

NEUROPSYCHIATRIC ASPECTS OF HIV/AIDS

OVERVIEW

- INTRODUCTION
- EPIDEMIOLOGY
- PSYCHIATRIC MANIFESTATIONS OF HIV
- HIV SPECIFIC PSYCHOTHERAPEUTIC ISSUES
- NEUROLOGICAL MANIFESTATIONS OF HIV
- SPECIAL ISSUES IN HIV
- CONCLUSION
- REFERANCES

INTRODUCTION

- The HIV epidemic continues to be a major public health problem more than 30 years after the initial discovery of the infection and the delineation of the routes by which it is spread.
- Psychiatric disorders play several roles in the HIV epidemic, in element and in comorbidity
- Since many of the behaviors that can result in HIV infection are those that are associated with the brain's reward systems, it is understandable that humans would be drawn to these behaviors
- Sex and substance use are indeed common behaviors of treatment.

INTRODUCTION

- Individuals with untreated mental illnesses are more likely to engage in high-risk behaviors and less likely to take their medications correctly, leading to greater viral loads in their blood and an increased risk of infecting others.
- This makes the recognition and treatment of mental illness crucial to putting an end to the spread of HIV and implies a critical role for psychiatry in integrated care for these patients.

EPIDEMIOLOGY

- HIV was originally recognized through a series of case descriptions involving young homosexual men with *Pneumocystis jiroveci*, pneumonia and other rare conditions, including an aggressive form of Kaposi sarcoma .
- The conditions seen were mostly infections associated with immune systems that had been compromised, termed “opportunistic” infections.
- HIV infects cells expressing the CD4 surface protein, mostly T lymphocytes and macrophages. The main disease mediator is the infection and destruction of T4 helper cells or CD4 cells critical in cell-mediated immunity.

EPIDEMIOLOGY

- Chances of becoming infected after a single exposure to an HIV-infected person:
 1. 0.8 to 3.2 % for unprotected receptive anal intercourse
 2. 0.05 to 0.15 % with unprotected vaginal sex
 3. 0.32 % after puncture with an HIV-contaminated needle
 4. 0.67 % after using a contaminated needle to inject drugs.
- Male-to-male transmission has been the most common route of sexual transmission in North America.
- Male-to-female and female-to-male transmissions are increasing, and they represent most transmission worldwide.

EPIDEMIOLOGY

- The populations at highest risk are:
 - Homosexual men
 - Intravenous drug users
 - Female partners of intravenous drug users
 - Those who trade sex for money or drugs.

Health workers

- India has about 3 million sufferers of AIDS and the southern states (TN, Andhra and Karnataka) and NE states of Manipur, Nagaland, Mizoram account for a large number of cases.

PSYCHIATRIC CONDITIONS IN HIV

- Psychiatric patients infected with HIV face a particularly difficult and complex problem.
- They may be unable to avoid high risk behaviors which increase chances of their contracting the disease at the first place.
- Also they may be vulnerable to non-adherence to pharmacological and non pharmacological treatment regimes thus placing them at high risk of drug resistance, high viral load, more morbidity and mortality.
- Patients with mental illness may also contribute to spreading the epidemic due to high risk activities
- People infected with HIV may develop various psychiatric, psychological and psychosocial problems either due to direct viral effect or by indirect mechanisms.

DELIRIUM

- Delirium is a state of global derangement of cerebral function.
- It occurs more frequently in medically ill, brain injured, or metabolically unstable patients.
- Prevalence of delirium in HIV-infected populations has been reported between 43 and 65 percent.
- It is characterized by inattention, disorganized thinking or confusion, and fluctuations in level of consciousness.
- Emotional changes are common and often unpredictable, and hallucinations and delusions are frequently seen.
- The syndrome has an acute or subacute onset, and remits fairly rapidly once the underlying etiology is treated.

DELIRIUM

- The differential diagnosis of delirium includes HAD, especially with AIDS mania, minor cognitive-motor disorder, major depression, bipolar disorder, panic disorder, and schizophrenia.
- Delirium can usually be differentiated from the above conditions based on its rapid onset, fluctuating level of consciousness, and link to a medical etiology.
- The cause of delirium should be aggressively sought by intensive medical examination.

