

CASE REPORT

9-Year Serial Follow-up of a HIV-Positive Man With Mild Neurocognitive Deficit

Sandeep Grover, Debasish Basu, Rama Malhotra, Anil Malhotra

Drug De-addiction & Treatment Centre (DDTC), Department of Psychiatry, Postgraduate Institute of Medical Education & Research, Chandigarh, India

Corresponding author: Dr. Sandeep Grover, Assistant Professor, Department of Psychiatry
Postgraduate Institute of Medical Education & Research Chandigarh 160012, India, E-mail:
drsandeepg2002@yahoo.com

Abstract

Background: Few long-term studies have been carried out to assess the serial change in cognitive functioning over time in HIV-positive but AIDS-free people. **Method and Result:** Case report. We report the case of a subject with opioid and alcohol dependence, who was found to be HIV positive at the age of 46 years and had mild neuropsychological deficit. He was followed up serially for next 9 years, with the same battery of cognitive function testing for cognitive functioning and it was found that there was a gradual decline in cognitive functioning initially but later stabilized. **Conclusion:** The case demonstrates that the deficits are not necessarily progressive (as is often assumed) (German J Psychiatry 2007;10: 88-91).

Keywords: HIV, cognitive impairment, drug addiction

Received: 2.1.2007

Revised version: 11.7.2007

Published: 24.8.2007

Introduction

Marked neuropsychological deficits and dementia are associated with acquired immunodeficiency syndrome (Miller et al, 1990; van Gorp et al, 1991). With the recognition that intravenous drug users (IDUs) as one of the largest group of patients with acquired immunodeficiency syndrome (AIDS), there has been growing interest in the question whether IDUs are at increased risk for developing cognitive impairment secondary to human immunodeficiency virus (HIV) infection. It has been hypothesized that IV drug users, by virtue of chronic effects of longstanding drug and alcohol intoxication on the brain, may have less "cerebral reserve capacity", resulting in an accelerated impact of HIV on cognitive functions (Selnes et al, 1997). However, the question of whether early signs of cognitive decline can be identified with any consistency in the asymptomatic HIV-positive population remains controversial and findings vary. Selnes et al. (1990), and Lunn et al. (1991) did not find any

cognitive deficits in their homosexual and bisexual, asymptomatic, HIV infected subjects compared with seronegative controls, other researchers have found evidence of subtle cognitive decline in asymptomatic, HIV infected populations (Stern et al, 1991; Grant et al, 1987).

Longitudinal studies can be very valuable in providing answers to such questions; unfortunately, few such long-term studies have been carried out to assess the serial change in cognitive functioning over time in HIV-positive but AIDS-free people, the longest one being of 8 years duration (Baldewicz et al, 2004).

We report the case of a patient with opioid and alcohol dependence, who was found to be HIV positive 12 years ago and presenting with mild neuropsychological deficit, and followed up serially with the same battery of cognitive function testing.

Case Presentation

GS, a 46-year (at the time of first presentation) married male, retired from the army, belonging to a Hindu nuclear family of low socio-economic status presented to our de-addiction clinic in July 1995, with gradually progressing alcohol consumption that started when he was 21 years old and developed into a dependence pattern by the age 40. Following increase in alcohol intake he started having epigastric pain, consulted a local doctor, who prescribed pentazocine injection for the same; patient liked the relaxing effect of the same and within 1-2 month started visiting the doctor daily for getting himself injected with pentazocine. Gradually over the period of 4-5 months he also developed dependence for the same also and started getting himself injected upto 2-3 ampoules/day (60-90 mg/day) without proper sterilization of the needle. Whenever he would not get himself injected he would have withdrawal features characteristic of opioids and would take excessive amount of alcohol to get relief of the same. The above pattern of taking alcohol and injectables continued for next 6 years, over the period he tried to cut down, but was never successful. He also had marked socio-occupational dysfunction due to the drug intake.

