Original Article

Clinical profile of central nervous system space-occupying lesions and their association with CD4 counts in patients with HIV: A prospective observational study

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Abstract

Background: Neurological manifestations are one of the major concerns for patients with human immunodeficiency virus (HIV). The secondary spectrum includes space-occupying lesions (SOL), including tuberculoma, cryptococcosis, candidiasis, toxoplasmosis, primary central nervous system lymphoma (PCNSL), and progressive multifocal leukoencephalopathy (PML). **Aim:** To assess the neurological manifestations, disease outcome, and their associations with cluster of differentiation 4 (CD4) counts in patients with HIV. **Materials and Methods:** This single-center, prospective, observational study was performed in the Department of General Medicine of a tertiary care institute, over a period of 2 years (January 2017 to December 2018). The study included 150 known or newly diagnosed HIV patients with CNS SOL. The physical examination, laboratory investigations, and imaging were conducted on every patient, and the findings were noted. **Results:** The patients mainly presented with hemiparesis (52%), had involvement of the frontal region (38.7%), and were diagnosed with tuberculoma (29.3%). Other diagnoses were toxoplasmosis (22.7%), PML (17.3%), PCNSL (15.3%), brain abscess (10%), and neurocysticercosis (5.3%). Of 150 patients, 136 (90.7%) were survivors, while 14 (9.3%) were non-survivors. The mean CD4 count was significantly less in patients with toxoplasmosis ($P < 0.0001$) and PCNSL ($P = 0.02$), and significantly higher in patients with tuberculoma ($P < 0.0001$) and brain abscess ($P = 0.0009$) relative to other causes of SOL. Moreover, the mean CD4 count was not significantly associated with survivors and non-survivors ($P = 0.28$). **Conclusion:** In patients with HIV, CD4 count was significantly low in toxoplasmosis and PCNSL, and high in tuberculoma and brain abscess.

Keywords: CD4 count, HIV, PCNSL, space-occupying lesions, toxoplasmosis, tuberculoma

Introduction

Human immunodeficiency virus (HIV) infection is a devastating condition that leads to the gradual loss of cluster of differentiation 4 (CD4) T cells, thereby damaging the immune system.[1] To date, more than 85.6 million individuals have been affected worldwide; around 39 million individuals in the world and 2.34 million in India are still living with HIV.[2,3] One of the major challenges

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posed by HIV is the involvement of the central nervous system (CNS), reportedly affected in 39–70% of the patients. Moreover, in these patients, the morbidity associated with CNS lesions is nearly 30%.[4]

Encephalitis, brain atrophy, white matter lesion, and HIV demyelination are the primary CNS lesions, while the secondary spectrum includes space-occupying lesions (SOL), including tuberculoma, cryptococcosis, candidiasis, toxoplasmosis, primary central nervous system lymphoma (PCNSL), progressive multifocal leukoencephalopathy (PML), and others.[4-6] Based on a recent study, the prevalence of SOL in patients with HIV is 2.2%.[7]

The reports from the Western world suggest that toxoplasmosis is the most common cause of CNS SOL in patients with acquired immunodeficiency syndrome (AIDS),[8] while, in the Indian context, tuberculosis appears to be the most common etiology of CNS SOL.[4,5,9] As India has the highest tuberculosis burden, evaluation of the clinical presentation of these patients can narrow down the differential diagnosis by a primary care physicians. Several studies have reported headache as the most common presentation,[9-11] while others have suggested hemiparesis, focal signs, and altered sensorium as the predominant presenting symptoms.[5,12,13] The opportunistic infections responsible for most CNS pathologies including SOL are frequently seen in patients with CD4 counts <200 cells/mm^3.[5] However, in these patients, the prevalence of SOL varies widely, from 52% to 86%.[4,11-13] In patients with toxoplasmosis, cryptococcosis, and PML, some of the authors have documented mean CD4 count of <100 cells/mm^3, while others have reported mean count >100 cells/mm^3.[14] In India, very few studies have evaluated CNS SOL in patients with HIV. Moreover, there is variability in the data reported from previous studies. Thus, we evaluated the clinical presentation of various SOLs and their association with CD4 count.

Materials and Methods

This prospective, observational study was performed in the Department of General Medicine of a tertiary care institute, over a period of 2 years (January 2017 to December 2018). The study began after obtaining approval from the Institutional Ethics Committee (No. IEC/PG/134/Dec/2016) and written informed consent from the enrolled patients.

