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Role of Neuroimaging in People Living with HIV and AIDS

Dr.Yevvari Sameera[1], Dr.Rajani Gorantla[2]
[1]*Department of radiology,NRI medical college and general hospital,Chinakakani,AndhraPradesh,India.*
[2]*Department of radiology,NRI medical college and general hospital,Chinakakani,AndhraPradesh,India.*
Corresponding Author: Dr.Yevvari Sameera

Abstract: *Nervous system is commonly involved due to HIV infection. It is paramount to distinguish whether the neurologic deterioration is due to opportunistic infection or immune reconstitution or the effect of virus itself.MR imaging greatly helps in narrowing the differential diagnosis.Neurological manifestations of retropositive patients is not uncommon. We present case series of People living with HIV and AIDS (PLHA) with varied imaging manifestations. Detailed clinical examination was done, CD-4 cell counts were obtained and correlated with the imaging features.Of the cases studied,majority were opportunistic infections,predominantly granulomatous infections,liketuberculosis,followed by toxoplasmosis.One case of CNS cryptococcosis was identified.Other cases were Primary CNS lymphoma,HIV encephalopathy and Progressive multifocal leukoencephalopathy.*

Keywords:*AIDS(Acquired immunodeficiency syndrome),HIV(human immunodeficiency virus),infection,MRI(magnetic resonance imaging).*

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I. Introduction

Human immunodeficiency virus (HIV) belongs to a subset of retrovirusescalled lentiviruses (or slow viruses), which means thatthere is an interval between the initial infection and the onset ofsymptoms. Upon entering the loodstream, HIV infects the CD4+ T cellsand begins to replicate rapidly. Acquired immunodeficiency syndrome(AIDS) is the final stage of HIV infection[1]. Approximately 40%-90% of patients with AIDS will developCNS manifestations during the courses of their illnesses[2].HIV-infection and particularly its late stage ofsevere immunodeficiency (AIDS) render thenervous system susceptible to an array ofneurological disorders[3].

The neurologic problems that occur in HIV-infectedindividuals may be either primary to thepathogenic processes of HIV infection or secondaryto opportunistic infections or neoplasms[3].Rarely,they may also manifest due to immune reconstruction of the host.

Magnetic resonance imaging (MRI) has been used to examine the impact of human immunodeficiency virus(HIV) on the central nervous system (CNS) since the beginning of the pandemic[4].Neuroimaging revolution has led to a much more rapid and accurate diagnostic approach to patients with suspected central nervous system (CNS) complications of HIV infection or AIDS.Applications of neuroimaging in this population include early identification of lesions, to establish a differential diagnosis and monitoring of treatment effects.

There is increasing ability to detect manifestations of direct effects of HIV infection to nervous system, opportunistic infections, immune reconstruction and neoplasia by combining clinical manifestations,laboratory findings and neuroimaging.

In our case series,westudied 15 people living with HIV and AIDS who presented with varied clinical manifestations involving the nervous system.Each of them were examined clinically in detail and then subjected to neuroimaging and laboratory investigations.We hereby present the varied clinical and imaging manifestations of people living with HIV and AIDS.

II. Aim

To study the various neuroimaging features of people living with HIV and AIDS and to cateogorise them under atleast one of the following:eitheroppotunistic infections or due to effects of virus itself or a vascular cause or neoplastic etiology.

III. Methodology

Fifteen patients were studied in last 12 months(from January 2017 to January 2018) who came to department of radiology for MRI brain from neurology out patient department of NRI Medical college and General hospital.

All the MRI sequences were obtained on 1.5 Tesla MRI machine 'GE Signa' 1.5T Signa Excite system (General electrical medical systems, Milwaukee, USA). A dedicated eight channel high resolution head coil was used.

MRI brain protocol:Axial sections of T1, T2 & FLAIR images were obtained using following parameters. Post contrast T1 images were obtained in required patients.

Table 1: Parameters for T1,T2,FLAIR and post contrast MR imaging:

Parameters	T1	T2	FLAIR	Post contrast
TE(msec)	9	85	140	20
TR(msec)	500	4080	7800	560
BAND WIDTH(kHz)	15.6	20.83	15.6	15.6
FOV(cms)	24	24	24	24
ST(mm)	5	5	5	5
SPACING(mm)	1.5	1.5	1.5	1.5
NO. OF SLICES	20	20	20	20
MATRIX	256X192	228X224	256X192	256X192

TR – time to repeat, TE – time to echo,ST-slice thickness.

