/ μ L, there was a relative reduction of 96% in the number of linked HIV transmissions, and a relative reduction of 41% in the number of HIV-related clinical events resulting from the early initiation of ART, when compared to delayed therapy. Further, benefit from more widespread HIV testing early in the course of infection was demonstrated in a recent report of increased life expectancy by more than 15 years in people treated for HIV infection early in the course of their disease.⁷ Similarly, in patients with HIV infection with PML, optimizing or initiation of ART may improve or stabilize PML leading to prolonged survival with a 1-year survival rate of about 50% compared to 10% in those not treated with ART.⁸ In patient 1 there was a 10-month delay in ART following seizure with MR FLAIR showing abnormal white matter suggestive of HIV encephalitis. The patient spent 45 days in the ICU and 10 days on a regular hospital floor. In

patient 2 there was an 11-week delay in starting ART after testing positive for HIV infection and a 16-day delay in starting ART after PML was diagnosed. He spent a total of 32 days in a regular hospital bed before he expired.

Determination of why some patients were HIV tested and others were not was not investigated in this study and can only be speculated on. In those who were tested, the presence of suggestive risk factors for HIV infection likely prompted testing. Targeted HIV testing based on individual risk factors has had diminished effectiveness due to the demographic evolution of the US HIV epidemic over the course of 30 years.⁴ As such, in 2006 the CDC issued revised recommendations for HIV screening to include all clinical encounters. Nevertheless, subsequent specialty practice guidelines as seen with stroke² and seizure³ do not include HIV screening in the routine evaluation of patients with these conditions. Considering that only 27 of 2806 patients seen at our stroke center were tested for HIV infection suggests that the CDC recommendations for HIV testing of all clinical encounters except for those who opt-out had little to no impact on physician behavior regarding HIV screening in clinical practice. These findings reflect the literature regarding delay in implementation of recommended practice guidelines in day-to-day clinical practice.^{9–11} We suggest that the inclusion of HIV screening in practice guidelines may improve early detection and treatment outcomes of HIV-related neurologic illness and be a step forward in translational medicine in neurology.

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Declaration of Conflicting Interests

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References

1. Branson BM, Handsfield HH, Lampe MA, et al. Centers for Disease Control and Prevention (CDC). Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Morb Mort Wkly Rep.* 2006; 55(RR-14):1-17.
2. Adams HP, del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke. *Stroke.* 2007;38(5):1655-1711.
3. Krumholz A, Wiebe S, Gronseth G, et al. Practice parameter: evaluating an apparent unprovoked first seizure in adults (an evidence-based review). *Neurology.* 2007;69(21):1996-2007.
4. Libman H. Screening for HIV Infection. *JAMA.* 2011;306(6): 637-644.
5. CDC. Results of the Expanded HIV Testing Initiative—25 Jurisdictions, United States, 2007-2010. *MMWR Morb Mort Wkly Rep.* 2011;60(24):805-810 (No.24).
6. Cohen MS, Ying Q, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med.* 2011;365(6):493-505.
7. May M, Gompels M, Porter K, et al. Impact of late diagnosis and treatment on life expectancy with HIV-1: UK Collaborative HIV Cohort (UKCHIC) Study. *BMJ.* 2011; 343: d6016.
8. Koranik IJ. Progressive multifocal leukoencephalopathy: prognosis and treatment. In: *UpToDate.* www.UpToDate.com. Accessed August 10, 2011.
9. McGlynn EA, Asch SM, Adams J, et al. The quality of health care delivery to adults in the United States. *N Engl J Med.* 2003; 348(26): 2635-2645.
10. Balas EA, Boren SA. *Year Book of Medical Informatics: Managing Clinical Knowledge for Health Care Improvement.* Stuttgart, Germany: Schattauer Verlagsgesellschaft mbH; 2000.
11. Westfall JM, Mold J, Fagan L. Practice-Based Research “Blue Highways” on the NIH Roadmap. *JAMA.* 2007;297(4): 403-406.