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The human immunodeficiency virus (HIV) infects the central nervous system (CNS), causing symptoms in most persons with AIDS-related complex (ARC) and AIDS, and in a significant proportion of those classified as asymptomatic seropositive. The most common clinical syndrome secondary to CNS infection is known as HIV encephalopathy. When sufficiently disabling, HIV encephalopathy is known as AIDS dementia, and must be reported to the Centers for Disease Control as a case of AIDS.

AIDS dementia is a complex of cognitive, affective, behavioral, and motor symptoms which varies widely in its presentation. In some persons, cognitive impairment predominates, manifesting in a loss of intellectual capacities such as short-term memory, information processing, and abstract thinking. When mood disturbance predominates, it may present as irritability, anxiety, depression, or mania. Behavioral complications are most often due to confusion or psychosis, and may render the patient difficult for caretakers to manage. Motor impairments include slowing, gait abnormalities, incontinence, and paralysis.

AIDS dementia presents a significant challenge to the public health system. Physicians, other health providers, and policymakers must be educated so that they may tackle the problems of diagnosis, acute and chronic care, and public safety which are related to this illness.

AIDS is one of a spectrum of disorders resulting from infection by the human immunodeficiency virus (HIV). In addition to AIDS, there exists a number of syndromes of immune dysfunction, such as AIDS-related complex (ARC). Furthermore, it has been established that HIV causes serious neurological dysfunction in most AIDS patients, in a significant number of persons with ARC,[1] in some otherwise asymptomatic seropositives, and occasionally in persons with a false-negative serologic test.[2, 3]

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Neurological Disorders: Phenomenology

Substantial evidence indicates that HIV infects the nervous system. HIV has been recovered from brain, cerebrospinal fluid, spinal cord, and peripheral nerve of patients with HIV infection and neurological disease. Over 90 percent of autopsied AIDS cases have histopathological changes in the brain.[4]

Sixty-three percent of AIDS patients have neurological symptoms during the course of their illness, and in 20 percent, these symptoms are the initial chief complaint leading to the AIDS diagnosis.[5] All levels of the nervous system may be affected, but cerebral involvement is the most common. Many factors may adversely affect neurological function in persons with an HIV infection, including prior neuropsychiatric disorders, concurrent drug treatment, systemic illness, malignancies (both primary and metastatic to the central nervous system), and opportunistic infections.

Infections afflicting immunocompromised hosts include bacterial, fungal, and viral types. The infectious agent most likely to impair nervous system function in an HIV-infected host is HIV itself. Many HIV-induced disorders, affecting each level of the nervous system, have been described.[6] In the peripheral nervous system, nerve palsies may produce painful sensory disturbance or motor weakness, or both. Autonomic neuropathy resulting in postural hypotension, with symptoms such as dizziness, is also frequently present. Damage to the spinal cord occurs in as many as 30 percent of AIDS patients, with consequent gait problems and urinary incontinence.[7]

The most common HIV-related disorder in the nervous system is known variously as nonfocal encephalopathy, subacute encephalitis, or AIDS dementia complex.[8] It is sufficiently prevalent that the Centers for Disease Control (CDC) recorded cases of AIDS dementia among its AIDS statistics as of September 1, 1987. Notably, the dementia may occur in the absence of concomitant immune disease; that is, in otherwise relatively symptom-free HIV-infected persons.

AIDS dementia is a complex of cognitive, affective, behavioral, and motor abnormalities. It usually begins with subtle alterations in mental status, such as poor concentration and mild, short-term memory loss. Patients may complain of forgetfulness, confusion, and mental slowing. Owing to attentional lapses, they may lose the train of a conversation or be unable to follow an entire television program or read a book.

Affective symptoms often include anxiety and severe depression, with loss of energy, diminished appetite, and sleep disturbance. Patients with these symptoms may be apathetic, socially withdrawn, mildly irritable, or inappropriate in their behavior. At times, behavioral changes may be more dramatic, marked by acute psychosis with agitation, hallucinations, paranoid ideation, and even mania.

Motor impairments are common and may include lower extremity weakness, ataxia, tremors, and difficulty with articulation. Patients may notice unsteadiness when walking, deterioration in handwriting, or slightly slurred speech.

The course of AIDS dementia is variable. In some individuals, it is indolent and slowly progressive. Concentration and memory may worsen, but individuals continue to work and live independently. In others, the course of AIDS dementia is rapid and catastrophic, progressing in a matter of weeks or months to severe intellectual deterioration, marked psychomotor slowing, and mutism. Hyperreflexia, urinary and fecal incontinence, and, occasionally, seizures may occur.