DWI TECHNIQUE:Diffusion weighted MR sequence was performed at two 'b' values, b = 0s/mm2 and b = 1000 $s/mm^2$to obtain axial index DW images. Then, by using asoftware application (FuncTool in 'GE Signa'), Apparent Diffusion Coefficient(ADC) maps were obtained for lesions. The imaging parameters of the diffusion sequence were as follows –TE* – minimum, TR*–9000, Number of shots – 1, FOV – 24, slice thickness – 5 mm, spacing – 1.5 mm, Planes – all, number of slices – 20.

Detailed clinical history was taken, clinical examination was done, CD-4 cell counts were obtained and correlated with the imaging features.

IV. Results

Out of the 15 patients included in our study, 9 are males,accounting to 60% and 6(40%) are females. Majority of them, approximately 73% aged between 31 to 40 years of age(Table2).On clinical examination they all showed a varied presentation with dominant features listed in table 3.CD-4 count of them was obtained it was between 50 to 100 cells/mm^3 in majority of the patients(Table 4).On MR imaging, they show characteristic features which are listed in table 3.

Based on the symptoms, their duration,CD 4 cell count and imaging findings, the cases were grouped into 4 cateogories as discussed in table 5.

Table 2: Age distribution of patients studied:

Age	No.of people	Percentage
20-30 yrs	2	13%
31-40 yrs	11	73%
41-50 yrs	2	13%

Table 3: Clinical presentation of the patients:

Cases	Presentation:	Imaging findings:
1	Flaccid paraplegia	Multiple T2 hypointense ring enhancing lesions in right thalamus, frontal region and dorsal spinal cord at D7 level
2	Seizures, Flaccid paraplegia	Ring enhancing lesions in left occipital and parietal regions and intensely enhancing ring lesion in conus with thickened and enhancing nerve roots .
3	Visual disturbances , cognitive disturbances.	Leptomeningeal enhancement basifrontal, opticochiasmatic and along the anterior cerebral arteries with small ring lesions.
4	Seizures.	T2 hypointense ring enhancing lesions in left basal ganglia, right frontal region with peri lesional edema.
5	Sudden onset of left hemiplegia.	Multiple ring and nodular enhancing lesions with target sign.
6	Fever,headache, vomitings Flaccid quadriparesis.	Meningeal enhancment at ambient and quadrigeminal cisterns.
7	Diplopia,Dysarthria, dysphagia, Vertical gaze palsy	T2 hypointense lesion , diffusion restriction and elevated choline on MR spectroscopy
8	Gradual painless loss of vision, altered behaviour with reduced memory	Diffuse white matter volume loss

9	**Sudden onset right hemiplegia**	**Diffusion restriction with T2 and FLAIR hyperintensity in left MCA territory.**
10	Headache, visual loss, difficulty in closing eyes with drooling of saliva, dysarthria	Diffusion restriction with T2 and FLAIR hyperintensity in right ACA territory.
11	Sudden onset left hemiplegia	MRV showing thrombosis of bilateral transverse and posterior aspect of superior sagittal sinuses.
12	Altered sensorium with paraparesis	T2 and FLAIR subcortical hyperintensity with patchy enhancement with LL peak on spectroscopy
13	Seizures	T2 and FLAIR relatively symmetrical white matter hyperintensities in bilateral cerebellar white matter , pons and bilateral cerebral white matter with angiocentric infiltrates on contrast.
14	Memory disturbances	Bilateral relatively symmetrical T2 and FLAIR non enhancing hyperintensities with Diffuse white matter volume loss.
15	Headache since 6 months	Multiple hyperintense psuedocysts in bilateral basal ganglia

Table 4:CD4 cell count in the patients:

CD 4 count(cells/mm3)	no.of patients	Percentage
<50	2	13
50-100	5	33
100-200	4	26
>200	4	26

Table 5: Cateogorising the patients into 4 groups:

Entity:	No. of patients:
1.Infection:	
A.Opportunistic infection	
Tuberculosis:	
Tuberculomas in brain	2
TB spine with chronic immune demyelinating polyneuropathy	1
Tubercular meningitis	1
CNS toxoplasmosis	1
Cryptococcosis	1
B.Reactivation of latent infection	
Progressive multifocal leukoencephalopathy	1
PML with IRIS	1
2.Effects of HIV virus on brain:	
HIV encephalopathy	2
3.Vascular	
MCA territory infarcts	2
Venous thrombosis	1
4.Neoplastic	
PCNSL	1

IRIS-Immune reconstruction inflammatory syndrome,TB-Tuberculosis,PML-Progressive multifocal leukoencephalopathy,PCNSL-Primary CNS lymphoma.