The study included patients aged 12–65 years, of either sex, and known or newly diagnosed HIV patients with CNS SOL admitted in the wards. HIV was diagnosed on enzyme-linked immunosorbent assay (ELISA), and SOL was confirmed on computed tomography (CT) and/or magnetic resonance imaging (MRI), while patients with focal radiological findings other than a mass lesion, including infarct, basal enhancement, or atrophy, were excluded.

A total of 150 patients fulfilling the eligibility criteria were analyzed for the clinical manifestations and presenting symptoms of SOL. Complete physical examination and laboratory investigations were performed. Clinically suspected patients were further evaluated with CT and/or MRI scans. Laboratory investigations, including complete blood count, liver profile, renal profile, HIV type, CD4 count, serum electrolytes, serum toxoplasma antibody, cerebrospinal fluid (CSF) toxoplasma IgM/IgG antibody as well as CSF adenosine deaminase, glucose, and protein, were performed in every patient. Blood pressure and blood sugar level were monitored daily.

Sample size calculation

The population size (n, for finite population correction factor) was considered as 1,000,000. Based on a previous study, percentage frequency of outcome factor in the population (p) was hypothesized as 14 ± 5%.[15] Confidence limits (d) and design effect (DEFF) were taken as 5% and 1, respectively.

Sample size (n) for confidence level of 90% was calculated as 131 using the formula:

$$n = DEFF * Np(1\text{-}p)]/\ [(d2/Z21\text{-}\alpha/2*(N\text{-}1)+p*(1\text{-}p)]$$

Considering 10% dropout, the sample size was 131 + 13 = 144, which was rounded off to 150.

Statistical analyses

Data obtained from the physical and laboratory investigations were further subdivided according to the diagnoses of SOL. Continuous and categorical variables were represented as means ± standard deviation (SD) and frequency (percentages), respectively. The Chi-square test and independent-sample *t*-test were used to compare the continuous and categorical variables, respectively. A $P < 0.05$ was considered as statistically significant. All analyses were performed with PRISM version 5.01 (GraphPad Software, San Diego, California, USA).

Results

The patients were predominantly males (69.33%) with a male-to-female ratio of 2.26. The mean age of the study population was 36.7 ± 8.4 years. HIV-1 (96%) was observed in most of the patients. The mean CD4 count was 331.98 ± 225.93 cells/mm^3, and the majority of patients had CD4 count >200 cells/mm^3 (53.33%). The SOLs were mostly located in the frontal (38.7%) and parietal (32.7%) regions. Of 150 patients, 136 (90.7%) were survivors, while 14 (9.3%) were non-survivors [Table 1].

The patients frequently presented with hemiparesis (52%) followed by seizure (46%), confusion (42%), and headache (37.3%). The most common diagnosis was tuberculoma (29.3%) followed by toxoplasmosis (22.7%), PML (17.3%), PCNSL (15.3%), brain abscess (10%), and neurocysticercosis (5.3%). The patients with tuberculoma, toxoplasmosis, PML, and brain abscess frequently presented with hemiparesis (61.8%, 47.7%, 42.3%,

and 66.7%, respectively). Seizure (65.2%) was the most common presenting feature in patients with PCNSL. Moreover, patients with neurocysticercosis mostly presented with hemiparesis and confusion (62.5% each) [Table 2].

Table 1: Demographic characteristics, CD4 count, and location of SOL

Parameters and characteristics (*n*=150)	Value
Age (mean±SD)	36.7±8.4 years
Sex, *n* (%)	
Male	104 (69.3%)
Female	46 (30.7%)
Type of HIV infection, *n* (%)	
HIV-1	144 (96%)
HIV-2	4 (2.7%)
HIV-1 and HIV-2	2 (1.3%)
CD4 count (cells/mm^3), *n* (%)	
Mean±SD	331.9±225.9 cells/mm^3
<100	34 (22.7%)
101-200	36 (24%)
201-300	12 (8%)
301-400	8 (5.3%)
>400	60 (40%)
Location of SOL, *n* (%)	
Frontal	58 (38.7%)
Parietal	49 (32.7%)
Basal ganglia	41 (27.3%)
Temporal	23 (15.3%)
Cerebellar	17 (11.3%)
Occipital	7 (4.7%)
Mid-brain	4 (2.66%)
Pons	2 (1.3%)
Outcome, *n* (%)	
Death	14 (9.3%)
Discharge	136 (90.7%)

CD4=Cluster of differentiation 4; SOL=Space-occupying lesion; HIV=Human immunodeficiency virus

The evaluation of the association between various clinical features and SOLs revealed no significant association of hemiparesis, seizure, confusion, and headache with any of the SOLs, except significantly higher seizures among patients with PCNSL (15 vs 8; $P = 0.04$) [Table 3].

