Original Research Article

Spectrum of central nervous system imaging findings in HIV/AIDS: Current scenario in India

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Abstract

Background: Next to Sub- Saharan Africa, India has the second largest burden of HIV related pathology. Central nervous system is one of the major targets of the neurotropic Human Immunodeficiency Virus (HIV). Although extensive studies on role of central nervous system imaging in HIV and AIDS have been done , this study was taken up again to discern the current status and spectrum of neurological pathologies encountered in HIV/ AIDS and elaborate how magnetic resonance imaging (MRI) aids in the characterization and differentiation of central nervous system abnormalities. **Materials and Method:** This was a cross sectional descriptive study carried out in the Department of Radiodiagnosis at a Tertiary care teaching Institution in Mumbai, India. 60 seropositive patients who presented with neurological complains underwent MRI and the imaging findings were studied. **Result:** Most common age group in our study was more than 40 years comprising 51.6 % of the total study population. Males (65%) were affected more than females (35%). HIV induced primary neurological illness were present in 25% cases, while opportunistic infections were seen in 60 % cases. Most common opportunistic infection in HIV was Tuberculosis (58.3%) followed by PML (22%), Toxoplasmosis (14 %) and fungal infections (6%). Primary CNS Lymphoma was found in 5% cases. The most common presenting symptom on admission was fever (41.6%) followed by altered sensorium (33.3%). The most common cause of meningitis in our study was tuberculosis. Most common cause of infarction (focal neurological deficit) were presumed to be tubercular meningitis and HIV vasculopathy. **Conclusion:** We came to the conclusion that Tuberculosis is still the most common CNS pathology encountered in HIV/AIDS in India. MRI is an excellent means of detection and characterization of brain lesions in Acquired Immunodeficiency Syndrome (AIDS) and should be considered as one of the first line investigations in a seropositive patient with neurological complains, in absence of any contraindication.

Keywords: Acquired Immunodeficiency Syndrome, HIV, MRI, Opportunistic infections, CNS Tuberculosis, Toxoplasmosis, Primary CNS Lymphoma, PML

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INTRODUCTION

Human Immunodeficiency Virus (HIV) is a neurotropic virus and crosses the blood brain barrier at early stages in the disease. Thus, the central nervous system (CNS) is the major target of HIV, with approximately two-third of the patients developing CNS involvement during the course of their disease. Neurological disease is the first manifestation of the symptomatic HIV infection in approximately 10-20% of persons. The spectrum of pathology affecting the Central Nervous System (CNS) in patients suffering from HIV disease can be broadly categorized into primary effects of HIV, opportunistic infections, neoplasms and vascular diseases. Clinical findings are non-specific, and are often unhelpful in distinguishing between the vast arrays of neurological disease processes in AIDS. In countries where HAART coverage is extensive, cognitive dysfunction and peripheral neuropathies caused directly by HIV represent the majority of cases of HIV-related neurologic disorders while in other countries, opportunistic infections of the

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CNS are more common. Immune reconstitution inflammatory syndrome (IRIS) is a complication of HAART that causes transient worsening or appearance of new signs, symptoms, or radiological manifestations of opportunistic infection after initiation of therapy. Occasionally, IRI vt5S may be associated with a fatal outcome. IRIS is thought to arise from restoration of immune response, and it impacts the imaging findings. Next to Sub- Saharan Africa, India has the second largest burden of HIV related pathology, essentially caused by HIV-1 class C in both the geographical locales, in contrast to USA and Europe. [3] In developing countries like India, opportunistic infections of the central nervous system (CNS) account for most of the reported neurological morbidity and mortality in AIDS. Although there is a considerable overlap in the imaging characteristics of different CNS pathologies, some findings are found to be very suggestive of a particular disease and imaging modalities, mainly Magnetic Resonance Imaging (MRI), play an important role in the diagnosis and follow up of AIDS patients with neurological disorders.[4] Magnetic resonance imaging has a high sensitivity in identifying lesions of the central nervous system. It is very useful, together with the results of other tests, in the final diagnosis of the lesions in the central nervous system. [5] Advanced techniques such as MR Perfusion study and MR spectroscopy (MRS) have been used to improve the sensitivity for characterizing the type, viability, and burden of the disease and the host tissue response.

MATERIALS AND METHODS

Study design: Cross sectional descriptive study.
Study site: Tertiary care teaching institute.
Study Timeline: 2 years from July 2018 to December 2020
Sample size: 60
Sampling method: Random
Inclusion criteria: All the patients who had their HIV status confirmed via ELISA/ western blotting presenting with neurological symptoms and willing to give informed written consent to take part in the study.
Exclusion criteria: Patients who were allergic to contrast media, those who had contra indications for MRI and those who were not willing were excluded from the study.
Study Protocol and Equipment used: All the patients satisfying inclusion criteria underwent Magnetic Resonance Imaging.All MR imaging examinations were performed on a Siemens 3 Tesla magnetom Verio MR system. Slice thickness was 4–5 mm; with an inter-slice gap of 0.5 mm.
The following sequences were obtained:
Pre-contrast

- Axial and coronal T1 weighted images
- Axial and sagittal T2 weighted images
- Axial fluid-attenuated inversion recovery (FLAIR)
- Diffusion weighted imaging (DWI)
- Susceptibility weighted imaging/ gradient recalled echo (SWI/GRE)

Post contrast

- T1 weighted fat suppressed images.
- MP RAGE(3D T1 gradient echo sequence)
- Axial fluid-attenuated inversion recovery (FLAIR)
- Additionally, MR-Spectroscopy, MR- Perfusion study, MR- Angiography/venography were done whenever required.