DELIRIUM

- Vital signs and oxygen saturation, careful history and physical exam, laboratory tests, EKG, radiological exams, and critical review of all medications are essential to the workup.
- Treatment consists of three parts.
- The first is the identification and removal of the underlying cause.
- The second is the reorientation of the patient by maintaining a normal diurnal variation of light cycles, providing orienting stimuli.
- The third, if necessary, is the management of behavior or psychosis.

DELIRIUM

- Low doses of high-potency antipsychotic agents work well.
- Newer, atypical antipsychotics are currently being used with some success, but those with more anticholinergic activity may worsen the condition.
- Benzodiazepines should be used with caution, as they may contribute to delirium in some patients, but are of particular use in alcohol or benzodiazepine withdrawal deliria.
- Physical restraint may be necessary if the patient becomes violent

HIV-ASSOCIATED DEMENTIA

Introduction and Neuropathology

- Early in the AIDS epidemic, some patients presented with rapidly progressing neurocognitive disturbances leading to an intensive search for etiology.
- Several CNS opportunistic conditions were identified
- HIV itself was the causative factor behind the dementia.
- These patients had a subcortical dementia characterized by increasing loss of attention and concentration, marked motor slowing, and variable behavioral components generally leading to death in less than a year.

HIV-ASSOCIATED DEMENTIA

- Autopsy studies of demented patients with AIDS revealed characteristic white matter changes and demyelination, microglial nodules, multinucleated giant cells, and perivascular infiltrates, but a marked absence of HIV within neurons
- It appears that basal ganglia and nigrostriatal structures are affected early in the dementia process, with diffuse neuronal losses following.
- Typical late findings show an approximate 40 percent reduction in frontal and temporal neurons.
- With the development of CART, there has been a dramatic reduction in HIV-induced dementia of the type seen earlier in the epidemic.

HIV-ASSOCIATED DEMENTIA

- It is now uncommon in populations in developed countries and less common even in underdeveloped settings.
- Patients with HIV-associated neurocognitive disorder (HAND) divided by severity into three classes:
- Asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND), and HIV associated dementia (HAD) in order of increasing severity.
- The confounds identified that may explain persistent cognitive impairment include both damage from the virus, damage from immune activation, drug toxicity, and many others.

HIV-ASSOCIATED DEMENTIA

- HAND in the current era involves both cortical and subcortical loss.
- Patients tend to show more impairment in memory (learning) and executive function including deficits in prospective memory (the ability to “remember to remember”) that has been shown to produce problems with medication adherence.
- Patients now have characteristics in common with cortical dementias such as Alzheimer disease.
- The course of HIV dementia prior to CART was clinical progression, while in the current longitudinal studies, some patients decline while others actually improve..

TREATMENT

- The best treatment is aggressive treatment with CART in patients who are untreated or inadequately treated.
- Depression can be treated with standard antidepressants, and in some cases.
- Methylphenidate (Ritalin) or other stimulants may be useful in the treatment of apathy..
- Despite numerous trials, no clear effective treatment for HAND has emerged.
- There are patients who individually respond to interventions, sometimes dramatically, but clinical trials have not yet shown reliable results in populations.

MAJOR DEPRESSION IN PATIENTS WITH HIV DISEASE

- Depression is a significant problem in HIV/AIDS. Major depression is a risk factor for HIV infection by virtue of its impact on behavior, intensification of substance abuse, exacerbation of self-destructive behaviors, and promotion of poor partner choice in relationships.
- In this way, depression can be seen as a vector of HIV transmission.
- Depression has been clearly shown to hinder effective treatment of infected individuals.
- HIV increases the risk of developing major depression through direct injury to subcortical areas of brain, chronic stress, worsening social isolation, and intense demoralization.

Differential Diagnosis of Major Depression

- Patients with complaints of depressive syndromes can have dysthymia, dementia, delirium, demoralization, intoxication, withdrawal, CNS injury or infection, acute medical illness, and a variety of other conditions.
- AIDS dementia and other HIV-related CNS conditions can produce a flat, apathetic state that is often misdiagnosed as depression.
- Cocaine withdrawal produces a depressive syndrome.
- CNS syphilis has been reappearing in medical centers with HIV specialty services and remains “the great imitator” as it was called when it was originally described.