Because the HIV-infected individual is vulnerable to numerous influences that can manifest in a disturbance of mental functioning, the advent of a change in mental status in

such a patient mandates a thorough evaluation to identify treatable causes such as tumors, opportunistic infections, drug toxicity, or metabolic imbalances. Once these have been ruled out, one is left with a diagnosis of AIDS dementia. There is no test that confirms the diagnosis, making it a diagnosis of exclusion.

As mentioned, the CDC now solicits reports of HIV encephalopathy/dementia, defined as follows: "clinical findings of disabling cognitive and/or motor dysfunction interfering with occupation or activities of daily living, or loss of behavioral developmental milestones affecting a child, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection that could explain the findings."[9] The appearance of this syndrome in an HIV-infected individual is now AIDS-defining; that is, its occurrence makes it a reportable case of AIDS.

The definition is necessarily vague, because the syndrome itself may have diverse manifestations, appearing singly or concurrently. In any one patient, motor, cognitive, affective, or behavioral features may predominate. Without a unique and predictable course, current knowledge prohibits the making of precise prognoses.

AIDS Dementia Complex: Epidemiology

We do not know the incidence of AIDS dementia. It is well known that most AIDS patients are grossly demented at the time of death; often, this mental decline declares itself dramatically in the last days or weeks of life. Less well known is the extent to which these same patients were functionally impaired prior to detection. This pattern is particularly apt to occur when more acute medical complications dominate the clinical picture.

Careful neuropsychological assessments of seropositives and persons with AIDS-related complex have revealed a high incidence of subclinical cognitive dysfunction. Despite the initial subclinical nature of the impairment, these individuals are coping with progressive intellectual decline that may ultimately undermine their capacity for work and social interaction.

Grant found a 44 percent incidence of neuropsychological impairment in otherwise asymptomatic seropositives, 54 percent in persons diagnosed with ARC, and 87 percent in persons with AIDS.[10] As the AIDS dementia complex becomes more widely recognized, early, subtler signs of intellectual impairment which have previously gone unnoticed or which have been understood as "functional," that is, as a psychological reaction to the diagnosis rather than organic in nature, will prompt earlier and more accurate diagnosis.

Clinical Vignette: *Mr. A., a forty-one-year-old single man, was referred to the psychiatry clinic for treatment of depression. Formerly employed as a public administrator, he had lost his job because of poor performance. Mr. A. had been in treatment for a year with a psychotherapist who was addressing issues of low self-esteem and social isolation.*

On evaluation, Mr. A. was a slovenly, mildly obese man with a slow and somewhat clumsy gait. His speech, though coherent and logical, was stuttering. Tearfully, Mr. A. described a persistent depressed mood and thoughts that others were out to get him because of past homosexual encounters. He admitted to intermittent suicidal ideation. He reported increased appetite, with a forty-pound weight gain over a year, and excessive sleep of up to fifteen hours a day, despite which he was chronically fatigued.

Mr. A. was admitted to a psychiatric hospital, where treatment with antidepressant medication was initiated. Routine psychological testing raised the question of cognitive

impairment. More comprehensive testing confirmed the presence of multiple intellectual deficits.

His medical evaluation included a CAT scan, which demonstrated cortical atrophy and a white blood count that was well below the normal range. An HIV antibody test was positive, and a diagnosis of AIDS dementia was made.

Mr. A. continued to suffer mental deterioration. He was unable to care for himself and was placed in a chronic care hospital, where he died some months later from pneumonia.

What features of this case might alert the clinician to a possibility of AIDS dementia? Once the possibility of this diagnosis has been raised, what type of evaluation is indicated? How can one now help the patient?

AIDS dementia should be considered when any patient presents with a new psychiatric condition that is accompanied by cognitive deficits or neurological impairments, or both. One must ascertain risk for HIV infection, and document its presence, if the patient consents. A medical evaluation must include CAT scan or magnetic resonance imaging (MRI), followed by lumbar puncture for analysis of cerebrospinal fluid (CSF).

The purpose of this evaluation is twofold: identification of treatable illness, such as cryptococcal meningitis and toxoplasmosis, and confirmation of the diagnosis of AIDS dementia. Making the diagnosis enables the physician to counsel the patient about his or her infectiousness and intellectual limitations; facilitate the acquisition of the necessary public assistance; and refer the patient to appropriate caretakers.

