

## MANIA IN HIV INFECTION

D. VENUGOPAL , P.B. PATIL, D. GUPTA, N. MURALI, N. KAR & P.S.V.N. SHARMA

### ABSTRACT

*Mania in HIV infected individuals is an uncommon clinical presentation. It can, however, complicate any stage of the HIV infection. We herewith report a set of three case reports of patients with HIV infection who developed manic episodes. The cases highlight some aspects of the plausible relationship between HIV infection and mania. HIV infection could be revealed by manic episode, it could itself also be associated with increased cycling in bipolar patients. Mania could be secondary to HIV or zidovudine therapy (though the etiological role of the latter is as yet unclear). Mania could also occur as a reaction to awareness to having HIV infection. These relationships are important for both the physician and the psychiatrist as they have important therapeutic and prognostic implications.*

**Key words :** Mania, HIV, AIDS, zidovudine

Mania in HIV infected individuals is an uncommon clinical presentation. However, it can complicate any stage of the infection - from the asymptomatic seropositive stage (category A) to symptomatic AIDS (category B) and HIV indicator conditions (category C) (CDC, 1993). The occurrence of manic illnesses in HIV infected individuals has been found to be associated with subsequent development of cognitive deficits and dementia (Lyketsos et al., 1993; Mijch et al., 1999).

There are several aspects are highlighted in the following three case reports.

**Case 1 :** Mr. A was a 43 year old male from a rural middle socio-economic background with past history of an episode of depression 16 years ago, and an episode of mania 4 years ago (both these remitted spontaneously). There was no contributory family history but there was history of several premarital unprotected heterosexual exposures with multiple partners. The patient presented to psychiatry outpatient department with one month duration of restlessness, increased activity levels, argumentativeness, overfamiliarity with strangers, excessive and loud talk, expansive ideas with respect to his career plans, disturbed

sleep and appetite. Patients was reportedly appearing excessively cheerful, spending money excessively, and had started smoking and consuming alcohol (which he never used to do previously). He was also preoccupied with his appearance and spent long periods of time in getting "ready". Above symptoms were of subacute onset and progressive course. There was history of significant loss of weight since the time of onset of illness.

Physical examination revealed signs of oral candidiasis, generalized lymphadenopathy and coarse crepitations in both lung fields. Cognitive functions were grossly intact when tested clinically. He had prolixity of speech, grandiose ideas and euphoric affect with absent insight. On investigating, the patient tested positive for HIV infection (by ELISA). Chest X-ray showed diffuse bilateral infiltration, suggestive of pneumonia and sputum was negative for acid-fast bacilli.

A clinical diagnosis of symptomatic AIDS with bipolar affective disorder - currently mania without psychotic symptom was considered. A differential diagnosis of secondary (organic) mania was also considered, but was considered unlikely

## MANIA IN HIV INFECTION

in view of past episodes of depression and mania. The infections were treated with antibiotics and antifungal agents. The manic episode was managed with lithium at dosage of 1200 mg/day (serum lithium level of 0.92 mEq/L), haloperidol 7.5 mg/day and trihexiphenidyl 2 mg/day. With the above treatment, the patient showed improvement in manic symptoms over the next 4 months.

After 4 months, the patient started reporting feelings of pervasive sadness, fatigue and loss of interest in most activities lasting for one month, and had ideas of helplessness and hopelessness, death wishes and slowness in activities. The patient was noticed to be withdrawn. On examination, he had depressed affect, reduced reactivity and depressive cognitions. A diagnosis of bipolar depression was made and the condition was managed by upward titration of the dosage of lithium to 1600 mg/day (as repeat lithium level on 1200 mg/day was 0.6 mEq/L). He improved with this treatment and is on regular follow-up for the past 2 years. There was no history to suggest any cognitive decline and clinical examination failed to reveal any cognitive deficits during the 2 year period.

**Case 2 :** Ms B was a 26 year old female from a semi-urban middle socioeconomic background with no past or family history of psychiatric illness. She was referred to the psychiatrist for complaints of abnormal behaviour of 15 days duration. She had been under treatment of the physician since nearly 4 years (with multiple admissions) for a number of opportunistic and cerebral toxoplasmosis - occurring in the context of HIV seropositive status and a CD4 lymphocyte count of 100 (normal range: 290-2600/cu mm). Antiretroviral drugs were initiated about 5-6 months prior to psychiatry consultation, but the patient had discontinued the same after she had two episodes of seizures. During the current admission, she was started on antiretroviral drugs (zidovudine and lamivudine) along with diphenylhydantoin about 3-4 days prior to onset of the abnormal behaviour that prompted psychiatric consultation.