V. Discussion

In the present study, we have divided the pathologies affecting the in people living with HIV into 4 cateogories as described in table 4.So,the first cateogory is infective, which is further divided into opportunistic infections and infections due to reactivation of latent virus due to immunosuppression.Firstly, among the opportunistic infections we have encountered,tuberculosis is the most common, followed by CNS toxoplasmosis and cryptococcosis.Progressive multifocal leukoenceohalopathy,though it is not an infection,was included under infections since the demyelination in this disease process is believed to be due to the reactivation of latent John Cunningham virus due to immunosuppression.

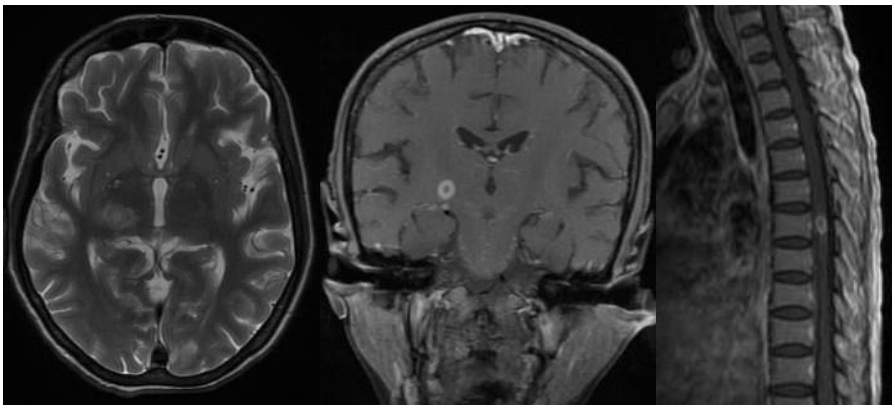
The second cateogory is the disease entities which follow due to the direct effects of HIV on brain tissue.This includes HIV encephalopathy and Aids dementia complex.

The third cateogory is vascular.In our study, we have encouontered 3 cases, out of which 2 of them had arterial territories involving the MCA territory which could be attributed to HIV vasculitis. One case,however, showed venous thrombosis.

Fourth cateogory is neoplastic.In this cateogory,we encountered a young male with primary CNS lymphoma.

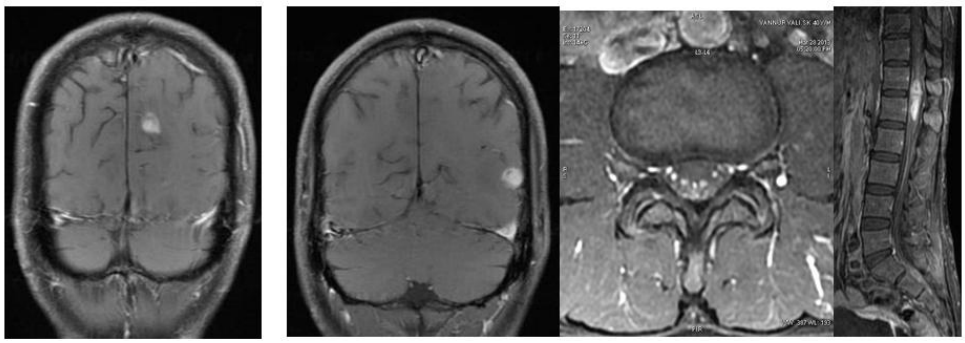
1.Tuberculosis:

TB is a common opportunistic infection and co infection in India. CNS manifestations of tuberculosis can be varied. In our study, we encountered tuberculomas and tubercular meningitis(Fig.1 and 2). The most common intracranial manifestationof tuberculosis is meningitis, which is usuallymore prominent in the basilar cisterns, especiallyaround the circle of Willis. However, tuberculomas,tuberculous abscess, and cerebral ischemiaand infarction are not uncommon findings[5].Tuberculomas are hypointense onT2-weighted MR images in the early stages; asthey mature, they develop a hypointense centersurrounded by an isointense capsule, which correspondsto solid caseation necrosis. They mayfurther progress to abscess formation with a hyperintense center[5].



