AIDS DEMENTIA & HIV NEUROCOGNITIVE DISORDERS

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AIDS DEMENTIA & HIV NEUROCOGNITIVE DISORDERS

Special Thank You To:

Elyse Singer, MD
Professor of Neurology
David Geffen School of Medicine at UCLA
Director, National Neurological AIDS Bank
OUTLINE

1. Definitions & Nosology (Types) of HIV Associated Neurocognitive Disorders

2. Epidemiology & Prevalence
   Changes Since Combined Antiretroviral therapy (cART)
   Associated Risks for HIV Neurocognitive Impairment

3. Pathophysiology

4. Clinical Presentation
   Early & Late Manifestations
   Contrast With Alzheimer’s
   Changes Since cART
OUTLINE

5. Diagnostic Assessment
   - History
   - Cognitive Exam
   - Laboratory & Imaging

6. Treatment Interventions
   - Antiretroviral Therapy
   - Other Medications
   - Psychiatric Medications for Symptom Management
   - Adjunct Non Medication Approaches

7. Three Cases
CASE ONE

Brian is a 42 year old HIV infected investment banker who is concerned that he is having problems focusing at work after a recent promotion to an more challenging position. He is worried that he is developing HIV associated dementia.

Although he has an AIDS diagnosis from Pneumocystis (carinii) jiroveci pneumonia and a CD4 nadir of 123 many years ago, he has had excellent response to antiretroviral therapy. He currently has a normal CD4 count and has had an undetectable plasma HIV viral load for the past 3 years.
CASE ONE

1. What is HIV associated dementia? Is it different from HIV associated neurocognitive disorders (HAND)?

2. How common is HIV associated dementia? Is it different since antiretroviral therapy has been available?

3. Who gets HIV associated dementia, what are associated risks?

4. How does HIV cause neurocognitive problems?

5. What is the clinical presentation of HIV associated neurocognitive disorder? What are early symptoms?
AIDS Dementia: AIDS Defining Condition

Definition 1
Clinical findings of disabling cognitive or motor dysfunction interfering with occupation or activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection that could explain the findings.

Lots of Names
AIDS Dementia Complex (ADC) 1986
HIV Encephalopathy (Dementia) 1987 2
HIV Associated Dementia (HAD) 2007 3

Spectrum Disorder - Mild to Severe Symptoms

1 MMWR 1992, 2 MMWR 1987, 3 Antinori 2007 Neurol
DEFINITION & NOSOCOLOGY (TYPES) OF HIV ASSOCIATED NEUROCOGNITIVE DISORDERS

Older Terminology

HIV Associated Minor Cognitive Motor Disorder –
  Early, Less Severe Symptoms
AIDS Dementia Complex (ADC) - Late Disabling Symptoms

Newest Terminology ¹ HIV-Associated Neurocognitive Disorders (HAND)

HIV Associated Dementia (HAD)
  Cognitive with **Disabling** Functional Impairment
Mild Neurocognitive Disorder (MND)
  Mild Cognitive with **Mild** Functional Impairment
Asymptomatic Neurocognitive Disorder (ANI)
  Cognitive But **No** Functional Impairment – Requires
  Neuropsychological Testing for Diagnosis

¹ Antinori 2007 Neurology
Incidence of AIDS Dementia Reduced >50% Since cART ¹

<table>
<thead>
<tr>
<th>Period</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988-1995 (Pre cART)</td>
<td>16.7%</td>
</tr>
<tr>
<td>2000-2007 (cART)</td>
<td>6.79%</td>
</tr>
</tbody>
</table>

¹ Heaton 2011 J Neurovirol
Severity & Incidence of Cognitive Impairment

Decreased Since cART
Attenuated Neurocognitive Impairment
  Slower Progression ¹

But Prevalence Increasing Due to Extended Life With Treatment ¹

High Burden of Cognitive Impairment Persists Even with cART ²
  2% HIV Associated Dementia
  12% Mild Neurocognitive Disorder
  33% Asymptomatic Neurocognitive Impairment
  47% With Cognitive Dysfunction (Total)

¹ Mc Arthur 2004 J Neuroimmunol, ² Heaton 2010 Neurol
Cognitive Dysfunction in HIV Infected Patients

