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HIV Encephalitis Simulating Huntington's Disease

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Abstract: **Complications from human immunodeficiency virus (HIV)/acquired immune deficiency syndrome are notorious for mimicking other neurological diseases. We describe a case of HIV encephalitis presenting with the classic clinical features of Huntington's disease in a woman without known HIV risk factors or other clinical stigmata suggestive of immunosuppression. This case reminds us that HIV should be part of the differential diagnosis in unexplainable neurological diseases.** © 2005 Movement Disorder Society

Key words: HIV; encephalitis; dementia; chorea

Pathological hyperkinetic movements in those infected with human immunodeficiency virus (HIV) are rare. Unilateral chorea or ballismus are the most reported forms, usually betraying a toxoplasmosis abscess in a contralateral basal ganglia.[1–6] We report a case of slowly progressive generalized chorea, behavioral changes, and

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dementia in an otherwise "healthy" woman without any "known" risk factors, signs, or symptoms of HIV in whom the differential diagnosis included Huntington's disease (HD), prion disease, an autoimmune disorder, or a paraneoplastic syndrome, but an autopsy revealed HIV encephalitis (HIVE).

CASE REPORT

A 49-year-old woman was referred to our Huntington's disease center with progressive dementia, chorea, and dystonia. She was an adopted child having no knowledge of her biological family's history. Her first husband had died 8 years earlier, and she was remarried. Her symptoms had started 6 years ago with insidious behavioral changes that included social withdrawal and emotional lability. Three years later, she underwent a multispecialty evaluation for the subacute onset of fatigue; paresthesias, pain, and weakness in her arms and shoulders; and gait impairment. Based on a cervical spine magnetic resonance imaging (MRI) scan and electromyographic/nerve conduction velocity studies, she was diagnosed with cervical arthritis, C-7 radiculopathy, and median and ulnar neuropathies. One year later, she developed chorea of her arms and head as well as short-term memory loss. Further work-up revealed an iron-deficiency anemia; a monoclonal gammopathy (immunoglobulin [Ig] G, 2220; IgM, 1190); an erythrocyte sedimentation rate of 122; normal white blood cell count and ceruloplasmin, B12, rapid plasma reagin, Lyme antibody values; a normal electroencephalogram; cortical and central atrophy on MRI scan; and an unremarkable bone marrow biopsy.

On examination at the HD center (6 years after symptom onset), she could no longer function independently, was disoriented to place, and could not perform serial 7's, spell "WORLD" backward, add change, recall two of three items, or copy figures (Mini-Mental State Examination score, 22/30). She made paraphasic errors. Her ocular pursuits were slow and saccades were interrupted; strength and sensation were intact; tone was normal; rapid alternating movements were slow throughout; and, except for absent ankle jerks, reflexes were 1+ with absent Babinski signs. Chorea and intermittent dystonic posturing of her head and extremities were present. Ambulation required assistance. Cerebrospinal fluid (CSF) analyses revealed the following: white blood cell count, 18 (96% lymphocytes and 4 monocytes); red blood cell count, 156; protein, 50; glucose, 50; elevated 14-3-3 protein; and negative Venereal Disease Research Laboratory test. Lupus anticoagulant was present and anticardiolipin IgG was elevated. Cerebral angiogram findings were normal. Genetic testing for HD, Huntington's disease-like (HDL-2), and dentatorubropallidoluysian atrophy was negative.

Over the ensuing year, she became nonambulatory and severely demented. A diagnostic right temporal lobe biopsy was performed. It revealed a chronic meningoencephalitis with microglial nodules. Granulomata, multinucleated giant cells, viral cytopathic inclusions, and spongiform changes were absent. Further CSF analyses revealed two oligoclonal bands; IgG synthesis rate of 163; negative polymerase chain reaction findings for Jakob–Creutzfeldt (JC) virus, human T-cell leukemia virus I/II, Herpes family, Arbo, Coxsackie, and entero viruses; and absent measles and Lyme antibodies. Serum anti-neuronal nuclear antibody types 1 and 2 and Purkinje cell cytoplasmic antibody type 1 were absent. A repeat bone marrow biopsy revealed a mild erythroid and megakaryocytic hyperplasia and plasmacytosis consistent with a myelodysplastic syndrome or monoclonal gammopathy. Computed tomography of the chest, abdomen, and pelvis revealed multiple enlarged axillary and retroperitoneal lymph nodes. An MRI scan of her brain revealed significant atrophy and subtle periventricular white matter changes. An HIV test was contemplated, but the patient was transferred to hospice before her husband could be deemed her legal proxy to consent for the test.

She died 1 month later. Autopsy of the brain revealed frequent microglial nodules, many associated with multinucleated giant cells, predominately involving white matter and gray–white junction regions. Virtually all sampled cortical and subcortical brain regions were affected. An immunohistochemical stain for HIV p24 antigen positively stained the microglial nodules and associated multinucleated giant cells (Fig. 1). Other central nervous system findings included a marked diffuse astrogliosis of the caudate nucleus, putamen, claustrum, amygdala, and thalamus; a diffuse microgliosis; a marked loss of Purkinje cells; and marked vacuolar myelopathy. The rest of the autopsy showed bilateral bronchopneumonia, retroperitoneal lymphadenopathy with reactive plasmacytosis, and wasting of distal and proximal muscles. A CSF HIV RNA level obtained on a stored postmortem sample was $\log_{10}$ 5.8. Plasma viral level and CD4 lymphocyte count were not obtained.

The results from the autopsy were discussed with her husband, who subsequently discovered from a friend that her previous husband had passed away from an unknown HIV-related complication. Our patient never shared this information with her family or her medical providers. Her husband tested HIV-negative, despite unprotected sex.