The patient's psychiatric symptoms consisted of excessive and loud talk, pervasive and persistent irritability over trivial provocation, increased religiosity, ideas of grandeur and hallucinatory behaviour. Social, occupational and biological functioning were significantly impaired. Mental status examination showed presence of distractibility, increased talk, religious preoccupations, predominantly irritable (and sometimes euphoric) affect, auditory hallucinations and absent insight. A psychiatric diagnosis of secondary mania (organic or drug induced) with mood congruent psychotic symptom was made. A primary mood disorder was considered to be unlikely in view of the absence of any contributory past or family history and literature evidence for mania associated with HIV infection and with antiretroviral drugs (Wright et al., 1989; Lyketsos et al., 1993; Maxwell et al., 1998; Mijch et al., 1999). The patient's symptoms partially improved with antipsychotic (risperidone 2-4 mg/day) along with antiparkinsonian agents over a period of 2 weeks. Antiretroviral drugs were continued and the patient is on follow-up. On clinical examination, she had no cognitive deficits either during or after the recovery from manic illness.

**Case 3 :** Ms C was a 34 year old female from semi-urban background. She had no past or family history of any psychiatric illness. She presented to the hospital with 7 months history of fever, dry cough, loose stools, non-specific abdominal pain, loss of weight and three months of amenorrhoea. Thereafter she was taken to a faith healer. During this visit she had a possession attack. This was immediately followed by the hospital consultation. In the hospital, she was found to have generalized lymphadenopathy, hepatosplenomegaly, coarse crepitations in both lung fields and lesions of oral candidiasis. On investigating, she was found to be positive for HIV (by ELISA). Stool examination showed presence of oocysts of cryptosporidium. chest X-ray showed diffuse infiltration; sputum was positive for acid fast bacilli and Mantoux test was negative. A diagnosis of AIDS (with HIV indicator condition - category C) with multiple opportunistic infections

was made and appropriate treatment was started for the infections.

Information regarding the patient's HIV infection status was revealed to her during the hospital stay. The patient initially became withdrawn, had crying spells and would reiterate that she was not at fault. Her sleep was also disturbed. About 4 days later, she started talking excessively and was noticed to be irritable. She was also noticed to be talking in English, instead of her usual language of communication i.e. Kannada. She reported that the faith-healer was doing some black magic on her and was attempting to harm her. She also started saying that Goddess Devi was protecting her from the ill effects of his magic, and that by virtue of this, her illness would also become alright soon. On mental status examination, she had pressure of speech with prolixity and was found to be irritable for most of the time. She also developed well-systematized delusion of persecution with an element of grandiosity in her thought content. A psychiatric diagnosis of secondary manic episode was made, considering the rather late age of onset of the illness, absence of contributory past and family history and the clear temporal correlation with revelation of her physical illness.

The patient was managed with haloperidol (5-10 mg/day) and trihexiphenidyl 4 mg/day. She improved over a period of next 3 months. On follow-up, manic symptoms were found to have improved. However, on clinical examination, patient was found to have impaired concentration, slowing of all mental activities, calculation and new learning deficits, in the absence of any prominent mood symptoms or active neurological infections.

## DISCUSSION

The occurrence of manic illness in the context of HIV infection has been reported to be uncommon. When it does occur, it has prognostic implications in terms of early, subsequent cognitive deficits (Lyketsos et al., 1993; Mijch et al., 1999). The case reports presented above are reflective of some aspects of the highly neurotropic

HIV infection, which can potentially contribute to the occurrence of mania.

Case 1 is interesting in the sense that for a naive observer the presentation looks like a coincidental occurrence of HIV infection in a known patient with bipolar disorder. The patient had only 2 episodes in the past 16 years, and developed 2 more episodes within a span of 6 months during which he was also detected to have HIV infection. This increased cycling could be attributed to the natural course of bipolar disorder. However, one cannot rule out the potential role of HIV infection in increasing the cycle frequency. This aspect highlights the need for a detailed physical examination with high index of suspicion for possibility of underlying organic conditions.