The mean CD4 count among patients with toxoplasmosis, PCNSL, and PML was <200 cells/mm^3, while it was >200 cells/mm^3 among patients with tuberculoma, neurocysticercosis, and brain abscess. Relative to other causes of SOL, the mean CD4 count was significantly lower in patients with specific causes of SOL, including toxoplasmosis ($P < 0.0001$) and PCNSL ($P = 0.02$); though similar trend was observed with PML, it did not reach statistically significant level ($P = 0.06$). Contrarily, tuberculoma ($P < 0.0001$) and brain abscess ($P = 0.0009$) had significantly higher mean CD4 count than other causes of SOL, while neurocysticercosis had no significant difference ($P = 0.23$) [Table 4].

Assessment of outcome, based on diagnosis, revealed mortality in patients with tuberculoma ($n = 8$, 57.14%) and toxoplasmosis ($n = 6$, 42.86%). Moreover, analysis of the association of outcome with CD4 count revealed no significant association between survivors and non-survivors in mean CD4 count (333.6 ± 226.9 cells/mm^3 versus 335 ± 227.95 cells/mm^3; $P = 0.28$).

Discussion

The principal findings of the study suggest that tuberculoma is the most common SOL (29.3%), hemiparesis (52%) is the most common clinical presentation, and mean CD4 count is significantly low in patients with toxoplasmosis and PCNSL relative to other SOLs.

Table 2: Distribution of patients according to the diagnosis and clinical features

Clinical features *n*=150 (%)	CNS space-occupying lesions					
	Toxoplasmosis (*n*=34)	PCNSL (*n*=23)	PML (*n*=26)	Tuberculoma (*n*=44)	Neurocysticercosis (*n*=8)	Brain abscess (*n*=15)
Hemiparesis (78; 52%)	21 (61.8%)	10 (43.5%)	11 (42.3%)	21 (47.7%)	5 (62.5%)	10 (66.7%)
Seizure (69; 46%)	17 (50%)	15 (65.2%)	10 (38.5%)	18 (40.9%)	2 (25%)	7 (46.7%)
Confusion (63; 42%)	14 (41.2%)	13 (56.5%)	10 (38.5%)	15 (34.1)	5 (62.5%)	6 (40%)
Fatigue (34; 22.7%)	10 (29.4%)	3 (13.1%)	5 (19.2%)	10 (22.7%)	2 (25%)	4 (26.7%)
Headache (56; 37.3%)	9 (26.5%)	10 (43.5%)	10 (38.5%)	16 (36.4%)	3 (37.5%)	8 (53.3%)
Neck stiffness (33; 22%)	7 (20.6%)	6 (26.1%)	4 (15.4%)	13 (29.5%)	2 (25%)	1 (6.7%)
Drowsiness (18; 12%)	7 (20.6%)	3 (13.1%)	2 (7.7%)	3 (6.8%)	2 (25%)	1 (6.7%)
Fever (27; 18%)	6 (17.6%)	1 (4.3%)	8 (30.8%)	10 (22.7%)	1 (12.5%)	1 (6.7%)
Altered sensorium (23; 15.3%)	4 (11.8%)	2 (8.7%)	7 (26.9%)	9 (20.5%)	1 (12.5%)	0 (0%)
Vomiting (12; 8%)	4 (11.8%)	3 (13.1%)	0 (0%)	4 (9.1%)	0 (0%)	1 (6.7%)
Aphasia (15; 10%)	3 (8.8%)	4 (17.4%)	2 (7.7%)	5 (11.4%)	0 (0%)	1 (6.7%)
UI (9; 6%)	3 (8.8%)	2 (8.7%)	1 (3.8%)	1 (2.3%)	0 (0%)	2 (13.3%)
Memory disturbance (5; 3.3%)	2 (5.9%)	1 (4.3%)	1 (3.8%)	1 (2.3%)	0 (0%)	0 (0%)
Paraplegia/paralysis (8; 5.33%)	2 (5.9%)	3 (13.1%)	0 (0%)	3 (6.8%)	0 (0%)	0 (0%)
VFD (6; 4%)	1 (2.9%)	1 (4.3%)	2 (7.7%)	2 (4.5%)	0 (0%)	0 (0%)