With Suppressed HIV Viral Load for 4 Years

- 4% HIV Associated Dementia
- 28% Mild Neurocognitive Disorder
- 42% Asymptomatic Neurocognitive Impairment
- 74% With Cognitive Dysfunction (Total)

“Hidden Epidemic of neurological disease in aviremic individuals”

1 Simioni 2010 AIDS (Switzerland), 2 McArthur 2010 AIDS
Epidemiology & Prevalence: Associated Risks for HIV Neurocognitive Impairment

Low CD4 With AIDS Dementia Patients 1991-1993

AIDS Dementia Unit, St Mary’s Hospital, San Francisco, CA

N=84, Median= 25.0, Mean= 45.9, SD= 63.1
Low CD4 Nadir (Since ART) \(^1,^2,^3\)

Increased Risk with HIV Subclade C \(^4\)

- Subclade C is Most Common HIV Clade
- 50% of HIV Infections Worldwide
  - China, India, Sub-Saharan Africa
  - USA & Europe – Mostly Subclade B

AIDS Mania Can Precede AIDS Dementia

Associated With Cognitive Decline \(^5,^6\)

\(^1\) Valcour 2006 J Neurovirol, \(^2\) Tozzi 2005 J of NeuroVirol (Italy),
\(^3\) Heaton 2011 J Neurovirol, \(^4\) Gannon 2011 Cur Opin Neurol
\(^5\) Lyketsos 1997 J Neuropsych, \(^6\) Nakimili 2006 Am J Psych (Uganda),
EPIDEMIOLOGY & PREVALENCE:
ASSOCIATED RISKS FOR HIV NEUROCOGNITIVE IMPAIRMENT

Non HIV- Specific Associations

Older Age

1. HIV Population is Aging - By 2015
   >50% of HIV Infected In US Will Be > 50

Drug & Alcohol Dependence

Lower Intelligence (IQ)

Traumatic Brain Injury (TBI)

Hepatitis C Virus Co-infection

1. ApoE4 Genotype

Unclear Association

Not Receiving Antiretroviral Therapy?

CNS Multidrug Resistant HIV Virus?

PATHOPHYSIOLOGY

HIV is Neuroinvasive, Neurotropic, and Neurovirulent ¹

Early HIV Entry to CNS
Within Hours to Days of HIV Infection
(1992 Autopsy Case ² & Animal Studies)

HIV Infects Non-Neurons
Infects Macrophages, Microglia, Astrocytes
HIV Infected Astrocytes Disrupt Blood Brain Barrier ³
No Infection of Neurons, Oligodendrocytes

¹ Singer 2010 Neuro Clin, ² Davis 1992 Neurol, ³ Eugenin 2011 J Neurosci
Sustained Chronic Brain Inflammation
Threshold Level Occurs Early HIV Infection and Persists
Unchanged With Combination ART, Likely Due to
Inadequate Penetration of cART and High Levels of Proviral HIV DNA in CNS Non Nuerons which is not lowered by cART

Magnetic Resonance Spectroscopy (MRS) \(^1\) Indicate Persistent Brain Degeneration and Inflammation in cART Treated Patients

Brain Injury with Neuronal Death & Demyelination
Subcortical Degeneration
(Basal Ganglia, Deep White Matter, Hippocampus,)
Emerging Cortical Involvement With cART \(^1,2\)

\(^1\) Harezlak 2011 AIDS, \(^2\) Heaton 2011 J Neurovirol
Indirect Neurotoxicity from Inflammatory Factors Secreted by HIV-Infected Monocytes, Macrophages and Astrocytes:

- TNF, Excitatory AA, Cytokines, Free Radicals,
- Apoptosis Inducers, \(^1\) Glutaminase \(^2\)

Direct Neurotoxicity from HIV Proteins

- Released from Infected Cells: gp 120, TAT, Nef, Vpr \(^3\)

MRS Changes in AIDS Dementia Patients: Decrease in N-Acetyl Aspartate/Creatine (Neuronal Marker) \(^4\)

Synaptodendritic Injury - Disruption in Neuron Circuitry (Pruning)

Correlates with Cognitive Impairment

Also in Alzheimer’s, Parkinson’s \(^5\)