Case 2 is that of a young woman presenting with a manic episode, for the first time within a few days of restarting antiretroviral drugs zidovudine and lamivudine on a background of pre-existing AIDS. Diagnostic possibilities of primary mania, AIDS induced mania as well as zidovudine induced mania could be considered. There was no family or past history of affective illness in the patient; she had been given zidovudine in the past, without any psychiatric complications; after restarting the drug she developed mania. There are reports of mania associated with both advanced HIV infection and also with zidovudine therapy (Wright et al., 1989; Lyketsos et al., 1993; Maxwell et al., 1998; Mijch et al., 1999). It is possible that both of these contributed to the emergence of manic symptoms in this patient. In this case, however, the indicated drug had to be continued after due consideration of the risk benefit profile of such a course of action. The patient showed improvement in her active symptoms with addition of antipsychotic (risperidone) alone.

Case 3 was a middle-aged woman who developed psychotic behaviour after being told about her illness i.e. AIDS. There was an initial period of withdrawn and depressed behaviour followed by a clear onset of manic symptoms. During the episode, the patient's thought content often reflected her belief of being persecuted by the temple priest and that her illness would

## MANIA IN HIV INFECTION

become alright by the grace of the goddess. In the absence of a positive past or family history and in the presence of HIV infection and cognitive deficits on clinical examination, a diagnosis of organic mania seems to be the most likely diagnosis, though this cannot be concluded with certainty. The cognitive deficits seen in this patient are in keeping with the widely reported cognitively deficits with HIV seropositivity (Butters et. al., 1990).

To sum up, the relationship between HIV infection can be of several kinds. Mania can be a presenting feature of the infection, (in otherwise "affectively predisposed" individual) and the frequency of affective episodes may increase following HIV infection in bipolar patients. The HIV infection and its treatment (zidovudine) can themselves induce mania. Mania can also occur as a reaction to awareness of having HIV infection. Thus, there are several facets to the understanding of occurrence of mania in an HIV seropositive individual. The implications of such an occurrence are manifold. Patients in the manic state can not only be disinhibited/promiscuous (as part of their psychopathology) but they may also deny their infection status and may pose a significant risk of transmission of the infection. So also, HIV infected individuals who develop mania are at risk to develop early subsequent cognitive deficits and extrapyramidal side effects of antipsychotic drugs. Psychiatrists and Physicians need to be aware of the intricacies involved in the occurrence of manic episodes in HIV seropositive individuals so as to deal with the same in an appropriate fashion. The above case also illustrate an urgent need to draw appropriate treatment guidelines in managing mania in HIV infection.

## REFERENCES

**Butters,N., Grant,I. & Haxby,J. (1990)** Assessment of AIDS related cognitive changes : recommendations of the HIMH work group in Neuropsychological Assessment Approaches. *Journal of Clinical and Experimental Neuropsychology*, 12, 963-978

**Centres for Disease Control (CDC) (1993)** Revised classification system for HIV infection and expanded surveillance case defined for AIDS among adolescents and adults. *Morbidity and Mortality Weekly Report*, 41, (Suppl.), 44-17.

**Lyketsos,A.M., Hanson,A.L., Fishman, M., Rosenblatt,A., Mchuge,P.R. & Treisman, G.K. (1993)** Manic syndrome early and late in the course of HIV. *American Journal of Psychiatry*, 150, 326-327.

**Maxwell,S., Schaftner,W.A., Kessler, H.A. & Busch,K. (1998)** Manic syndrome associated with zidovudine. *Journal of American Medical Association*, 259, 3406-3407.

**Mijch,A.M., Judd,F.K., Lyketsos,C.G., Ellen,S. & Cockram,A. (1999)** Secondary mania with HIV infection : are antiretrovirals protective? *Journal of Neuropsychiatry and Clinical Neuroscience*, 11, 475-480.

**Wright,J.M., Sachdev,P.S., Perkins,R.J & Rodriguez,P. (1989)** Zidovudine related mania. *Medical Journal of Australia*, 150, 339-341.

---

D. VENUGOPAL\*, P.B. PATIL, D. GUPTA, N. MURALI, N. KAR & P.S.V.N. SHARMA, Department of Psychiatry, Kasturba Medical College, Manipal - 576119

\* Correspondence