PML=Progressive multifocal leukoencephalopathy; CNS=Central nervous system; PCNSL=Primary central nervous system lymphoma; VFD=Visual field defect; UI=Urinary incontinence

Table 3: Association of various clinical features with different space-occupying lesions

Diagnosis	Features present	Features absent	OR	*P*
Hemiparesis				
Toxoplasmosis	21	13	1.68	0.19
PML	11	15	0.62	0.29
Neurocysticercosis	5	3	1.57	0.72
Brain abscess	10	5	1.97	0.28
Tuberculoma	21	23	0.78	0.59
Seizure				
Toxoplasmosis	17	17	1.27	0.53
PML	10	16	0.71	0.51
PCNSL	15	8	2.61	0.04
Tuberculoma	18	26	0.77	0.58
Confusion				
Lymphoma	13	10	2.00	0.16
Neurocysticercosis	5	3	2.41	0.28
Headache				
Brain abscess	8	7	2.07	0.25

PML=Progressive multifocal leukoencephalopathy; OR=Odds ratio; PCNSL=Primary central nervous system lymphoma

Table 4: Association of CD4 count with specific SOL

Diagnosis	*n*=150 (%)	CD4 count (mean±SD)	*P*
Toxoplasmosis	34	82.41±9.87	<0.0001
Except toxoplasmosis	116	412.35±191.67	
PML	26	190.92±32.71	0.06
Except PML	124	361.55±238.39	
PCNSL	23	180.5±27.39	0.02
Except PCNSL	127	360.37±234.75	
CNS tuberculoma	44	605.18±76.99	<0.0001
Except CNS tuberculoma	106	218.57±161.58	
Brain abscess	15	522.93±106.14	0.0009
Except brain abscess	135	310.76±226.56	
Neurocysticercosis	8	441.25±76.18	0.23
Except neurocysticercosis	142	325.82±230.67	

PML=Progressive multifocal leukoencephalopathy; CD4=Count in cells/mm^3

Hematogenous spread of the primary tuberculous lung infection to CNS leads to small tuberculous lesions or granulomas in the brain. These lesions then coalesce to develop tuberculomas which are firm, avascular, and spherical granulomatous masses containing central core of caseous necrosis surrounded by a wall of inflammatory cells.[16] In this study, tuberculoma (29.3%) was the most common SOL followed by toxoplasmosis (22.66%). Studies by Luma *et al.* and Azovtseva *et al.* also demonstrated toxoplasmosis as the most common SOL in patients with HIV.[10,17] Toxoplasmosis, caused by *Toxoplasma gondii*, has been regarded as the leading cause of SOL in patients with HIV. The ubiquitous nature of the parasite along with the weakened immune system makes it the most common cause of SOL worldwide.[5] In the Indian context, CNS tuberculosis is more frequent among patients with AIDS than the Western world.[18] Toxoplasmosis occurs at a later stage in HIV-positive patients, but tuberculosis can occur at any stage of the disease. Moreover, with high prevalence of tuberculosis in India, as in this study, it is not surprising that the most common cause of CNS SOL in HIV-positive patients is tuberculoma.[14,19] This finding is in consensus with the Indian studies conducted by Ray *et al.* and Sharma *et al.*, where CNS tuberculosis was the most common cause of CNS manifestations of HIV.[4,9]

We observed that hemiparesis (52%) and seizure (45.33%) were the two most common clinical presentations. Other common features were headache, neck stiffness, fatigue, fever, and urinary incontinence. These findings are in consensus with the study conducted by Pillay *et al.*, who reported hemiparesis (48.19%) as the most common presentation, followed by seizure and confusion.[5] However, Luma *et al.* reported headache as the most common clinical finding in patients with HIV-associated CNS disease.[10] In this study, headache was found in 37% of the patients, the fourth most common finding. This might be due to the fact that in resource-limited country such as India, common complaint such as headache is ignored by patients and they present late with more serious symptoms. The results indicate that although manifestations such as seizures and hemiparesis are considerably serious clinical findings, headaches in an HIV-infected patient should raise the suspicion in clinician's mind about the possibility of a SOL and such symptoms should be given due consideration.[5]