(A) **(B)** **(C)**

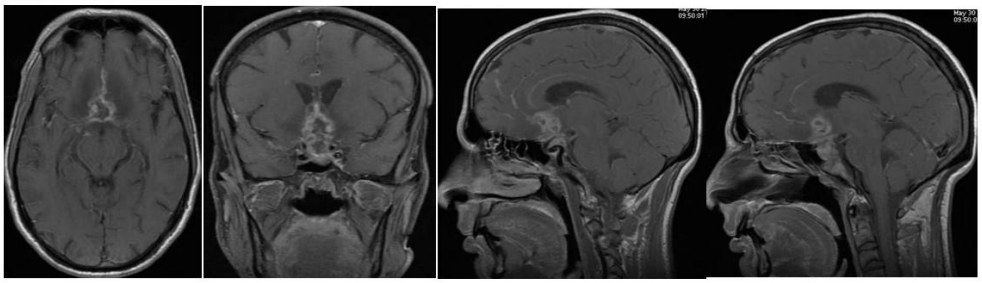
Fig 1: T2 weighted axial image(A),Post contrast T1 coronal(B) shows smooth thin walled ring enhancing lesion in the right thalamus. Post contrast Saggital section of dorsal spine(C) shows similar ring enhancing lesion that are consistent with tuberculomas in dorsal spine in a case of CNS tuberculosis.



(A) (B) (C) (D)

Fig 2: Post contrast T1 weighted coronal(A and B)show nodular enhancing lesion in the left parietal region, Post contrast T1 axial at lumbar spine(C)shows thickened and enhancing nerve roots and post contrast saggital(D) shows solid nodular enhancing lesion in the lower dorsal spinal cord.Tuberculous etiology was confirmed by CSF cytology.

We have encountered a rare type of tubercular meningitis in a patent who presented with diminution of vision of right eye, drooping of right eye lid and behaviouraldisturbances.Clinically,the symptoms are localized to right III cranial nerve and frontal region.MR imaging revealed thick nodular enhancement of meninges in basifrontal, opticochiasmatic and along the anterior cerebral arteries with small ring enhancing lesions in frontal region.CSF was done and it was confirmed to be tuberculous etiology.



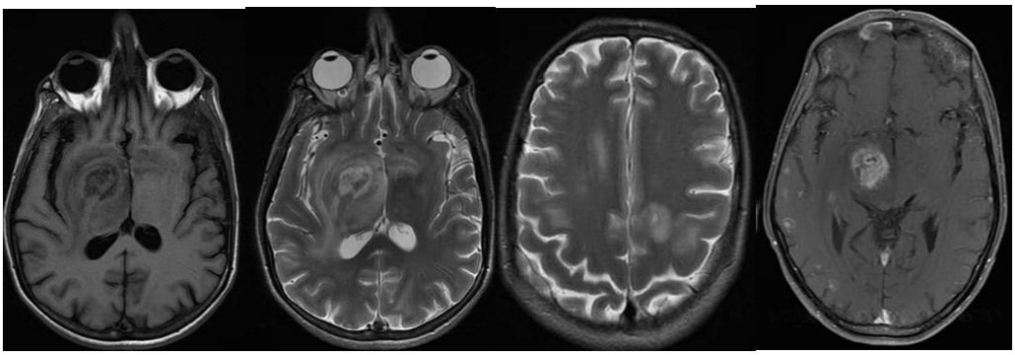
(A) (B) (C) (D)

Fig.3: Post contrast T1 weighted Axial(A),Coronal(B) and Saggital images(C,D) show bilateral relatively symmetrical leptomeningeal enhancement in bilateral basifrontal,opticochiasmatic and along the anterior cerebral arteries with small ring enhancing lesions which on correlation with CSF cytology was proven to betuberculous infection with optochiasmatic arachnoiditis.

