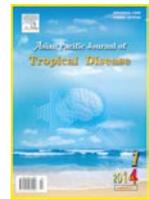




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Neurological manifestations in HIV positive patients in Tehran, Iran

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PEER REVIEW

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Comments

The present study is highly valuable regarding the setting (a referral hospital in Tehran) and also included retrospective and prospective parts. Also, regarding the scarce data in the country about the topic, the results can help clinicians in the setting for evaluation of the mentioned complaints and manifestations.

Details on Page S484

ABSTRACT

Objective: To evaluate the neurological complications among Iranian HIV-positive patients.

Methods: This cross-sectional study was conducted among 428 patients diagnosed with HIV infection between 2006 and 2009 at Imam Khomeini hospital, Tehran, Iran. Demographic and clinical variables as well as laboratory tests were extracted and analyzed. Also, another 100 patients referred to Voluntary Counseling and Testing center of the hospital were visited and evaluated for neurological complications.

Results: Among the patients, neurologic manifestations were observed in 34 (7.94%) patients. Twenty three percent of the patients received antiretroviral therapy. Identified causes included brain toxoplasmosis (14.7%), progressive multi-focal leuko encephalopathy (5.9%), HIV encephalopathy (5.9%), TB meningitis (5%) and unknown etiologies (11.8%). Also, among 100 patients who were admitted and visited at the Voluntary Counseling and Testing center, no one was diagnosed for any neurological manifestations.

Conclusions: According to our results, toxoplasmosis is the most frequent cause of neurological conditions among Iranian HIV infected patients and should be considered in any HIV/AIDS patient with neurological manifestations.

KEYWORDS

HIV, Neurological manifestations, Prevalence

1. Introduction

By the end of 2009, HIV infection had infected over 33 million people worldwide^[1]. Development of highly active antiretroviral therapy (HAART) revolutionized the care of HIV infected patients and reduced mortality and morbidity associated with HIV infection^[2]; however, improvement of the neurological complications remains a challenge in this regard. For example, application of HAART reduced the frequency of toxoplasmosis – the most common neurologic condition among people living with HIV/AIDS (PLWHA) – from 0.54% in 1990 to 0.2% in 1998^[3]. Either cause of direct

HIV invasion or manifestation of an opportunistic infection, neurological complications are among the most important causes of death among PLWHAs^[4,5], and they are the most common complication in 10%–20% of PLWHAs with low CD4 counts^[6]. In fact, about 60% of patients with advanced HIV disease will show at least a clinical evidence of neurological diseases^[7].

Neurologic manifestations among PLWHA include confusion, forgetfulness, behavioral changes, headaches, progressive weakness, loss of sensation in the extremities, cognitive and motor impairment, peripheral neuropathy, pain, seizure, shingles, spinal cord involvement, lack of

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coordination, dysphagia or odynophagia, mood disorders (*i.e.* depression and anxiety), fever, vision loss, gait disorders, encephalitis, dementia and coma^[8]. Toxoplasmosis is the most common cause of neurological involvement among PLWHAs. It is common among Asian PLWHAs, especially in Iran, where anti-retroviral therapy (ART) is relatively available. Another common cause of neurologic manifestations is HIV-associated cognitive dysfunction which accounts for a considerable proportion of neurologic diseases burden^[9].

We conducted this study to investigate distribution of neurological manifestations among Iranian PLWHAs.

2. Materials and methods

This study included two parts. In the first part, we retrospectively studied the medical profiles of 428 HIV infected patients who have been admitted to the infectious disease department in Imam Khomeini hospital from 2006 to 2009. Also, among the HIV positive patients who prospectively referred to Voluntary Counseling and Testing center of the hospital for daily visits and prescription, 100 individuals were selected randomly for screening of probable neurological manifestations. Informed consent for participation was obtained from all the participants and Institutional Review Board of Tehran University of Medical Sciences approved this study protocol.

Data collection was performed based on the medical documents gathered through a 4-year follow up of patients. All of the patients underwent precise clinical evaluation, followed by relevant laboratory investigations and appropriate neuro-imaging studies, including computed tomography and magnetic resonance imaging, electromyography and nerve conduction velocity and cerebrospinal fluid examination. The prevalence and incidence of neurologic disorders were assessed and recorded among admitted patients. Socio-demographic and clinical variables were obtained and analyzed. In addition, the first and the last CD4 level of patients were collected. The data were collected by semi-structural questionnaire and then analyzed by SPSS software 17.