\(^1\) Lindl 2010 J Neuroimmune Pharmacol, \(^2\) Huang 2011 J Neurosci, \(^3\) Van de Bovenkamp 2002 Eur J Clin Invest, \(^4\) Harezlak 2011 AIDS, \(^5\) Ellis 2007 Nat Rev Neurosci
CLINICAL PRESENTATION: COGNITIVE FUNCTIONS

EARLY – Mild Neurocognitive Disorder
- Forgetfulness
- Slowed Processing of Information
- Impaired Attention
- Loss of Concentration
- Sequencing Problems

LATE – HIV Associated DEMENTIA
- Severe Memory Loss
- Word Finding Problems or Speech Arrest
- Severe Attention & Concentration Problems
- Poor Judgment
CLINICAL PRESENTATION: BEHAVIORAL

EARLY – Mild Neurocognitive Impairment
  Withdrawal
  Apathy
  (associated with atrophy of caudate nucleus)
  Disinhibition
  Impetuous Actions

LATE – HIV Associate Dementia
  Extreme Withdrawal
  Irritability
  Apathy
CLINICAL PRESENTATION: AFFECTIVE

EARLY – Mild Neurocognitive Impairment
  Depression
  Hypomania
  Personality Change

LATE – HIV Associated Dementia
  Extreme Depression
  Mania (Rare)
  Psychosis (Rare)
CLINICAL PRESENTATION: MOTOR

EARLY –
- Slowing
- Unsteady Gait
- Weakness (Lower Extremities)
- Poor Coordination
- Handwriting Change

LATE –
- Marked Slowing
- Tremor
- Spasticity & Paraplegia
- Incontinence
- Muteness
- Parkinsonian Picture (Particularly in Older Males)
# CLINICAL PRESENTATION: CONTRAST WITH ALZHEIMERS

<table>
<thead>
<tr>
<th>AIDS DEMENTIA</th>
<th>ALZHEIMERS</th>
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<tbody>
<tr>
<td><strong>Memory</strong></td>
<td></td>
</tr>
<tr>
<td>↓ Working/Short Term</td>
<td>↓ Delayed</td>
</tr>
<tr>
<td>↓ Retrieval Information</td>
<td>↓ Encoding New Info</td>
</tr>
<tr>
<td>Improves With Cueing</td>
<td>Cueing Does Not Help</td>
</tr>
<tr>
<td><strong>Language-</strong></td>
<td></td>
</tr>
<tr>
<td>Spared</td>
<td>Impaired</td>
</tr>
<tr>
<td><strong>Visuospatial</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Motor</strong></td>
<td></td>
</tr>
<tr>
<td>Impaired</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>Speed</strong></td>
<td></td>
</tr>
<tr>
<td>Slow</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>Tremor</strong></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Coordination</strong></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>Reflexes</strong></td>
<td></td>
</tr>
<tr>
<td>Hyperreflexia</td>
<td>Normal</td>
</tr>
</tbody>
</table>

1 Singer 2010 Neurol Clin
**CLINICAL PRESENTATION: CHANGES SINCE COMBINATION ANTIRETROVIRAL TREATMENT (cART)**

<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Executive Functioning</td>
<td>Impaired</td>
<td>More Impaired</td>
</tr>
<tr>
<td>Learning</td>
<td>Impaired</td>
<td>More Impaired</td>
</tr>
<tr>
<td>Motor Skills</td>
<td>Impaired</td>
<td>Less Impaired</td>
</tr>
<tr>
<td>Information Processing</td>
<td>Impaired</td>
<td>Less Impaired</td>
</tr>
<tr>
<td>Speed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Heaton 2011 J Neurovirol
CASE ONE

1. What is HIV associated dementia? Is it different from HIV associated neurocognitive disorders (HAND)?

A. HIV associated dementia, also called AIDS dementia, includes disabling cognitive but not motor dysfunction.

B. HIV associated neurocognitive disorder includes a spectrum from mild to severe symptoms: asymptomatic neurocognitive disorder, mild neurocognitive disorder, and HIV associated dementia.

C. Both A & B
CASE ONE

1. What is HIV associated dementia? Is it different from HIV associated neurocognitive disorders (HAND)?

   A. HIV associated dementia, also called AIDS dementia, includes disabling cognitive but not motor dysfunction.

Correct answer: B

   B. HIV associated neurocognitive disorder includes a spectrum from mild to severe symptoms: asymptomatic neurocognitive disorder, mild neurocognitive disorder, and HIV associated dementia.