Hemiparesis and seizure were the two most common presenting features in patients with toxoplasmosis, and the odds ratio indicates that they are more likely to occur in these patients. Though the association of symptoms has not been evaluated in most of the studies, a meta-analysis of six studies showed an association (odds ratio ranging from 1.17 to 5.35) between seizures and toxoplasmosis. The neuropathogenesis of seizure development is not well understood; however, chronic infection by *T. gondii* results in the formation of tissue cysts containing the parasite in the bradyzoite stage. Later, these cysts release large number of bradyzoites which infect new cells (neurons, microglia, and astrocytes) and cause localized inflammation producing microglial scars. This scar tissue formation is hypothesized to be the cause of seizure in patients with toxoplasmosis.[20] A recent review on toxoplasmosis in patients with HIV states that headache followed by focal deficit and seizures are the most common manifestations.[8] Though a wide variety of clinical manifestations are possible, depending on size, number, and location of lesions, hemiparesis and seizure are reported among the top three clinical features in patients with toxoplasmosis.[5,8,14]

In patients with PCNSL, seizure and confusion were the two most common presenting features in this study, whereas a study conducted by Bayraktar *et al.* showed headache, memory loss, and seizure as the common presenting feature in 60%, 50%, and 38%, respectively.[21] We observed that hemiparesis was the most common presenting features in patients with PML. This was in accordance with the study conducted by Fanjul *et al.* which found motor deficits in the majority of the patients.[22] We further observed that hemiparesis and seizure were the two most common presenting features in patients with CNS tuberculoma. Similar results were reported by Marais *et al.*, where focal

neurological deficit was found in 66% of the patients followed by headache (62%) and seizure (34%).[16] Hemiparesis and confusion were the two most common presenting features of patients with neurocysticercosis. This contrasted with the record-based study conducted by Jewell *et al.*, which mentioned seizures and headache as the most common symptoms of neurocysticercosis in patients with HIV.[23]

We observed that the mean CD4 count was 331.9 ± 225.9 cells/mm^3, and the majority of the patients had CD4 count >200 cells/mm^3 (53.3%). The mean CD4 count among patients with toxoplasmosis (82.41 ± 9.87), PCNSL (175.17 ± 38.19), and PML (190.92 ± 32.71) was <200 cells/mm^3 and was statistically significant, whereas the count in those with tuberculoma, neurocysticercosis, and brain abscess was >200 cells/mm^3. Similar results were reported in a study conducted by Pillay *et al.*, where the mean CD4 count was lowest in toxoplasmosis (94 ± 8.5 cells/mm^3) and was on higher side in tuberculoma (187.5 ± 53 cells/mm^3) and brain abscess (235.3 ± 301.6 cells/mm^3).[5] We also observed that the mean CD4 cell count in patients with tuberculoma (605.18 ± 76.99 cells/mm^3) and brain abscess (522.93 ± 106.14 cells/mm^3) were on the higher side. Though the mean CD4 count in tuberculoma patients was higher, in this study, relative to other studies, it is not surprising as even in individuals with preserved cell-mediated immune responses and CD4 count of >200 cells/mm^3, caseating rich foci in the brain cortex can cause tuberculomas especially in endemic regions such as India.[24]

Latent *T. gondii* bradyzoites are converted active tachyzoites, based on the level of immunosuppression, and the occurrence of toxoplasmosis increases in HIV-infected individuals with CD4+ cell counts of <100 cells/mm^3. This finding is documented in most of the studies[5,9] and has been established in this study as well. PML, a demyelinating disease of the brain, is caused by the John Cunningham virus infection. This virus is ubiquitous in >50% population and gets reactivated typically at a decreased CD4 cell count.[24] In agreement with this study, Sharma *et al.* reported a mean CD4 count of <200 cells/mm^3 in patients with PML.[25] In the late stage of AIDS, *Epstein–Barr virus* (EBV) infection may cause PCNSL due to dysregulation of the immune system and B-cell stimulation of decrease in CD8 T cells by HIV and mutations in tumor suppressor genes by EBV. PCNSL occurs late in HIV when the CD4 count is very low (usually <50 cells/mm^3). Bayraktar *et al.* reported 75 ± 13 cells/mm^3 as the mean CD4 count in HIV-positive patients with PCNSL, which is less than that found in this study.[21] The mean CD4 count, in this study, was 175.17 ± 38.19 cells/mm^3, which was a surprising finding as most of the literature has reported counts below 50 cells/mm^3 in PCNSL.