Differential Diagnosis of Major Depression

- Neuro vegetative symptoms are commonly associated. These include difficulties with sleep, appetite, concentration and memory.
- Patients with HIV suffering from major depression frequently present with multiple somatic symptoms.
- These include, but are not limited to, headache, gastrointestinal (GI) disturbances, inexplicable musculoskeletal or visceral pain, cardiac symptoms, dizziness, tinnitus, weakness, and anesthesia.

Differential Diagnosis of Major Depression

- Certain HIV-related medical conditions and medications can cause depressive symptoms.
- Of the antiretroviral agents, efavirenz is most often associated with depressive symptoms, which may remit spontaneously in a number of patients but persist in a few.
- More recently, raltegravir has been implicated in depression as well.

Differential Diagnosis of Major Depression

- Patients receiving interferon are at risk of depression from this agent.
- Metoclopramide, clonidine, propranolol, sulfonamides, muscle-relaxants and many others, have all been reported to produce major depression or similar syndromes.
- While these depressive syndromes often respond to withdrawal of the offending drug, when they do not, they should be treated as major depression with appropriate antidepressant medication.

TREATMENT

- Pharmacotherapy is the mainstay of treatment for major depression.
- No single antidepressant has been found superior in treating HIV-infected patients
- Start at low doses of any medication, titrating up to a “full” dose or therapeutic serum level.
- Patients who show only partial response to antidepressant medication should be offered an augmentation strategy.
- The best studied is lithium, but its side-effect profile often prevents its use in the HIV setting.
- Triiodothyronine, have shown to be of benefit, and may be of particular advantage in patients complaining of fatigue.

- Atypical neuroleptics and pindolol have also been reported to be effective augmenting agents
- If no benefit is gained from the primary antidepressant, even after augmentation, or if it must be abandoned due to intolerable side effects, a new primary agent should be chosen, titrated slowly, and augmented as necessary.
- Since depression is associated with reductions in adherence to HAART, untreated depression may be equally or more detrimental to disease progression than any medication interaction.

Psychotherapeutic Treatment.

- Psychotherapy is an important and integral part of the treatment of major depression.
- Treatment with medication plus psychotherapy has been shown to be more effective for patients than either modality alone.
- Interpersonal psychotherapy and cognitive behavioral psychotherapy are quite popular for the treatment of depression and have the best evidence to support their efficacy.

BIPOLAR (MANIC-DEPRESSIVE) ILLNESS IN PATIENTS WITH HIV DISEASE

- Patients may have this condition after developing AIDS or already have preexisting bipolarity prior to developing AIDS
- A spectrum of symptoms from hypomanic features to frank psychotic mania may be encountered with elevated or irritable mood, decreased need for sleep, talkativeness, increased activity and even delusions and hallucinations.
- Some patients may have a delusion that they have discovered a cure for HIV and go into euphoria
- **AIDS Mania** - a slightly different condition with onset in late stages of disease, lack of family history or past episodes and presence of cognitive impairment. Patients tend to have cognitive slowing or dementia.

BIPOLAR (MANIC-DEPRESSIVE) ILLNESS IN PATIENTS WITH HIV DISEASE

- In AIDS Mania, irritable mood is more typical than euphoria and psychomotor slowing may be observed. It has more severe and has a chronic course with infrequent remissions and tends to relapse after cessation of therapy.
- Treatment of classical mania early in AIDS is with mood stabilizers eg. lithium, valproate, carbamazepine, lamotrigine and antipsychotics (esp.SGAs).
- AIDS mania patients typically respond to treatment with antipsychotic agents alone
- Late-stage patients are far more sensitive to the therapeutic effects but even more so to the toxic side effects of antipsychotic agents.
- In late-stage disease the dose of antipsychotic needed may be much lower than normally.