   C. Both A & B
2. How common is HIV associated dementia? Is it different since antiretroviral therapy has been available?

A. The incidence of HIV associated dementia has been reduced.

B. Cognitive dysfunction is rare with HIV suppression and undetectable HIV viral load.

C. Asymptomatic neurocognitive disorder is less prevalent than HIV associated dementia.
2. How common is HIV associated dementia? Is it different since antiretroviral therapy has been available?

Correct answer: A

A. The incidence of HIV associated dementia has been reduced.

B. Cognitive dysfunction is rare with HIV suppression and undetectable HIV viral load.

C. Asymptomatic neurocognitive disorder is less prevalent than HIV associated dementia.
3. Who gets HIV associated dementia, what are associated risks?

A. Smoking cannabis
B. Younger age
C. Low CD4 count
D. Low CD4 nadir
3. Who gets HIV associated dementia, what are associated risks?

A. Smoking cannabis
B. Younger age
C. Low CD4 count

Correct answer: D
D. Low CD4 nadir
4. How does HIV cause neurocognitive problems?

A. HIV penetrates the brain many years after seroconversion.

B. HIV infects neurons and is directly neurotoxic.

C. HIV interrupts neuronal circuits and unlike Alzheimer’s disease has increased neuron pruning.

D. HIV infects brain monocytes, macrophages, and astrocytes, which generate both neurotoxic viral proteins and neurotoxic cytokines that cause neuronal dysfunction and neuronal apoptosis.
4. How does HIV cause neurocognitive problems?

A. HIV penetrates the CNS many years after seroconversion.

B. HIV infects neurons and is directly neurotoxic.

C. HIV interrupts neuronal circuits and unlike Alzheimer’s disease has increased neuron pruning.

Correct answer: D

D. HIV infects brain monocytes, macrophages, and astrocytes, which generate both neurotoxic viral proteins and neurotoxic cytokines that cause neuronal dysfunction and neuronal apoptosis.
CASE ONE

5. What is the clinical presentation of HIV associated neurocognitive disorder? What are early symptoms?

A. Severe memory and concentration problems
B. Personality changes
C. Incontinence
D. Hyperactivity
5. What is the clinical presentation of HIV Associated Neurocognitive Disorder? What are early symptoms?

A. Severe memory and concentration problems.

Correct answer: B
B. Personality changes

C. Incontinence

D. Hyperactivity
CASE TWO

Jeff is a 27 year old homeless HIV infected man with methamphetamine dependence with a low CD4 count of 98. Because of his chronic poly substance and alcohol dependence, he has not engaged in HIV care and he is not on antiretroviral therapy.

He is brought to clinic by a Mission shelter case worker because he was observed to be confused. He appears somnolent, has a fever, and has left arm hyperreflexia.
1. Is it possible that he has an opportunistic infection or tumor causing his symptoms?

2. What is the appropriate history and cognitive assessment?

3. What laboratory tests and imaging studies are appropriate?
DIAGNOSTIC ASSESSMENT

Early Neurocognitive Changes are Deceptive
Screening Indicated With $^1$

- Low CD4 Nadir (CD4 $\leq$ 200)
- Advanced Disease Without ART Treatment “Late Entry to Care”
- Complaints in High Functioning Individuals With Complicated Jobs
  Intolerant of Executive Functioning Impairment

Rule Out Treatable Opportunistic Infections
  Tumors, Metabolic Problems, Drugs

Diagnosis of Exclusion - There are No Biomarkers
  for HIV Neurocognitive Disorder $^2$

$^1$ Singer, personal communication $^2$ McGuire 2009 Neurology
DIAGNOSTIC ASSESSMENT - HISTORY

GOAL = ESTABLISH BASELINE

Collateral Information From Family & Friends
   About Personality & Behavior Changes

Highest Level of Education & Occupation

Psychiatric Affective & Mood Disorders
   Hospitalizations & Suicide Attempts
   Depression Heralds Many Types of Cognitive Problems