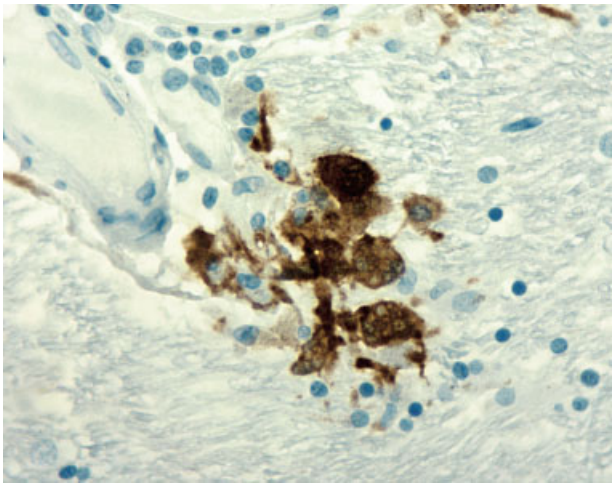

FIG. 1. Microglial nodule with multinucleated giant cells in internal capsule immunohistochemically stained for HIV p24 antigen. Scale bar = 50 μm. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

DISCUSSION

This report is an unusual case of chronic, slowly progressive HIVE simulating the cardinal features of HD in a woman not known to be HIV infected. The clinical correlate of HIVE is HIV-associated dementia (HIVD),[7] which, like HD, is classified as a "subcortical" dementia and typically manifests with behavioral changes, cognitive impairment (e.g., slowed processing and executive function), and motor abnormalities. Phenotypic differences in the motor abnormalities can usually enable one to discriminate between the two diseases.

One commonly cited study suggests that movement disorders among acquired immune deficiency syndrome (AIDS) patients are rare.[1] However, extrapyramidal signs such as bradykinesia and rigidity are common neurological abnormalities associated with AIDS, particularly among those with HIVD.[8] What is uncommon among those with AIDS are hyperkinetic movements such as chorea. When present, it is usually unilateral and associated with an underlying space-occupying lesion such as toxoplasmosis.[1–6]

Three cases of generalized chorea attributed to HIVE have been reported. In the only biopsy proven case, a subject with known HIV and a CD4 count of 383 cells/mm^3 presented with rapidly progressive encephalopathy and generalized chorea.[9] In the two presumed cases of HIVE, 1 subject with AIDS and a CD4 cell count of 50 cells/mm^3, developed rapid onset of chorea that improved with zidovudine (AZT),[10] whereas the other, who was previously undiagnosed with HIV and had a CD4 cell count of 42 cells/mm^3, presented with a 6-month progressive course of chorea, personality changes, and cognitive impairment and also improved with AZT.[11]

HIV is considered "the great mimicker" in contemporary medicine. Despite advances in antiretroviral therapy, the central nervous system is affected, directly or indirectly, by HIV in over 70% of AIDS patients, and the hallmark pathological features of HIVE, namely microglial nodules with multinucleated giant cells, perivascular infiltrates, and astrogliosis, can be found in up to 60% in autopsy series.[12] HIVE can affect the entire brain, but for reasons not yet fully elucidated, it has a predilection for the subcortical structures, particularly the globus pallidus.[13] In our patient, the basal ganglia, including caudate, putamen, globus pallidus, and claustrum, showed a diffuse astrogliosis and numerous microglial nodules. In untreated patients, the dementia rapidly progresses and death usually ensues within months.

The ultimate diagnosis of HIVE was overlooked for several reasons: its unusual presentation and the long duration of illness; the lack of identifiable or reported HIV risk factors; and the absence of laboratory (e.g., leukopenia), clinical (opportunistic infections), or imaging (e.g., HIV-associated leukopathy) abnormalities suggestive of HIV infection. Therefore, the leading diagnoses considered reflected those likely to manifest with generalized chorea and dementia, including Huntington's disease, dentatorubropallidoluysian syndrome, prion disease, autoimmune disorders, or paraneoplastic syndromes. Further complicating the picture were the presence of "red herrings" on diagnostic testing. The lupus anticoagulant and elevated anticardiolipin IgG antibodies suggested an autoimmune disorder, while the elevated CSF 14-3-3 protein suggested Jakob–Creutzfeldt disease, although antiphospholipid antibody syndrome and elevated 14-3-3 protein have been reported in HIV.[14–16]

Diagnosis and treatment with antiretroviral therapy might have prevented progression and indeed reversed the symptoms, as reported in the two presumed cases noted above and further suggested by recent studies on HIVD.[17,18] This case reminds us that HIV testing is warranted in unexplained neurological disease, irrespective of seemingly mitigating historical or clinical factors.

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Parkinsonism in the Course of HTLV-I-Associated Myelopathy

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Abstract: **Parkinsonian syndromes may represent a complication of viral infection. Human T cell lymphotropic virus I (HTLV-I) is a cause of a chronic myelopathy in which encephalic involvement has been also found. We report on the case of a 60-year-old man with HTLV-I-associated myelopathy, complicated with bradykinesia, resting tremor, and cogwheel rigidity. These findings suggest that parkinsonian features may represent a neurological disorder associated with HTLV-I infection.** © 2005 Movement Disorder Society

Key words: Parkinson syndrome; HAM/TSP; HTLV-I; CSF

Parkinson's disease (PD) is a progressive disease of the extrapyramidal system, characterized by degeneration of pigmented neurons in substantia nigra and other pigmented brainstem nuclei with dopamine deficiency transmitter in basal ganglia.[1] The syndrome includes bradykinesia, cogwheel rigidity, postural instability, and resting tremor. The most important problem is to differentiate PD from other parkinsonian syndromes related to other causes. Postencephalitic parkinsonism has been reported after viral encephalitis.[2]

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