3. Results

In the retrospective part of study, the mean age of patients was 39.06 years (the range was from 24 to 60 years old) and 88.9% of them were self-employed. Injection drug use (IDU) was the major route of HIV acquisition (81.3%) and most of them (81.5%) were in AIDS phase. Hepatitis C virus was the

most prevalent co-infection which was reported among 32.4% of patients. Additionally, the first reported CD4 level of most patients was below 100/ μ L. From a total of 428 participants who were retrospectively approached, 34 (7.94%) had neurological manifestations directly associated to HIV infection, among which 29 (85.3%) were male. Besides, more than half of the patients with neurological manifestations received ART. Table 1 shows socio-demographic characteristics of the participants.

Table 1

Demographic, laboratory and therapeutic characteristics of 34 HIV infected patients with neurological manifestations.

Characteristics	Frequency (%)	
Gender	Male	29 (85.3)
	Female	5 (14.7)
Occupational status	Staff	2 (7.4)
	Self-employee	24 (88.9)
	Jobless	1 (3.7)
Marital status	Single	16 (47.1)
	Married	18 (52.9)
Co-infection	HCV	11 (32.4)
	HBV	2 (5.9)
	Candidiasis	3 (8.8)
Taking anti-retroviral therapy		17 (50.0)

HCV: hepatitis C virus; HBV: hepatitis B virus.

Regarding neurological complications, toxoplasmosis was reported in 55.9% of patients with neurological manifestations. The most common presenting symptoms of toxoplasmosis were loss of consciousness, weakness, seizure and fever. Table 2 shows the reported neurological complications of the patients. Moreover, Table 3 shows some of the most common neurological complaints of the patients.

Table 2

Neurological complications of 34 HIV infected patients.

Manifestations	Frequency (%)
Toxoplasmosis	19 (55.9)
Progressive multifocal leuko encephalopathy	5 (14.7)
Undiagnosed	4 (11.8)
HIV encephalopathy	2 (5.9)
TB meningitis	2 (5.9)
CLP-PCP	1 (2.9)
Mononucleosis meningitis	1 (2.9)

Through the follows up, 30 patients with neurologic manifestations (88.2%) eventually expired after admission. Furthermore, among those who survived during the period of our study, two patients (11.8%) were recognized as the known cases of toxoplasmosis.

In the prospective part of the study, out of 100 patients, 77 were male and the mean age of participants was 33.4 years (ranging from 20–64 years). Besides, the major route of HIV acquisition was IDU (69%). Additionally, hepatitis C virus

Table 3

Neurological complaints of HIV–infected patients.

Manifestations	Weakness (%)	Seizure (%)	Loss of consciousness (%)	Fever (%)	Urine incontinency (%)	Fatigue (%)
Toxoplasmosis	3 (15.8)	4 (21.1)	5 (26.3)	5 (26.3)	5 (26.3)	5 (26.3)
PML	1 (20.0)	3 (60.0)	4 (80)	1 (20.0)	3 (60.0)	0 (0)
HIV encephalopathy	1 (50.0)	1 (50.0)	0 (0)	1 (50.0)	0 (0)	1 (50.0)
TB meningitis	0 (0)	0 (0)	1 (50)	1 (50.0)	0 (0)	0 (0)
CLP–PCP	0 (0)	1 (100.0)	0 (0)	0 (0)	0 (0)	0 (0)
Mononucleosis meningitis	0 (0)	0 (0)	0 (0)	1 (100.0)	0 (0)	0 (0)
Undiagnosed	1 (25.0)	0 (0)	3 (75)	1 (25.0)	1 (25.0)	0 (0)

PML: progressive multifocal leuko encephalopathy.

was the most prevalent co–infection (67%). Also, the mean CD4 level of patients was 243.5/ μ L and all of them received ART. Furthermore, none of the patients presented with any neurologic condition during the study period. Eight of them had neurological symptoms (*e.g.* headache and dizziness), with no laboratory, imaging or objective evidence.

4. Discussion

Although HIV is a neurotropic virus which can cause a large variety of neurological manifestations involving the nervous system^[10], only 7.9% of PLWHAs in our survey showed neurological signs and symptoms and there was no patient with HIV induced dementia.

In our study, the prevalence of neurological manifestations among PLWHAs was lower than those reported in other studies. For example, in studies performed by Levy *et al.* and Teja *et al.*, neurologic manifestations were identified in 39% and 26% of patients, respectively^[11,12]. Furthermore, in a study conducted by Janssen *et al.*, the prevalence of HIV dementia was between 7.3%–11.3%^[13]. Some other investigators have declared that neurologic symptoms might be present among 70% to 90% of HIV–infected patients during the course of infection^[14–16]. Such observed differences in the reported prevalence rates are due to different epidemiology of the infections in each study population and ART accessibility as well as diversity of the neurological signs, the accuracy of diagnosis and consideration of either both or only one of the presentations related to the central and peripheral nervous systems. We speculate that the reason for the observed differences in spectrum of opportunistic infections of nervous system in PLWHAs could be accessibility and application of HAART which has increased patients' survival rates and improved their overall quality of life.