He presented to the out patient service of the hospital 12 years back and was admitted for the first time. On investigation patient was found to have diabetes mellitus and HIV seropositive. He was provided with psychoeducation and relapse prevention counseling. During the same admission the patient was found to have cognitive deficits. His cognitive functions were assessed using Indian adaptation of Wechsler Adult intelligence scale (Verma et al, 1984), Standard Progressive Matrices (SPM) for IQ (Raven et al, 1998), PGI memory scale (PGIMS) for memory (Pershad, 1977), and Nahor-Benson test (NBT) for perceptuomotor functions (Nahor & Benson, 1970)(Table 1). Indian adaptation of Wechsler Adult intelligence scale includes tests for performance in the form of picture completion test, digit symbol, block design, picture arrangements, and object assembly. Standard Progressive Matrices (SPM) consisted of sixty matrices divided into 5 sets A, B, C, D and E of 12 problems each and it tests the ability to apprehend meaningless figures, see the relation between them, conceive the nature of figure and complete each system of relations presented. PGI memory scale (PGIMS) is a reliable scale for assessment of memory in Indian subjects with 10 subtests. The Nahor-Benson test consisted of 8 cards in which patient was asked to draw the shape of the objects (card I to V) and follow the instructions (card VI to VIII) on the cards. The scoring is based on the principle of 'all or none' and depending upon the performance the error score can vary from 0 to 8. Dysfunctional rating is done depending upon the patient's educational status. In those who can read fluently error score of ≤ 2 is considered to have 0 dysfunctional rating, scores between 3 to 4 are given a dysfunctional rating of 2 and those with scores ≥ 5 are rated as having dysfunctional rating of 3 (Nahor & Benson, 1970).

At initial evaluation his Verbal Adult Intelligence Scale (VIQ) was 65, his IQ was 76 by using standard progressive matrices (SPM), had raw score of 62 on PGI memory scale

(PGIMS) for memory, and error score was 2 on Nahor-Benson test (NBT). Over the next 10 years he was admitted 8 times in the deaddiction centre, for periods varying from 2-4 weeks during which he would be provided with detoxification, psychoeducation and relapse prevention counseling. Mostly the patient would have lapse in 1-2 months of discharge, and would come back with full-blown relapse for opioids and alcohol abuse/dependence. Over this period his compliance with antidiabetic drugs was also poor. He tested negative for hepatitis-B and hepatitis-C antigen throughout this period. His CD4+ count in July 2004 was 408 (CD8 count 1517; CD4/8 ratio 0.27, CD3 total Average 1985) after 9 years of seropositivity. His CT scan Brain immediately after being found to be positive for HIV showed cerebral atrophy and a MRI brain after 9 years showed cerebral atrophy keeping in with the age. After 9 years of being seropositive, he for the first time manifested herpes zoster lesion and oral candidiasis. Over the years he did not receive any antiretroviral treatment because of poor socioeconomic status.

Over the years his cognitive functions were assessed serially using the same instrument after every 6 months - 2 years, after completion of detoxification. The same clinical psychologist under standard conditions, avoiding stress, fatigue and other factors/events influencing mental performance, administered the neuropsychological tests. Administration of all neuropsychological tests took approximately 1.5 hours every time. The tests selected were easy to complete, had relatively short administration times, were sensitive to acquired impairment and measured cognitive impairment associated with HIV infection. The tests included Verbal adult intelligence scale (VIQ) (Verma, 1984), which includes subtests for information, digit span, arithmetic and comprehension, standard progressive matrices (SPM) for intelligence (Raven et al, 1998), thinking and visuo-spatial organisation, PGI memory scale (PGIMS) for memory (Pershad, 1977), and Nahor-Benson test (NBT) (Nahor & Benson, 1970) for perceptuomotor tasks. Over the years he showed gradual decline in all the cognitive functions for initial 68 months, after which the deficits seems to have stabilized (Table-1).