SCHIZOPHRENIA IN PATIENTS WITH HIV DISEASE

- Prevalence rates of between 4 and 19 percent in both inpatient and outpatient samples.
- Schizophrenia contributes to behaviors that may lead to HIV infection.
- Patients with schizophrenia may have high rate of unprotected sex, multiple sex partners, trading sex for money and have sex while intoxicated.
- Patients with more positive symptoms and more impulsive behaviors may be prone to high risk sexual activities.
- Management employs antipsychotics for symptom control and psychological support and rehabilitation

Personality in Patients Infected with HIV

- Personality disorder prevalence among HIV infected is 19-36% and the most common is antisocial personality disorder which itself is a risk factor for HIV infection
- Knowledge of HIV and its transmission is insufficient to deter these individuals from engaging in HIV risk behaviors, suggesting that certain personality characteristics may enhance their vulnerability to practice such behaviors.
- Unstable extroverts are more prone to engage in HIV risk behavior despite having knowledge of the consequences, for them the immediate removal of pain/ obtaining of pleasure assumes paramount importance (60% patients in Johns Hopkins AIDS Service, JHAS)

Personality in Patients Infected with HIV

- Second most common (25%) type is the stable extrovert . Their emotional condition generates a kind of indifference to HIV risk more than an immediate need for pleasure.
- Unstable introverts (14%) consist of the next most common group, who are anxious, moody and pessimistic; they seek drugs or sex not for pleasure but for relief from pain. They are concerned about the future and consequences but think they have little control over their fate.
- Stable introvert (1%) they are controlled and even tempered persons who are least likely to engage in risky behavior.
- Personality factors may have significant implications for treatment like non adherence to medication regimes, engaging in high risk behaviors etc.

Personality in Patients Infected with HIV

- Personality traits were not directly related to HAART adherence. However, clinical experience suggests that non adherence is more common among extroverted or unstable patients.
- A cognitive-behavioral approach is most effective in treating patients. Five principles guide standard care:
 1. Focus on thoughts, not feelings.
 2. Use a behavioral contract.
 3. Emphasize constructive rewards.
 4. Use relapse prevention techniques.
 5. Coordinate with medical care providers

Substance Abuse and Addiction in HIV Disease

- Substance abuse is a primary vector for the spread of HIV. This impact is directed not only at those who use intravenous drugs and their sexual partners but also at those who are disinhibited or cognitively impaired by intoxication and are driven by addiction to impulsive behaviors and unsafe sexual practices.
- Diagnosis of substance dependence may be difficult to make because physical symptoms of HIV infection overlap with those of substance abuse or dependence.

Substance Abuse and Addiction in HIV Disease

- Neurological symptoms can overlap between HIV infection and substance abuse.
- Triple diagnosis refers to a dual diagnosis patient who also has HIV.
- Most HIV-positive substance abusers would be classified as “unstable extroverts.” These can be found in as many as 49 percent of all substance abusers.

Substance Abuse and Addiction in HIV Disease

- The clinician must be especially mindful of interactions between these medications and the abused substances.eg.(Stavudine can cause neuropathy as a side effect which can be exacerbated by alcohol).
- Treatment of Substance Use Disorders in Patients Infected with HIV
 - 1. Role induction and motivation
 - 2. Detoxification
 - 3. Treatment of co-morbid conditions
 - 4. Rehabilitation
 - 5. Relapse prevention

Psychological Problems in Patients Infected with HIV

- **Acute stress reaction** may be seen, most commonly at the time of learning a positive test result.
- **Depressive** features with insomnia, suicidal ideas and depersonalization may be seen. Other reactions may include anger, despair, guilt, increased drug/ alcohol use, social withdrawal and high risk sexual behavior
- **Adjustment disorder** may occur in 5-20 % of patients. Risk factors include past history of psychiatric problem, poor support, lack of social acceptance.
- **Obsessive compulsive disorder** may occur with or without depressed mood involving repeated bodily scrutiny for evidence of disease progression

Psychological Problems in Patients Infected with HIV

- Repeated ruminations may occur about death and dying and thoughts of having spread the virus to others may be present
- Other anxiety disorder like GAD, panic disorder may occur. HIV diagnosis can lead to PTSD in some patients.
- Psychological difficulties of everyday life in AIDS patients are very complex and include grief, social isolation, family problems, workplace difficulty, peer rejection, stigma and many others and they need to be managed appropriately.