Drug & Alcohol Use
Attention (Serial Sevens)
Short Term Memory (3 of 3 at 3 Min)
Spell WORLD Backwards
Judgment (Situational)
Proverb Interpretation
Shifting Sets (1A, 2B, 3C, etc)

Orientation, Conversation, Remote Memory,
& Fund of Knowledge Often Appear Normal

Neuropsychological Testing – Requires Literacy
Not Normed for Ethnic Minorities
CD4 Count – CD4 Nadir is More Important
HIV Viral Load - Both Serum & CSF
  Positive HIV CSF is not diagnostic of HAND
  High HIV viral load in CSF Plus Cognitive Impairment
    Indication for More CNS Penetrating ART
Lumbar Puncture with CSF Studies - Send for Everything
  Neopterin & Beta 2 – Correlates with Intrathecal Inflammation
Serum & CSF Cultures for CNS Infections
Always Check for Syphilis!
Screen for Metabolic & Endocrine
  (B12, Thyroid, Folate, Hepatic Encephalopathy)
Toxicology Screen
Cranial MRI with and without Contrast
HIV Associated Dementia

Atrophy – Enlarged Ventricles & Sulci

Non Enhancing “Dirty White Matter”

MRI T2-WI, Medscape 2002
AIDS Lymphoma

Ring Enhancing Lesion

MRI w/Gad JS 1993, St Mary’s
Toxoplasmosis

Multiple Focal
Ring Enhancing Lesions

MRI w/Gad, JW 1990, CMF
PML

Focal Non Enhancing Sub-Cortical Lesion

MRI w/Gad, TO 1992 St Mary's
PML
Focal Non Enhancing Sub-Cortical Lesion

MRI T2 WI, OG 1993 St Mary’s
CASE TWO

1. Is it possible that he has an opportunistic infection or tumor causing his symptoms?

   A. Somnolence and confusion are common with HIV associated dementia.

   B. A normal cranial CT rules out an opportunistic infection.

   C. Non HIV causes must always be considered and ruled out.
CASE TWO

1. Is it possible that he has an opportunistic infection or tumor causing his symptoms?

A. Somnolence and confusion are common with HIV associated dementia.

B. A normal cranial CT rules out an opportunistic infection.

Correct answer: C

C. Non HIV causes must always be considered and ruled out.
2. What is the appropriate history and cognitive assessment?

A. Neuropsychological testing is needed to identify HIV associated dementia.

B. Family members notice early cognitive changes and are therefore very helpful for collateral information.

C. Baseline function is irrelevant with mild neurocognitive impairment.
CASE TWO

2. What is the appropriate history and cognitive assessment?

A. Neuropsychological testing is needed to identify HIV associated dementia.

Correct answer: B

B. Family members notice early cognitive changes and are therefore very helpful for collateral information.

C. Baseline function is irrelevant with mild neurocognitive impairment.
CASE TWO

3. What laboratory tests and imaging studies are appropriate?

A. Cranial MRI with atrophy is suggestive but not diagnostic of HIV associated dementia.

B. A normal cranial CT rules out opportunistic infections.

C. Lumbar puncture with CSF studies is unnecessary with a normal neurological examination.
3. What laboratory tests and imaging studies are appropriate?

Correct answer: A

A. Cranial MRI with atrophy is suggestive but not diagnostic of HIV associated dementia.

B. A normal cranial CT rules out opportunistic infections.

C. Lumbar puncture with CSF studies is unnecessary with a normal neurological examination.
CASE THREE

Tom is a 38 year old alcohol and methamphetamine dependent man diagnosed 3 years ago with HIV infection while in prison. Although his initial CD4 was low at 97 he declined antiretroviral treatment and did not seek HIV care when he paroled last year.

He recently completed inpatient chemical dependency treatment, is now clean and sober, and living with his mother. She has noticed that he is very forgetful and is “just different.” She explained that he has been withdrawn, apathetic, very depressed, has unsteady gait, and very poor judgment.

After a complete diagnostic evaluation he was diagnosed with HIV associated dementia. He would like to be treated.
CASE THREE

1. How is HIV associated dementia treated?
2. How can psychiatric symptoms be managed?
3. What non medication interventions can help him?
TREATMENT INTERVENTION: ANTIRETROVIRAL THERAPY

Goal - Preserve Immune Function & Lower Viral Load

Antiretroviral Treatment Improves Neurocognitive Function $^{1,2,3}$
It is the Who and Which That Are Controversial

Who Should Be Treated With ART?
Which Antiretroviral Medications?