The most common neurological disease observed in our survey was cerebral toxoplasmosis with a prevalence of 56%, which corroborates the results of Rezza *et al.*^[17]. According to their findings, the most common central nervous system

diseases among PLWHAs included cerebral toxoplasmosis, cryptococcal meningitis and progressive multifocal leukoencephalopathy (PML), in addition to HIV dementia^[17–19]. Literature shows some differences among the prevalence of underlying neurological conditions among PLWHAs. The most common central nervous system disorder of adult HIV infected patients include dementia complex (33%–67%), acute meningitis (5%–10%), cerebral toxoplasmosis (3%–40%), cytomegalovirus infection (2%–20%), cryptococcal meningitis (5%–10%), PML (2%–5%), primary brain lymphoma (2%) and tuberculosis (2%)^[20]. However, in line with our results, most researchers point to cerebral toxoplasmosis as the most common neurological complication^[19,21,22]. Some studies have shown that 24%–47% of toxoplasmosis–seropositive patients with HIV infection aggravate to toxoplasmosis encephalitis^[23,24], which is related to low CD4 counts (<100/ μ L)^[13, 24]. This fact is vindicator of what occurred in our patients, considering that most of our patients had a CD4 count less than 100/ μ L.

The most common clinical complains related to neurologic disorders in PLWHAs include headache (91%), fever (75%), focal neurologic deficits (61%), speech disorders (42%), cognitive disorders (41%), visual disturbances (36%) and seizure (15%)^[19]. On the other hand, most of our patients presented with loss of consciousness, fever and urine incontinency. Diagnosis was established based on patients' presentation and magnetic resonance imaging that showed multiple lesions in 90% of our patients.

Acute encephalitis and dementia presenting with headache and mental changes are common among HIV infected patients^[25]. Literature discusses that the prevalence of HIV encephalopathy as the most frequent cause of central nervous system damage in PLWHAs^[26,27], is rising despite the wide administration of ART. This can be a result of worldwide emerging HIV drug resistance^[2,28,29]. Our study showed that encephalopathy is one of the most common neurological manifestations in our patients (5.9%). Among the other neurological diseases, PML is one of the most common neurological manifestations among PLWHAs with advanced disease that can affect approximately 4%–8% of patients^[30].

We diagnosed PML in 14.7% of our patients.

One limitation of this study is that we were not able to obtain the detailed data for all of the patients because of missing some reporting files. Considering that toxoplasmosis is still a prevalent infection in some developing countries and HIV infection is also expanding among such nations, in addition to the more severe and complicated HIV infection in co-infected patients, the timely diagnosis of toxoplasmosis among HIV infected patients with neurological symptoms would be a principal action. Taking into consideration that our data supported the idea that IDU is still the main route of HIV transmission in Iran^[31], the practice of risky sexual behaviors among IDUs should be considered in this context. Moreover, to establish an early diagnosis of neurological manifestation, a complete screening for neurologic problems is recommended for all HIV-positive patients in order to increase their quality of life and survival.

Conflict of interest statement

We have no conflict of interest.

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Comments

Background

This study included two sections, including retrospective and prospective parts for evaluation of prevalence and incidence of neurological complications. Since neurological manifestations are common among PLWHAs, and also the complications are one of substantial causes for morbidity and mortality among PLWHAs, this survey is very important. Additionally, there is paucity of valuable data in Iran regarding this topic.

Research frontiers

Since current therapies are going to increase quantity and quality of life in HIV positive patients, prevention of major morbidities including neurological complications has been become a very important issue. So, doing early treatment interventions for prevention of the complications regarding different setting in countries is a high priority.

Related reports

In the present study, only 7.9% of PLWHAs showed neurologic manifestations which the prevalence was lower than those reported in other studies because of missing some data. Also, in line with other studies, toxoplasmosis is still a prevalent infection in the developing countries.

Innovations & breakthroughs

This survey studied both prevalence and incidence rate in the setting. Also, regarding the paucity of data about the neurological manifestations in Iran, the results are very beneficial and valuable.

Applications

The present study suggests taking history and doing physical exam for early diagnosis of neurological manifestations among all HIV-positive patients. Also, the timely diagnosis of toxoplasmosis among PLWHAs with neurological symptoms is very important action.

Peer review

The present study is highly valuable regarding the setting (a referral hospital in Tehran) and also included retrospective and prospective parts. Also, regarding the scarce data in the country about the topic, the results can help clinicians in the setting for evaluation of the mentioned complaints and manifestations.

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