HIV-SPECIFIC PSYCHOTHERAPEUTIC ISSUES

- Pretest, test, and posttest counseling issues;
- Risk behavior reduction in patients at risk or infected with HIV;
- Partner notification in patients infected with HIV;
- Impaired patients with issues of capacity and competence;
- HAART adherence issues.

PRE TEST COUNSELLING

- Discuss meaning of a positive test & clarify distortions
- Discuss meaning of a negative result
- Discuss why test is necessary
- Discuss patient's fears and concern
- Explore patient's potential reaction to a positive result
- Discuss confidentiality issues relevant to testing
- Discuss how positive result may affect social life
- Explore high risk behavior and recommend risk reduction
- Document discussion
- Allow patient time to ask questions

POST TEST COUNSELLING

- Interpretation of test results.
- Recommendation for prevention of transmission.
- Recommendation for follow up of sexual partners and needle contacts.
- If result is positive recommendation against donating blood, sperm or organs.
- Referral for appropriate psychological support.

RISK BEHAVIOR REDUCTION INPATIENTS AT RISK OR INFECTED WITH HIV

- Men with sexual contacts with other men was the largest subgroup in terms of new AIDS diagnoses in the United States in the year 2000.
- Interventions include :
 - o stress management and relaxation techniques
 - o education cognitive self-management training
 - o negotiation skills training
 - o psychotherapy directed at emotional distress reduction
 - o relapse prevention models of high-risk behavior reduction
 - o education directed at eroticizing safer sex
 - o assertiveness training
 - o peer education in bars.

PARTNER NOTIFICATION

- Partners should be notified of exposure risk and potential infection as well.
- Physicians or health department officials to notify partners of HIV-infected patients of their risk.
- Sex care workers and their clients can make their own decisions and should be responsible for their own behavior all the way to the sentiment that HIV-infected sex workers should be arrested and jailed for attempted murder.

CAPACITY TO CONSENT/COMPETENCE

- Patient must understand that there is a decision before him or her regarding some aspect of care and must understand the consequences not only of each option but also of refusal to make a choice.
- The patient must be able to manipulate the information involved in a rational way.
- Patterns of prior behavior, severity of illness, poor judgment, and psychiatric vulnerabilities complicate these decisions and play an important role in tempering the way in which patients are managed.

HAART ADHERENCE

- Intervention such as cognitive-behavioral psychotherapy, structured psycho educational psychotherapy, supportive psychotherapy, and group interventions have all been used to improve patient adherence to office visits and medication regimens.
- HIV medication adherence focuses on technical interventions such as pill box and timer reminders, less complex pharmacological interventions, decreased pill burdens, and increased access to care.
- Psychotherapy has been shown to improve clinic visit adherence, the best indirect predictor of medication adherence.

NEUROLOGICAL COMPLICATIONS OF HIV/AIDS

- **OPPORTUNISTIC INFECTIONS**

- **Toxoplasmosis:**

- When CD4 < 200 cells per microliter.
- most common reason for intracranial masses.
- Ring-enhancing lesions in the basal ganglia or at gray–white matter junction.

Acute focal or diffuse meningoencephalitis -
headache, fever, altered consciousness and focal
neurological signs.

Cytomegalovirus:

- CD4 < 50 cells per microliter.
- Two distinct syndromes of CMV CNS infection.
- Encephalitis with dementia -subacute onset, periods of delirium, confusion, apathy & focal neurological deficits.
- Ventriculoencephalitis -infects the ependymal cells, causing a rapid progression from delirium to death.
- Treatment- supportive, gancyclovir, foscarnet

Cryptococcal meningitis:

- 8 -10%.
- Present with fever and delirium.
- Treatment- amphotericin B and flucytosine.

Progressive multifocal leukoencephalopathy:

- Demyelinating disease of white matter.
- Polyoma virus, named JC virus.
- CD4 < 100 cells per ml.
- Treatment-supportive , HAART

CNS Neoplasms

- Lymphoma is the most common neoplasm seen in AIDS patients, affecting between 0.6 and 3 percent.
- Clinical features- afebrile, mental status change, Seizures present in about 15 percent of patients.
- Brain biopsy is required for confirmation of the diagnosis of CNS lymphoma.
- Management includes radiation therapy and steroids with adjunctive chemotherapy.
- HAART has somewhat improved the prognosis which was earlier limited to 3-4 months of survival after diagnosis.