As of January 18, 1988, 51,361 cases of AIDS had been identified in the United States (1,095 in Massachusetts) with 28,683 deaths. Two hundred and seventy thousand cases are anticipated by 1991, with 54,000 cases in that year alone.[11] Given an average period of four years from infection to disease manifestation, this number of AIDS cases would occur by 1991 even if no new transmissions of HIV were to take place. The incidence of ARC is thought to be two to four times that of AIDS, and the number of infected persons in the United States totals at least 1.5 million.[12] In view of the incidence of neuropsychological impairment found by Grant and others, we must confront the likelihood that thousands of persons are afflicted with AIDS dementia.

AIDS Dementia Complex Treatment

Unfortunately, there is no cure for this disorder. Early experience with Azidothymidine (AZT) in AIDS patients suggests that the drug may retard or even reverse impairments in some individuals. Controlled trials are under way to determine whether these preliminary findings are significant.

Since the virus is known to reside and replicate in the central nervous system (CNS), any effective antiviral drug must cross the blood-brain barrier and achieve sufficient levels to eradicate virus. In the absence of such penetration, the CNS could serve as a sanctuary for HIV despite its eradication elsewhere in the body. The establishment of such a sanctuary introduces additional risks to the patient and raises a series of policy-related issues. The risks are the potential for the virus to break out of its sanctuary and affect other organs; to increase damage to the central nervous system, and thereby to cognitive abilities; and to go unnoticed or undiagnosed.

The policy implications of the sanctuary problem include at least the efficacy of new treatments or vaccines and the potential for occupational impairment and consequent threats to public safety, owing to cognitive problems.

Meanwhile, such therapies as do exist are palliative, that is, they provide some symptomatic relief and enhance functioning but do not alter the course of the disease. They consist of drugs already used for patients with medical and psychiatric disorders, and include psychostimulants, antidepressants, and antipsychotics.

Given the limitations of our pharmacopoeia, appropriate therapy must include accurate appraisal of cognitive and functional capacity and assistance in adapting to individual limitations. Because of the progressive nature of the dementia complex, patients require close follow-up. Good medical care requires a multispecialty approach that may include infectious disease, neurology, psychiatry, neuropsychology, and social service expertise.

Public Health Issues

Education

Updated training and increased awareness concerning the neuropsychiatric consequences of HIV are essential for an adequate response to the epidemic. The field of knowledge is growing rapidly. Efforts to inform health professionals are especially important. Many physicians who were trained before the AIDS epidemic feel particularly uneasy tending to AIDS patients and may choose to refer them to persons they regard as AIDS "experts." It will not be possible for such specialists to provide all care. Every physician must attain a working knowledge of AIDS, making him or her prepared to provide basic care and ready to refer to other practitioners when such referrals are appropriate.

State planning committees, as well as involvement from the private sector, labor, and other social organizations, will be necessary to increase understanding and enroll support for legislative and other governmental and private solutions to the needs of these patients.

Early Diagnosis

The hallmark of successful control of disease is diagnostic sophistication. In this disease, the early manifestations may be subtle and are often in the neuropsychiatric sphere. Most health professionals have limited familiarity with the clinical and laboratory assessments of such impairments. The psychiatric specialty within medicine can respond to this diagnostic challenge but must be ready itself to accept the challenge and the central role of psychiatry in the treatment of HIV patients.

Any change in mental status in an HIV-infected individual necessitates immediate evaluation to identify treatable causes. As mentioned earlier, there are multiple possible causes for such a change, some of which are medical emergencies requiring acute intervention. A proper diagnostic workup may include CAT scan, lumbar puncture, and electroencephalogram (EEG).

Increased Demands for Care

Several problems present major challenges. First, the complexities of diagnosis, infectious and neuropsychiatric, require technical know-how from several specialties that are not organized to function together in health care settings.

Second, the kinds of clinical problems that patients have after diagnosis require medical and psychiatric input for successful management. Currently, many HIV patients are difficult to manage on a general medical ward, owing to their agitation or psychosis, or both; because their symptoms fall into the psychiatric range, there is pressure to refer them to a psychiatric facility. Unfortunately, neither public nor private psychiatric hospitals are equipped to diagnose and treat emergent medical conditions in HIV patients.

Third, HIV patients referred to public inpatient and outpatient facilities because of neuropsychiatric disturbances could create excessive demands on these services, which are already pressed by growing numbers of chronically ill and homeless mentally ill patients.

Fourth, the range of clinical presentations calls for a range of services. Some individuals are only mildly impaired, with ongoing needs for medical and psychiatric follow-up, while others are functionally incapacitated, unable to work or adequately care for themselves. HIV-infected patients have died from undiagnosed, treatable illnesses while in psychiatric facilities, underscoring the need for appropriate sites for evaluation and treatment of such patients with neuropsychiatric symptoms. Specialized treatment centers, home care support, and outpatient programming for individual, group, and rehabilitative therapy represent other services that need to be part of the solution to these problems.

