AIDS Dementia Complex

Definition

- Also referred to as AIDS-related dementia, AIDS encephalopathy, HIV encephalopathy.
- Characterized by a progressive impairment in cognitive function that is accompanied by behavioral changes and motor abnormalities.
- Diagnosed only when other causes of CNS pathology have been excluded.
- The word *complex* has been added to denote the association of cognitive changes with motor and behavioral signs.

A Diagnosis of Exclusion: other causes of encephalopathy in AIDS:

- Most common diagnoses to exclude are CNS opportunistic infection, neoplasm or substance abuse
- Also must consider toxic, metabolic causes: B12 deficiency, heavy metals, systemic infection
- Cryptococcal meningitis, CNS toxoplasmosis when CD4 <100
- Primary CNS lymphoma with CD4 less than 50
- PML (JC virus) can be similar with personality changes, cognitive deficits, aphasia, ataxia, motor deficits—CT more likely discrete, asymmetric, hypodense, nonenhancing lesions in white matter.
- In patients with higher, even normal CD4: TB meningitis, HSV encephalitis, neurosyphilis
- Less common infections: CMV encephalitis, histoplasmosis

Epidemiology

- The most common cause of cognitive decline in HIV-infected patients.
- Prevalence increases with declining immune function, but can be seen as initial AIDS defining illness, with CD4 in range of 200-500.
- Higher risk in patients >50 years.
- Depending on sensitivity of criteria used, has been detected in 25% to 90% of all patients with AIDS; and minor neurocognitive deficits have been seen at all stages of HIV
- CDC Data: prevalence of 7.3% in pre-HAART era
- Multicenter AIDS Cohort Study Group reported a 7% annual incidence in AIDS patients and a 15% cumulative incidence between AIDS diagnosis and death.
- Strongest predictors of ADC: CD4 <100, onset of other AIDS-defining infection / neoplasm
- Aggressive treatment of the systemic disease has decreased the incidence (although perhaps not the prevalence) of this HIV complication
- HAART has increased survival, decreased incidence of OI's but various series have suggested that the prevalence of ADC has increased (ie longer survival has increased prevalence)

Clinical Features

- Subclinical phase has been shown on neuropsych testing—minimal effects on ADL's, job performance
- Early signs include impairments in cognitive function: forgetfulness and inability to concentrate, as well as personality changes: apathy, diminished libido, withdrawal, emotional lability and depression.
- In moderate disease motor abnormalities become more prominent; leg weakness, slowed movement, tremor and ataxia in upper and lower extremities, Parkinsonian features have been reported
- Late in the course, psychiatric disturbances, mutism, paraplegia, seizures, incontinence, myoclonus, frontal release signs.
- This is a subcortical dementia (like Lewy Body or vascular dementia), responsible for the combination of cognitive and motor systems being affected

Pathogenesis

- HIV has been shown to invade CNS in as early as primary infection
- In CNS, HIV infects the monocyte/macrophage lineage, including monocytes that have migrated from the peripheral blood and microglial cells
- Pathology well studied: abnormalities include microglial nodules, giant cells, focal perivascular demyelination and gliosis.
    - MGCE (multinucleated giant cell encephalitis) is most specific finding (in 25%),usually present in basal ganglia, other subcortical regions
- Most commonly cited theories of pathogenesis include: direct toxicity of gp 120 on neurons, neurotoxins (arachodonic acid, platelet activating factor) and cytokines released from infected mononuclear cells (inducing apoptosis)
- Clinical severity and extent of pathologic abnormalities do not correlate

Imaging studies (no specific test)

- CT reveals cortical atrophy in about 75% of patients with ADC
- Also seen on CT is attenuation of white matter, appears like microvascular PVWM disease (symmetrical and less demarcated as opposed to PML)
- MRI shows hyperintense white matter lesions on T2 imaging: from discrete foci to large confluent periventricular lesions, often frontal lobe predominant.

Laboratory Findings (no specific test)

- The CSF is usually normal or shows mild pleocytosis, protein elevation, and oligoclonal bands.
- Elevated CSF IgG corresponds to intrathecal synthesis of antibody to viral antigens.
- CSF viral load has not been correlated with degree of impairment or onset of dementia, and + PCR for HIV RNA seen in non-demented patients

Treatment

- Antiretrovirals chosen should penetrate BBB: these are AZT, ddI, d4T
- NNRTI's and protease inhibitors have seemed beneficial in studies, but thought to be secondary to decreasing plasma viral load, and thus decreasing CNS invasion.

Prognosis

- Usually progressive, eventually to severe terminal dementia; function may plateau on HAART, complete reversal rare

- In one large cohort study of prognosis, mean survival in pre-HAART era after Dx of ADC was 11.9 months, in post-HAART era was 48.2 months (no RCT's—unethical, thus no NNT)

- Smaller cohort study of patients followed with standardized scales severity scales, all on HAART—40% progressed despite HAART, 60% improved

References

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