DIRECT CNS MANIFESTATIONS OF HIV

Guillain- -é Barré Syndrome

- It is an inflammatory demyelinating polyneuropathy causing symmetrical paralysis and few if any sensory symptoms, usually beginning in the lower extremities and progressing upward.
- The condition becomes especially serious if abdominal musculature is involved, as it may impair respiration.
- Thought to be autoimmune in etiology and generally self-limited.
- Intravenous immunoglobulin and plasmapheresis have been used to shorten the course.

Vacuolar Myelopathy

- Associated with history of *P. carinii* and *M. avium-intracellulare* infections, suggesting that the development of vacuolar myelopathy is related to more severe immunosuppression.
- Multinucleated giant cells are seen on histological examination.
- Clinical manifestations appear when the disease progresses to affect the lateral and posterior columns and thus includes:
 - o spastic paraparesis
 - o loss of proprioception and vibration sense
 - o bowel and bladder urgency or incontinence
 - o Impotence
- Management is mainly supportive , myelopathies in HIV donot respond well to HAART.
- L- methionine has shown promise in one trial.

PERIPHERAL NEUROPATHY

- Involves most often feet but occasionally can occur in the hands.
- The neuropathy may range from paresthesia to burning pain, and patients will have a vibratory-sense gradient with decreased sensation in the distal extremity compared to more proximal points.
- Treatment of peripheral neuropathy may include :Tricyclic antidepressants, Pregabalin, Gabapentin (Neurontin), Other antiepileptic drugs used to treat neuropathic pain.,
- Opiate analgesics should be used sparingly-tolerance and dependence.
- Benzodiazepines are of no use

Special Issues in HIV

Fatigue

- Fatigue is a common symptom in HIV-infected patients.
- It may have multiple causes:
 - direct effect of virus
 - medical causes like anemia
 - Infection
 - side effect of medications eg. ART medicine.
 - due to psychiatric disorder such as depression, substance withdrawal, or as a result of demoralization.
- Testosterone has been used to treat fatigue in HIV infected men. Depression may be treated by activating antidepressants (fluoxetine).

HIV/HCV Coinfection

- Hepatitis C virus (HCV) is a blood-borne pathogen that is currently most commonly transmitted by injection drug use.
- 50 percent of HIV-infected patients are also infected with HCV.
- HIV infection is likely to make individuals more susceptible to contract HCV if exposed, likely due to immunosuppression, and also to cause more rapid progression of liver disease.
- Interferon-alpha has been associated with depressive syndromes, suicide, and, on rare occasions, mania.
- Depressive symptoms associated with interferon-alpha have been successfully treated with both SSRIs and tricyclic antidepressants.

Diagnosis Implicated agents

- **Depression**- Abacavir, Efavirenz(mc), Indinavir, Nevirapine, IFN- α , Steroids, INH.
- **Mania**- Didanosine, Efavirenz, Zidovudine.
- **Psychosis**- Abacavir, Efavirenz, Nevirapine, Acyclo/Ganciclovir, Prednisone.
- **PTSD**- Efavirenz.
- **Anxiety**- Didanosine, Ganciclovir.
- **Vivid dreams** -Abacavir, Nevirapine, Efavirenz.
- **Suicidal ideation**- Abacavir, Efavirenz.
- **Miscellaneous symptoms**- Efavirenz.

CONCLUSION

- HIV & AIDS are closely related to psychiatry with the infection giving rise to many psychiatric problems and psychiatric illnesses leading to risk of acquiring HIV.
- Hence the approach to such a situation must be holistic with good coordination between medical specialists and psychiatrists, psychologists to bring maximum possible benefit to people with such a difficult illness.

REFERENCES

- KAPLAN & SADOCK'S COMPREHENSIVE TEXTBOOK OF PSYCHIATRY, 10 TH EDN
- LISHMAN'S ORGANIC PSYCHIATRY

THANK YOU