In this study, the majority of the CNS lesions were located in the frontal region (38.66%) followed by the parietal (32.66%) region. The frontal lobe was the most common region in toxoplasmosis, PCNSL, neurocysticercosis, and brain abscess, while the patients with tuberculoma and PML had the involvement of the parietal lobe. Although SOL can affect any part of the CNS, results similar to this study were reported by Pillay *et al.*, where frontal, parietal, and basal ganglia were the three most common regions affected.[5] Bayraktar *et al.* reported frontal, periventricular, and temporal as the most common location for PCNSL.[21] Mohammadian and Butt reported frontal and parietal lobes as common site for tuberculoma.[26] Sharma *et al.* reported supratentorial white matter lesions in cerebral hemispheres as the most common site for PML.[25]

We observed that 9.33% of the patients died during the hospital stay. Toxoplasmosis and tuberculoma were the two conditions that led to mortality. Almost similar results were reported in a study conducted by Pillay *et al.*, where the mortality rate was 8.18%.[5] In two other studies, mortality was reported in around 20% of the patients with SOL.[12,27] The low mortality in this study might be due to the lack of long-term follow-up of the patients.

The study had certain limitations, including lack of collection and analysis of data on treatment, correlation of symptoms with location of SOL, lack of analysis of HIV viral load, and lack of long-term follow-up.

Conclusion

To conclude, tuberculoma followed by toxoplasmosis was the most common cause of CNS SOL. The majority of the CNS lesions were in the frontal and parietal regions. Hemiparesis and seizure were the two most common clinical presentations. The mean CD4 count was significantly low in toxoplasmosis and PCNSL relative to other etiologies of SOL in patients with HIV.

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Conflicts of interest

There are no conflicts of interest.

References

1. Vidya Vijayan KK, Karthigeyan KP, Tripathi SP, Hanna LE. Pathophysiology of CD4+ T-Cell Depletion in HIV-1 and HIV-2 Infections. Front Immunol 2017;8:580.
2. UNAIDS. Fact sheet - Latest global and regional statistics on the status of the AIDS epidemics. Available from: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf. [Last accessed on 2023 Nov 15].
3. Shri N, Bhattacharyya K, Dhamnetiya D, Singh M, Jha RP,

Patel P. Long-term trends of HIV/AIDS incidence in India: An application of joinpoint and age-period-cohort analyses: A gendered perspective. Front Public Health 2023;11:1093310.