$^1$ Cysique 2011 BMC Neurol (Australia), $^2$ Tozzi 2009 JAIDS (Italy),
$^3$ Smurzynski 2011 AIDS
TREATMENT INTERVENTION: ANTIRETROVIRAL THERAPY

WHO

Combination ART Recommended for Symptomatic Neurocognitive Disorder (MND & HAD)

No Established Recommended treatment for Asymptomatic Neurocognitive Disorder

Should Asymptomatic Neurocognitive Disorder be on ART?

Probably, But There is No Research Information

WHICH

Antiretrovirals with Good CNS Penetration More Effective in Suppressing CSF HIV

Combinations Should Include More than One CNS Penetrating to Avoid Resistance

1 Letendre 2008 Arch Neurol
### TREATMENT INTERVENTION: ANTIRETROVIRAL THERAPY

#### CNS PENETRATION $^{1,2}$

<table>
<thead>
<tr>
<th></th>
<th>High</th>
<th>Medium</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTI</td>
<td>Abacavir</td>
<td><strong>Emtricitabine</strong></td>
<td>Didanosine</td>
</tr>
<tr>
<td></td>
<td>Zidovudine</td>
<td>Lamivudine</td>
<td><strong>Tenofovir</strong></td>
</tr>
<tr>
<td>NNRTI</td>
<td>Delavirdine</td>
<td><strong>Efavirenz</strong></td>
<td>Zalcitabine</td>
</tr>
<tr>
<td></td>
<td>Nevirapine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI</td>
<td>Amprenavir/R</td>
<td>Atazanavir/R</td>
<td>Nelfinavir</td>
</tr>
<tr>
<td></td>
<td>Indinavir/R</td>
<td></td>
<td>Saquinavir/R</td>
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<tr>
<td></td>
<td>Lopinavir/R</td>
<td></td>
<td>Tripanavir/R</td>
</tr>
<tr>
<td></td>
<td>Darunavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusion</td>
<td></td>
<td></td>
<td><strong>Enfuvirtide</strong></td>
</tr>
</tbody>
</table>

$^1$ Letendre 2008 Arch Neurol, $^2$ Wright 2011 Cur Opin HIV & AIDS
TREATMENT INTERVENTION: ANTIRETROVIRAL THERAPY

Poor Correlation of Cognitive Impairment and HIV Viral Load (Serum or CSF) Since cART $^{1,2}$

CNS Penetrating ART may Be Neurotoxic and Worsen Cognitive Performance $^{3,4}$

Controversial - Studies in Non Demented Persons

1 Sevigny 2004 Neurol, 2 McArthur 2004 Arch Neurol,

3 Marra 2009 AIDS, 4 Robertson 2010 Neurol
TREATMENT INTERVENTION: ANTIRETROVIRAL THERAPY

WHY IS THIS?

Limitations Of HIV Viral Load Assessment:

Threshold Problems – Undetectable Virus is **Not** Zero Virus

Does Not Measure Brain Infection – Sequestered Reservoir

Plasma, CSF, Brain are Separate and Poorly Communicating Areas

Measures only HIV RNA – Not Cell Integrated HIV Proviral DNA or HIV Neurotoxic Proteins

Whole HIV Virus Not Needed for Neuropathology

Incomplete, Defective Virus and Viral Proteins

Can be Neurotoxic
TREATMENT INTERVENTION: OTHER MEDICATIONS

Nothing Good Yet

**Valproic Acid** – Potentially Neuroprotective

Non Statistical Cognitive Improvement \(^1\)

**Lithium** – Potentially Neuroprotective

Statistical Improvement But Small 8 Patient Study \(^2\)

**Selegiline** - Antioxidant Potentially Reduce Oxygen Free Radicals

No Cognitive Improvement \(^3\)

**Memantine** - NMDA Antagonist Approved for Alzheimer’s

Non Statistical Cognitive Improvement \(^4\)

**Minocycline** - Anti-Inflammatory Potentially Neuroprotective

No Cognitive Improvement \(^5\)