Clinical Vignette: *Mr. D., a twenty-six-year-old man who had been diagnosed with AIDS four months earlier, was brought to his internist's office by three friends after he disrobed in a public park. Mr. D. was extremely agitated, talking rapidly and pacing. He admitted to auditory hallucinations and believed that God and Satan were warring within him. He refused to cooperate with a physical examination and threatened to strike anyone who came near him. The patient was brought to the emergency room by hospital security, where he was placed in a locked room.*

Mr. D.'s internist instructed emergency room physicians to refer Mr. D. to a psychiatric hospital for treatment of manic psychosis. The hospital's psychiatric unit refused Mr. D. admission, citing the unmanageability of his agitation and the potential for violence in an unlocked psychiatric facility. Mr. D. was refused admission to other general hospital and private psychiatric units.

Mr. D. was sent to a state mental hospital, where he was placed in seclusion and treated with neuroleptic medications. Twenty-four hours after admission, he developed a temperature of 104 degrees Fahrenheit, a stiff neck, and severe obtundation. He was transferred to the general hospital, where medical evaluation revealed cryptococcal meningitis. Mr. D. was admitted to the medical floor, where antibiotic therapy was initiated.

This case illustrates the dangers of preemptive diagnosis — in this instance, of "functional" psychiatric illness. When an HIV-infected patient presents with psychiatric symptoms, serious medical illness may well be present. The patient becomes a diagnostic and treatment dilemma. No one hospital or facility is prepared to meet the challenge of caring for the patient, and, all too often, the patient is transferred from one facility to another without proper and thorough evaluation.

Limited Support for Individual Patients

HIV patients are often less likely to have family involvement in their care than, for instance, Alzheimer's patients. The stigma of the illness entity contributes to this alienation, but many of those with the illness are already socially alienated, for example, many intravenous drug users and homosexual males. Lacking supports such as family increases the morbidity (suffering) of the disease. The inability to qualify for health or life insurance because of positive antibody test results is an additional obstacle to obtaining adequate support.

The issue of disability income is also a major concern. It is not currently known to what extent otherwise asymptomatic seropositives and ARC patients may develop disabling

cognitive impairment. Some are partially incapacitated, while others are completely unable to work or to adequately care for themselves.

Because our current programs do not allow for distinctions between partial and full disability, patients may be forced either to (1) conceal or deny deficits until the condition becomes so advanced that such efforts are no longer possible, at which time patients must quit or lose a job and turn to the public welfare system, or (2) go on complete disability upon receiving an AIDS-related diagnosis, even though they are capable of continuing to work at the same or at a reduced level.

Because the system fails to make allowance for the subtle distinctions among HIV-infected individuals, it is often impossible for persons to continue working at a reduced capacity. Income from part-time work often causes discontinuation of disability payments, even though full-time employment is not possible.

Safety

Public safety is a policy issue, because impaired individuals may hold positions wherein their neuropsychiatric impairment may jeopardize the welfare of others. Should such individuals be restricted in their work? Should patients with impairments be allowed to drive? Currently, the answers to these and related questions are unclear; yet, the safety issue remains.

Clinical Vignette: *Mr. X., a thirty-two-year-old respiratory therapist, was diagnosed with ARC after a year of low-grade temperatures, enlarged lymph nodes, and recurrent oral thrush. Although he felt chronically ill, he was able to continue working full-time as a respiratory technician. Formerly married, he had two young children whom he supported in cooperation with his ex-wife, who worked part-time as a typist. Mr. X. was without life or disability insurance at the time of his diagnosis. He applied for both but feared that any investigation into prior conditions would disqualify him.*

Mr. X. was referred for evaluation of increasing difficulties with attention, concentration, and short-term memory. He reported "spacing-out" at work, and on one occasion mistakenly administered a medication in a dose ten times greater than ordered, not aware of the error until reviewing his paperwork from the previous day. Mr. X. felt that his cognitive difficulties reflected his anxiety and depression over his medical condition as well as his preoccupation with his financial situation.

Neuropsychological testing revealed moderate short-term memory deficits, psychomotor slowing, and difficulty with abstract reasoning. A CAT scan of the brain was consistent with a loss of brain tissue. Analysis of cerebrospinal fluid was unremarkable. A diagnosis of HIV-related encephalopathy was made. Treatment with methylphenidate, a stimulant medication, enhanced mental alertness and improved mood, but neuropsychological test results were unchanged three months later.