Discussion

Longitudinal studies limited to HIV-positive, but AIDS-free subjects have not found evidence of progressive decline in performance over time (McKegney et al, 1990; Selnes et al, 1992). Studies that have included subjects with AIDS have reported decline in psychomotor speed (Silberstein, 1993), concentration and memory (Egan et al, 1992), but these studies did not control for the influence of practice effects on longitudinal test performance. Baldevicz et al (2004), compared cognitive functions of HIV-infected seropositive and seronegative men longitudinally over an 8-year period of time, assessed semiannually for fine motor speed, attention, verbal memory, executive functioning, and speed of information processing. They found that symptomatic AIDS patients scored significantly worse on fine motor speed and speed of information processing than asymptomatic seropositive and seronegative patients. Further, asymptomatic seropositive performed more poorly than the seronegative group on speed of information processing. In another study Selnes et al. (1997), compared cognitive functions of HIV-

infected injection drug users (IDUs) and seronegative controls longitudinally for 4.5 years, assessed semiannually. They

Table 1. Serial Neurocognitive Testing Results. VIQ, Verbal Adult Intelligence Scale; SPM/IQ, Standard Progressive Matrices (SPM) for Intelligence; PGIMS; PGI Memory Scale; NBT, Nahor-Benson Test

Serial no. (Month/year of testing)	Time Interval of As- sess- ment (months)	VI Q	SPM IQ	PGIMS Raw Score	NBT Error Score
1. July, 1995	0	65	76	62	2
2. Aug, 1995	1	68	80	67	1
3. April, 1996	9	68	75	57	4
4. Jan, 1997	18	58	65	55	2
5. Aug, 2000	61	58	65	44	3
6. Aug, 2002	85	54	<65	52	5
7. July, 2004	109	54	<65	45	5

found improvement in performance over time, consistent with practice effects for all measures. The only subtest for which the magnitude of the practice effects was mildly attenuated relative to the seronegative controls was Grooved Pegboard, dominant hand. After adjusting for disease progression and antiretroviral therapy use, none of the time trends for the neuropsychological test scores were significant, suggesting no decline in performance of the seropositive patients relative to the seronegative controls. With development of clinical symptoms, there was a trend in the direction of declining performance. Subjects having two or more symptoms and using antiretroviral therapy had significantly poor performance on tests of psychomotor speed and memory. Silberstein et al (1993) assessed cognitive functions at base line and after mean follow up of 47 months, found seropositivity at baseline was associated with statistically significant declines in neuropsychological functioning on the Finger Tapping and Trail Making B tests. They concluded that subtle cognitive deficits develop over time and can be identified early, but their course is slow and appears generally to parallel that of non-CNS symptoms/signs of HIV infection.

A wide range of cognitive deficits have been reported in subjects with alcohol dependence, which are directly proportional to severity and duration of alcoholism (Parsons, 1998). Most of the studies which have examined the cognitive functions in opioid users have been done on the subjects who are on methadone maintenance treatment (Mintzer & Stitzer, 2002) and it has been shown that cognitive deficits in opioid abusers improve with abstinence (Davis et al, 2002). Over the year's index patient's predominant substance of abuse was opioids with off and on use of alcohol. On every cognitive testing patient was abstinent from the drugs, hence the stable decline in cognitive functioning cannot be attributable to the drug abuse.

Conclusion

The longest study that has followed HIV seropositive subjects for the cognitive dysfunctions is of 8 years (Baldewicz et al., 2004). This case represents the longest duration of follow-up for the cognitive functions in HIV seropositive IDU's. This case shows that the cognitive deterioration occurs gradually in seropositive but asymptomatic patients, which tends to stabilize after 68 months. Furthermore, it demonstrates that only by following the same HIV-infected individuals over several years studies will be able to define the onset and severity of cognitive decline related to HIV. Future studies will benefit from more frequent cognitive assessment, even longer follow-up, and larger cohorts.