2.CNS Toxoplasmosis:

CNS toxoplasmosis is considered the most common opportunistic infection in people living with HIV and AIDS in the United States presenting as mass lesion[5]. However,we encountered only one case in our study.

Unenhanced CT reveals multiple areas of abnormallow attenuation that appear most frequently inthe basal ganglia, thalamus, and corticomedullaryjunction. These areas demonstrate ring ornodular enhancement on postcontrast CT images.At MR imaging with T2-weighted sequences,toxoplasmosis lesions are typically hypo- to isointenseand are surrounded by high-signal-intensityvasogenic edema.Postcontrast MR imaging reveals multiplenodular lesions or ring-enhancing lesions. Occasionally, a small eccentric nodulerests alongside an enhancing ring: the "targetsign"[5].



(A) (B) (C) (D)

Fig. 4: Case of 35 year old male who presented with sudden onset left hemiplegia.T1 weighted axial section(A),T2 axial sections(B and C) and Post contrast T1 axial sections show multiple ring enhancing lesions with mural enhancing nodules that represents "target sign" that is specific for CNS toxoplasmosis.

3.CNS cryptococcosis:

Cryptococcus is the third most common cause ofCNS infection in AIDS patients, ranking behindHIV and Toxoplasma[5]. On MR imaging,dilatedperivascular spaces resulting from the presence ofgelatinous pseudocysts are a frequent finding, andtheir presence in an immunocompromised patientshould raise a red flag[5].

In present study, we encountered a 26 year old male patient who presented with headache since 6 months with a CD 4 cell count of 86 cells/mm^3 who on MR imaging revealed multiple T2 hyperintense gelatinous pseudocysts in bilateral basal ganglia.

4.Progressive multifocal leukoencephalopathy:

PML is a progressive demyelinating disorderthat results from a viral infection of the myelinproducing oligodendrocytes. The infecting agentis the John Cunningham virus, which is a DNApapovavirus[5].The greatest risk of developing PML occurs among patientswith CD4 counts in the range of 50–100 cells/L^5.

On MR images, there aretypically multifocal, asymmetric areas of T1 andT2 prolongation in the periventricular and subcorticalwhite matter.These lesionsare frequently bilateral and multiple, although

they may occasionally be solitary. Subcortical Ufiber involvement is frequently seen, a findingthat provides a sharp contrast with the overlyinggray matterTypically, PML lesions do notenhance, but faint peripheral enhancement hasbeen described. On DWI, there is leading edge of high signal intensity with low ADC values.

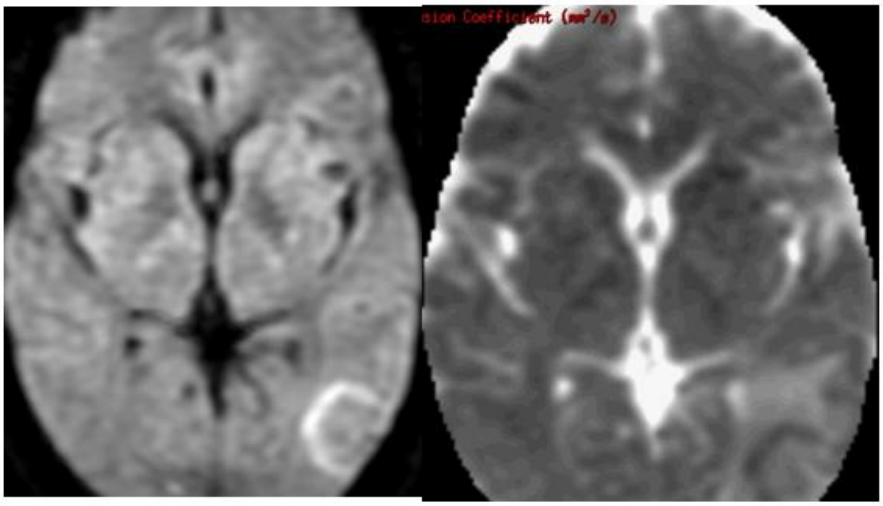


Fig. 5: DWI(A) and corresponding ADC image shows diffusion retriction at the advancing end of the lesion in a known case of PML. PML-Progressive multifocal leukoencehalopathy.

5. HIV Encephalopathy:

It is also called aids-dementia complex.Patients with CD4 counts less than 200 cells/L, longer duration of HIV infection,andolder age at seroconversion are at most risk for developing AIDS dementia complex.