4. Ray J, Debbarma P, Debbarma T. Magnetic resonance imaging evaluation of CNS diseases in AIDS patients and correlation of CD4+ cell count with the opportunistic infections. Int J Contemp Med Surg Radiology 2021;6:B6-11.
5. Pillay S, Ramchandre K. Audit of computed tomography brain findings in HIV-infected patients with space occupying infective lesions at a regional level hospital in KwaZulu-Natal. SAGE Open Med 2018;6:2050312118801242.
6. Javadi S, Menias CO, Karbasian N, Shaaban A, Shah K, Osman A, *et al.* HIV-related malignancies and mimics: Imaging findings and management. Radiographics 2018;38:2051-68.
7. Omar AT 2nd, Nepomuceno MJ, Salvana EMT, Chua AE. Intracranial mass lesions in human immunodeficiency virus patients in the Philippines: A retrospective cohort study. World Neurosurg 2021;145:e149-54.
8. Vidal JE. HIV-Related cerebral toxoplasmosis revisited: Current concepts and controversies of an old disease. J Int Assoc Provid AIDS Care 2019;18:2325958219867315.
9. Sharma SR, Hussain M, Habung H. Neurological manifestations of HIV-AIDS at a tertiary care institute in North Eastern India. Neurol India 2017;65:64-8.
10. Luma HN, Tchaleu BC, Temfack E, Doualla MS, Ndenga DP, Mapoure YN, *et al.* HIV-associated central nervous system disease in patients admitted at the Douala General Hospital between 2004 and 2009: A Retrospective Study. AIDS Res Treat 2013;2013:709810.
11. Sharma SK, Dwivedi NC, Kumar N, Bharti A, Meena LP. Neurological manifestation of HIV infection in North-Eastern part of India. Natl J Physiol Pharm Pharmacol 2014;4:4-8.
12. Modi M, Mochan A, Modi G. Management of HIV-associated focal brain lesions in developing countries. QJM 2004;97:413-21.
13. Jagtap SB, Patil PM. Clinical profile of neurological manifestations and CD4 counts in patient living with HIV cases and its outcome with treatment with ART at a tertiary hospital. Med Int J of Medicine. 2021;21:78-84. Available from: https://www.medpulse.in/Medicine/Article/Volume20Issue3/Medicine_20_3_3.pdf. [Last accessed on 2023 Jul 19].
14. Attili SVS, Gulati AK, Singh VP, Varma DV, Rai M, Sundar S. Neurological Manifestations HIV-Infected Patients Around Varanasi, India. Afr J Neurol Sci. 2006;25:4-8. Available from: https://www.ajol.info/index.php/ajns/article/view/7579. [Last accessed on 2023 Jul 19].
15. Berger JR. Mass lesions of the brain in AIDS: The dilemmas of distinguishing toxoplasmosis from primary CNS lymphoma. AJNR Am J Neuroradiol 2003;24:554-5.
16. Marais S, Roos I, Mitha A, Patel V, Kalincik T, Bhigjee AI. Presentation and outcome of patients with intracranial tuberculoma in a high HIV prevalence setting. Int J Tuberc Lung Dis 2020;24:224-32.
17. Azovtseva OV, Viktorova EA, Bakulina EG, Shelomov AS, Trofimova TN. Cerebral toxoplasmosis in HIV-infected patients over 2015-2018 (a case study of Russia). Epidemiol Infect 2020;148:e142.
18. Modi M, Garg A. Tuberculosis of Central Nervous System. J Postgrad Med Edu Res 2013;47:202-13. Available from: https://www.jpmer.com/doi/pdf/10.5005/jp-journals-10028-1086. [Last accessed on 2023 Jul 19].
19. Satischandra P, Mathew T. Neurological manifestations associated with HIV infection Indian persective, Med. Update 2010;10:760-5.
20. Ngoungou EB, Bhalla D, Nzoghe A, Dardé ML, Preux PM. Toxoplasmosis and epilepsy--Systematic review and meta analysis. PLoS Negl Trop Dis 2015;9:e0003525.
21. Bayraktar S, Bayraktar UD, Ramos JC, Stefanovic A, Lossos IS. Primary CNS lymphoma in HIV positive and negative patients: Comparison of clinical characteristics, outcome and prognostic factors. J Neurooncol 2011;101:257-65.
22. Fanjul F, Riveiro-Barciela M, Gonzalez J, Delgado E, Murillas J, Payeras Cifré A, *et al.* Evaluation of progressive multifocal leukoencephalopathy treatments in a Spanish cohort of HIV-infected patients: Do protease inhibitors improve survival regardless of central nervous system penetration-effectiveness (CPE) score?. HIV Med 2013;14:321-5.
23. Jewell PD, Abraham A, Schmidt V, Buell KG, Bustos JA, Garcia HH, *et al.* Neurocysticercosis and HIV/AIDS co-infection: A scoping review. Trop Med Int Health 2021;26:1140-52.
24. Bowen LN, Smith B, Reich D, Quezado M, Nath A. HIV-associated opportunistic CNS infections: Pathophysiology, diagnosis and treatment. Nat Rev Neurol 2016;12:662-74.
25. Sharma SK, Soneja M, Ranjan S, Miglani S, Hari S, Sinha S, *et al.* Progressive multifocal leucoencephalopathy in HIV/AIDS: Observational study from a tertiary care centre in northern India. Indian J Med Res 2013;138:72-7.
26. Mohammadian M, Butt S. Symptomatic central nervous system tuberculoma, a case report in the United States and literature review. IDCases 2019;17:e00582.
27. Omar AT 2nd, Nepomuceno MJ, Salvana EMT, Chua AE. Intracranial mass lesions in human immunodeficiency virus patients in the Philippines: A retrospective cohort study. World Neurosurg 2021;145:e149-54.