References

- Baldewicz TT, Leserman J, Silva SG, Petitto JM, Golden RN, Perkins DO, Barroso J, Evans DL. Changes in neuropsychological functioning with progression of HIV-1 infection: results of an 8-year longitudinal investigation. *AIDS Behav.*, 2004; 8:345-355.
- Davis PE, Liddiard H, McMillan TM. Neuropsychological deficits and opiate abuse. *Drug Alcohol Depend.* 2002;67:105-108.
- Egan V, Brett RP, Goodwin GM. The Edinburgh cohort of HIV-positive drug users: pattern of cognitive impairment in relation to progression of disease. *Br J Psychiatry* 1992; 161:522-531.
- Grant I, Atkinson JH, Hesselink JR, Kennedy CJ, Richman DD, Spector SA, McCutchan JA. Evidence for early central nervous system involvement in the acquired immunodeficiency syndrome (AIDS) and other human immunodeficiency virus (HIV) infections: Studies with neuropsychologic testing and magnetic resonance imaging. *Ann Intern Med*, 1987;107, 828-836.
- Lunn S, Skydsbjerg M, Schulsinger H, Parnas J, Pedersen C, Mathiesen L. A preliminary report on the neuropsychologic sequelae of human immunodeficiency virus. *Arch Gen Psychiatry*, 1991;48:139-142.
- McKegney FP, O'Dowd MA, Feiner C, Selwyn P, Drucker E, Friedland GH. A prospective comparison of neuropsychologic function in HIV-seropositive and seronegative methadone maintained patients. *AIDS* 1990; 4: 565-569.
- Miller EN, Selnes OA, McArthur JC, Satz P, Becker JT, Cohen BA, Sheridan K, Machado AM, Van Gorp WG, Visscher B. Neuropsychological performance in HIV-1-infected homosexual men: The Multicenter AIDS Cohort Study (MACS). *Neurology*, 1990; 40:197-203.
- Mintzer MZ & Stitzer ML. Cognitive impairment in methadone maintenance patients. *Drug Alcohol Depend*, 2002; 67:41-51.
- Nahor A & Benson DF. A screening test for organic brain disease in emergency psychiatric evaluation. *Behav Neuropsych*;1970; 1, 2 : 23-26.

- Parsons OA. Neurocognitive deficits in alcoholics and social drinkers: a continuum? *Alcohol Clin Exp Res*, 1998;22: 954-961.
- Pershad, D. Construction and standardization of clinical test of memory in simple Hindi. Agra: National Psychological Corporation, 1977.
- Raven, J, Raven, JC, Court, JH. Manual for Raven's Progressive Matrices and Vocabulary scales. Section 3. The Standard Progressive Matrices, San Antonio, Tx: The Psychological Corporation, 1998.
- Selnes OA, Galai N, McArthur JC, Cohn S, Royal W 3rd, Esposito D, Vlahov D. HIV infection and cognition in intravenous drug users: long-term follow-up. *Neurology*, 1997;48:223-230.
- Selnes OA, McArthur JC, Royal W 3rd, Updike ML, Nance-Sproson T, Concha M, Gordon B, Solomon L, Vlahov D. HIV-1 infection and intravenous drug use: longitudinal neuropsychological evaluation of asymptomatic subjects. *Neurology*, 1992;42:1924-1930.
- Selnes OA, Miller E, McArthur J, Gordon B, Munoz A, Sheridan K, Fox R, Saah AJ. HIV-1 infection: no evidence of cognitive decline during the asymptomatic stages. The Multicenter AIDS Cohort Study. *Neurology*, 1990;40:204-208.
- Silberstein CH, O'Dowd MA, Chartock P, Schoenbaum E, Friedland G, Hartel D, McKeegney P. A Prospective Four-Year Follow-up of Neuropsychological Function in HIV Seropositive and Seronegative Methadone-Maintained Patients. *Gen Hosp Psychiatry* 1993; 15:351-359.
- Stern Y, Marder K, Bell K, Chen J, Dooneief G, Goldstein S, Mindry D, Richards M, Sano M, Williams J, et al. Multidisciplinary baseline assessment of homosexual men with and without human immunodeficiency virus infection. III. Neurologic and neuropsychological findings. *Arch Gen Psychiatry*, 1991;48:131-138.
- van Gorp WG, Satz P, Hinkin C, Selnes O, Miller EN, McArthur J, Cohen B, Paz D. Metacognition in HIV-1 seropositive asymptomatic individuals: self-ratings versus objective neuropsychological performance. Multicenter AIDS Cohort Study (MACS). *J Clin Exp Neuropsychol*. 1991; 13:812-819.
- Verma SK, Pershad D, Gupta LN, Khorana D, Misra MN, Ojha KN, Shukla TR. Standardization of Hindi WAIS-R Verbal short scale. *PGI Bulletin*, 1984; 18:70-79.