On magnetic resonance (MR) images, a diffuse cerebral atrophy with symmetric, patchy or confluent areas of T1 and T2 prolongation are seen within the periventricular and deep white matter of patients with AIDS dementia complex.Often, there is a frontal predominance that may include involvement of the genu of the corpus callosum[5].

In the present study, there are 2 patients with of 30-35 years of age who were diagnosed as affected with HIV since 10 years.Both of them presented with memory disturbances.One of them had a CD 4 count of 74 cells/mm^3 and the other had 189 cells/mm^3.On MR imaging one patient revaled diffuse volume loss of cerebrum and the other showed bilateral confluent symmetrical T2 and FLAIR hyperintensities in the periventricular region in addition.

6.HIV Vasculitis:

HIV-related vasculitis including a primaryHIV vasculitis has been describedin pathologic studies of AIDS patients.The lenticulostriate vessels are the mostVulnerable[1,6].This panarteritis couldthen lead to stenosis and/or aneurysmaldilatation[1,7]. Resultant infarcts orhemorrhages can occur[1,8].

In present study, the two cases of arterial infarcts are thought to probably be due to vasculitis.Venous thrombosis ,however, was thought to be due to be "de-novo" and not due to the HIV virus.

7.Primary CNS Lymphoma:

Primary CNS lymphoma without extracranialinvolvement occurs in approximately 5% of AIDSpatients. These tumours are usually aggressive,high-grade, diffuse B-cell neoplasms, whichconsist of either large immunoblastic or smallnoncleaved cells[3]. *Epstein-Barr virus* (EBV) DNA hasbeen detected by *in situ* hybridization in most AIDSrelatedprimary CNS lymphomas[3,9].

On CT scan, lymphomas appear as iso- tohyperdense space-occupying lesions with masseffect and uniform contrast. With MRI, lesionsappear hypo- to isointense on T1-weighted imagesand are obscured by surrounding oedema. Signalintensity may be variable on T2-weighted images,with lesions appearing isointense, hyperintense,or with mixed increased and decreased signalintensity[3].Spinal fluid examination is abnormal with somecombination of mild pleocytosis, protein elevation,and hypoglycorrhachia; however, tumour cells are identified in fewer than 25%[3,10].

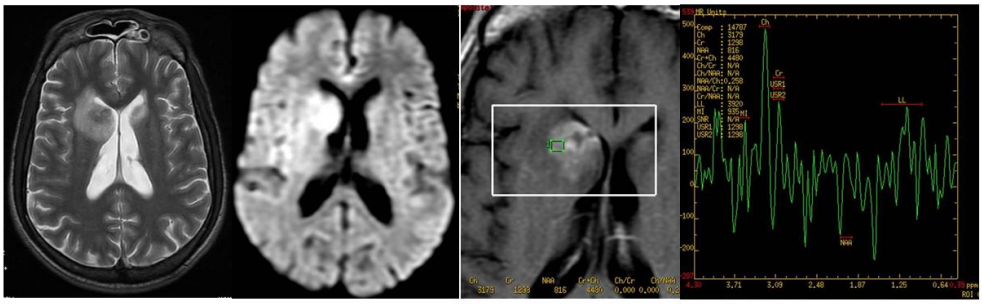


Fig. 6: Case of 36 year male patient with PCNSL.T2 weighted axial(A)shows predominantly hypointense lesion in bilateral frontal regions in periventricular location,DWI image(B)shows diffusion restriction,post contrast T1 weighted Coronal image(C)shows solid heterogenous enhancement and MRS shows increased choline.

VI. Conclusion

Nervous system is the most common and serious target of HIV infection, even in the era of effective antiretroviral treatment. Now a days successful treatment for virologic control raised the survival of HIV patients.

MRI is excellent meansof detection of cerebral lesions in AIDSpatients, useful in initial diagnosis andin therapeutic follow-up evaluation and has high sensitivity.

Radiologist often needs to distinguish whether the neuroimaging findings are due to opportunistic infection or immune reconstitution or the effect of virus itself. Therefore the adequate knowledge of different CNS imaging manifestations in HIV patients is necessary for timely recognition and management to reduce the morbidity and to improve the quality of life of HIV patients.

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