Mr. X. joined an ARC support group and began weekly psychotherapy with a psychiatrist. He experienced recurrent depression with suicidal ideation, and after several months stopped responding to methylphenidate. Trials of several antidepressant medications were discontinued, owing to intolerable side effects. Mr. X. was advised repeatedly that he should work at a less demanding job, but he continued to work for one year, at which time he developed AIDS. He is currently unemployed and on disability.

This case raises complex treatment and public health issues. Is this patient competent to continue working at his present job? Who is mandated to make that decision? If he is not

competent to continue working, should he be considered completely disabled? What will be the course of his illness? What type of follow-up is indicated for him? What are the psychological consequences when such an individual stops working yet remains relatively well for months or years? And what are the consequences for his family and for society?

The problem of intellectually compromised persons in positions of responsibility is not a new one; substance abuse in the workplace has been of sufficient public concern that drug testing has been instituted in a number of settings. Unfortunately, there is no simple diagnostic test for AIDS dementia. Widespread HIV antibody testing would offer no answer to intellectual functioning; cognitive state can be measured only with neuropsychological testing, a time-consuming and costly endeavor. Furthermore, the results of such tests must be interpreted in view of the specific demands of the individual's work.

Psychologically, it can be devastating to a productive, self-supporting individual to be removed from the work force. Many persons on disability become profoundly depressed. Careful thought must go into developing methods for assessing the intellectual capacity of infected individuals. Rational, nondiscriminatory policies must evolve to protect the individual and society from the untoward effects of cognitive impairment.

Ongoing Psychiatric Care

HIV patients, particularly those with cognitive impairment, are at great risk for psychiatric disorders. Common diagnoses in this population include adjustment disorder; major depression; anxiety; panic disorder; organic affective, delusional, anxiety, and personality disorder; and dementia.

Individual and group psychotherapy have both been shown to be valuable in the care of these patients. Furthermore, when appropriate psychiatric services are available, utilization of other medical services may decrease.

Clinicians from a variety of disciplines (including social work, psychology, and nursing) have been working effectively with this population. However, they must always be closely allied with a psychiatrist who can recognize organic syndromes, prescribe medication, and refer for neuropsychiatric evaluation when such a referral is appropriate.

Housing

Many patients with dementia lose their housing. Financial depletion may be part of the cause, but the dementia itself may render these patients unable to live safely without supervision. Such persons would do well in a structured home setting. Currently, there is a dearth of such placements.

Persons with advanced dementia are often no longer able to perform basic activities of daily living, such as hygiene and eating. Motor impairments such as paralysis and urinary incontinence may necessitate intensive nursing care. Such patients will require a total care facility, such as a hospice, a chronic care hospital, or a nursing home.

Conclusion

We have indicated that a serious feature of HIV infection is its manifold effects on neurological, cognitive, and psychiatric functioning. These effects are frequent in this population and represent a major source of the suffering and disability associated with AIDS.

We may be encouraged that the rate of new HIV infections has slowed in certain populations; yet, at the same time, we need to soberly recognize the magnitude of the needs of persons already infected. We now diagnose and treat at an earlier point opportunistic

infections and malignancies, thereby increasing life expectancy, and, with it, the incidence of clinical neuropsychiatric disorders. It is essential that we prepare ourselves to optimally care for this patient population.

We cannot rely on the medical and public health systems as they stand today; they are inadequate for the task of caring for persons who are already ill. Through education and careful planning, we must prepare ourselves for the increased demands to come.

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Glossary

Chemotherapeutic ablation. Immune deficiency that is secondary to drugs given to treat an underlying disorder.

Cytomegalovirus. A distinct virus, but a member of the herpes family of DNA viruses.

Embryopathy. A morbid condition in the embryo or in a fetus which may become apparent after birth.

Hepato-splenomegaly. Enlargement of the liver and spleen.

Histology. The science that deals with the minute structure of cells, tissues, and organs in relation to their function.

Intravenous immunoglobulin. A processed blood product with known antibody activity, given directly into the vein of an individual.

Lymphadenopathy. Swollen glands that can be located anywhere in the body.

Lymphoid interstitial pneumonitis. A particular lung disease that is commonly seen in children with AIDS. The exact etiology of this condition is not clear at present.

Mucocutaneous candidiasis. Yeast infection of the mucous membranes; commonly known as thrush.

Parotitis. Inflammation and swelling of the salivary glands.

Pathogen. Any virus, bacteria, parasite, or other microorganism or other substance that causes disease.

Pneumonitis. An infection of the lung which causes a diffuse change on a chest x-ray.

Sepsis. An infection of the blood which can be carried to internal organs via the bloodstream.