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\(^1\) Schifitto 2006 Neurol, \(^2\) Letendre 2006 AIDS, \(^3\) Schifitto 2009 Neurol,
\(^4\) Zhao 2010 HIV Clin Trials, \(^5\) Sacktor 2011 Neurol
TREATMENT INTERVENTION: SYMPTOM MANAGEMENT

Impulse Control
Low Dose Antipsychotics:
- Queitapine (Seroquel) – Least Risk for EPS
- Risperidone (Risperdal) \(^1\) – Few Interactions with Antiretrovirals
  Higher Risk for EPS

Mood Stabilizers: Lithium
- Caution With Lamotrigine, Valproic Acid, Aripiprazole, Carbamazepine Due to Interations with Antiretrovirals \(^2\)

Anxiety
- Clonazepem (Klonopin)
- Lorazepam (Ativan)

\(^1\) Maher 2011 JAMA, \(^2\) Clarke 2011 HIV Web Study,
(http://depts.washington.edu/hivaids/drug/case 1/index.shtml)
TREATMENT INTERVENTION: SYMPTOM MANAGEMENT

**Depression**
SSRI & Mirtazapine/Remeron

**Mania**
Lithium

**Lethargy, Withdrawal, Psychomotor Slowing**

Psychostimulants:

Methylphenidate (Ritalin)¹
Dextroamphetamine (Dexedrine)

¹ Hinkin 2001 J Neuropsychiatry Clin Neurosci
# TREATMENT INTERVENTION: Adjunct Non Medication

<table>
<thead>
<tr>
<th>Cueing</th>
<th>Labels, Timers, Reminders, Medisets</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supervision, DOT Meds</td>
</tr>
<tr>
<td></td>
<td>Program Smart Phones</td>
</tr>
<tr>
<td></td>
<td>Emergency Numbers, Directions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Safety</th>
<th>Restricted Environment-Avoid Wandering</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Secure Dangerous Items (Knives, Poisons)</td>
</tr>
<tr>
<td></td>
<td>Secure Things that Can be Misused</td>
</tr>
<tr>
<td></td>
<td>(Stoves, Credit Cards, Medications)</td>
</tr>
</tbody>
</table>

## Family Support & Relief
1. How is HIV associated dementia treated?

A. Antiretroviral treatment can improve neurocognitive function.

B. Antiretrovirals must have good CNS penetration to be effective.

C. Studies with valproic acid, lithium, seligiline, and memantine demonstrate cognitive improvement in HIV associated dementia.
1. How is HIV associated dementia treated?

Correct answer: A

A. Antiretroviral treatment can improve neurocognitive function.

B. Antiretrovirals must have good CNS penetration to be effective.

C. Studies with valproic acid, lithium, seligiline, and memantine demonstrate cognitive improvement in HIV associated dementia.
CASE THREE

2. How can psychiatric symptoms be managed?

   A. Antipsychotics can reduce behavioral problems.
   B. Benzodiazepines do not relieve anxiety.
   C. Psychostimulants are addictive and should be avoided.
2. How can psychiatric symptoms be managed?

**Correct answer: A**

A. **Antipsychotics can reduce behavioral problems.**

B. Benzodiazepines do not relieve anxiety.

C. Psychostimulants are addictive and should be avoided.
CASE THREE

3. What non medication interventions can help him.

A. Cueing is helpful with Alzheimer’s and HIV associated dementia.

B. Dangerous objects should be secured and not available.

C. Both A & B

D. Neither A or B
CASE THREE

3. What non medication interventions can help him.
   
   A. Cueing is helpful with Alzheimer’s and HIV associated dementia.
   
   Correct answer: B
   
   B. Dangerous objects should be secured and not available.
   
   C. Both A & B
   
   D. Neither A or B
HIV Neurocognitive Disorder is a Diagnosis of Exclusion, There are No Biomarkers

Severity & Incidence of Cognitive Impairment Has Decreased Since Combination Antiretroviral Treatment (cART)

High Burden of Cognitive Impairment Persists Even with cART and HIV Suppression

Antiretroviral Treatment Can Improve Neurocognitive Function

Treatment of Asymptomatic Neurocognitive Disorder Remains Elusive
Thank you.

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