Contrast Administration: After proper consent, history taking and information to the patient, Intravenous Gadolinium DTPA was administered following the recommended dose i.e. 0.1mmol/kg or 0.2 ml/kg.
Data analysis:
The final diagnosis was made after considering clinical features, laboratory investigations, and radiological findings. Quantitative data were represented in the form of values and percentages. Also the qualitative data will be presented in the form of visual impression like bar-diagram, pie-diagram.

OBSERVATION AND RESULTS

In our study of total 60 patients, maximum i.e 20 (33.3%) were in the age group of 41-50 years followed by 31-40 years age group which included 18(30 %) . Least number of patients were 2 in the age groups of 11-20 years and more than 60 years. Males (65%) were affected more than females (35%) .Male: Female ratio was 1.86:1 The most common clinical presentation was that of fever present in 41.6 % of total patients followed by altered sensorium (33.3%) ,headache (26.6%) , stroke (26.6 %) and dementia (20 %). Opportunistic infections were the most common finding seen in 60% (36/60) patients. Primary effects of HIV like cerebral atrophy, HIV encephalopathy were seen in 25%(15/60) patients. CNS lymphoma was seen in 5% (3/60) of patients. 18.3% (11/60) patients showed Cerebrovascular complications -infarcts. Other findings like arachnoiditis, Pott's spine with para-vertebral abscesses were seen in 5% (3/60) patients.

Table 1: Diagnosis and frequency of CNS pathologies in HIV patients

Sr No	Pathologies	No. of patients	%age
1.	**Primary effects of HIV**	**15**	**25 %**
	Cortical Atrophy	06	
	HIV encephalopathy	09	
2.	**Opportunistic Infections**	**36**	**60 %**
	CNS Tuberculosis	21	
	Toxoplasmosis	05	
	Fungal Infections	02	
	PML	08	
3.	**Lymphoma**	**03**	**5 %**
4.	**Cerebrovascular complications**	**11**	**18.3 %**
	Infarction	11	
	Hemorrhage	00	
5.	**Any other**	**03**	**5 %**
	Arachnoiditis	01	
	Pott's spine	02	

In our study 38% (08/21) patients with **CNS tuberculosis** presented with isolated Tuberculous meningitis. Isolated Tuberculomas were seen in equal percentage of patients while 9.5 % (2/21) patients had tuberculous meningitis with tuberculomas. Tubercular abscess was seen in 14.3 % (03/21) cases. 08/21 i.e 38% patients had hydrocephalus, all being communicating hydrocephalus. Vasculitic infarcts were seen in 28.3 % (5/21) cases. Other findings like arachnoiditis (1/21) and Pott's spine (2/21) were seen in 14.2% (03/21) patients.

Table 2: Spectrum of Neurotuberculosis in HIV patients (n =21)

Imaging Diagnosis	Number of patients	%age
Tuberculoma	08	38.0 %
Tubercular meningitis	08	38.0 %
Tuberculomas with tubercular meningitis	02	9.5 %
Tubercular abscess	03	14.3 %
Total	**21**	

In our study,five cases of **toxoplasmosis** were encountered. 80% (04/05) patients showed multiple lesions and gangliocapsular region was the most common location. Ring enhancement was seen in 80% (04/05) patients. Blooming on SWI was noted in 60% (03/05) cases. Two patients showed eccentric target lesion like enhancement. All patients showed surrounding edema and mass effect. We did not find meningeal enhancement in any of the patients. **Progressive multifocal leukoencephalopathy** an opportunistic infection caused by JC virus was seen in eight patients. White matter lesions were asymmetric in distribution and bilateral in all the cases. Sub cortical white matter was the most common location (87.5%) followed by brain stem (50%).Single case showed patchy diffusion restriction. None of the lesion showed mass effect or enhancement. Associated cerebral atrophy and ventricular prominence were present in 75% (06/08) cases. Three cases of **CNS lymphoma** are present in our study. All the cases showed multiple lesions. Out these 3 cases 2 were involving supratentorium (periventricular and subcortical white matter). All the lesions were isointense on T1W images. Single case showed hypo to isointense lesions on T2W images and rest were hyperintense on T2W images. Variable enhancement patterns were seen with each case showing homogeneous, ring pattern and heterogeneous enhancement. Two cases showed surrounding edema, while single case showed mass effect. 66.6 %(02/03) cases showed hyper perfusion on perfusion study.

Total 9 patients had **HIV encephalopathy**.Bilateral symmetrical lesions were seen in all 9 (100%) patients. Periventricular lesions were seen in 8 (88%) . None of them showed contrast enhancement. Associated cerebral cortical atrophy was seen in 4 (44.5 %) of patients Out of 60 patients, 6 % (10/60) showed meningitis. All the cases of meningitis were associated with CNS tuberculosis. We did not come across aseptic meningitis or meningitis due to other opportunistic infections.

In our study 11 (18.3 %) patients had imaging feature suggestive of Infarct. Five patients had infarct secondary to tuberculosis infection.In another five patients etiology of infarct was not clearly established but these patients had no other risk factors such as hypertension, diabetes, hyperlipidemia or smoking. In this particular group in absence of obvious etiological factors and after ruling out other predisposing factors to CV stroke, presumed diagnosis of HIV Vasculopathy was considered.

Table 3: Correlation between CD4 Count and Neurological manifestations

CD4 Level	TB	Cryptococcosis	Toxoplasmosis	PML	HIV Encephalopathy	Lymphoma
0-50	00	01	01	01	00	01
51-100	01	00	02	02	00	01
101-150	03	00	02	03	01	01
151-200	01	00	00	00	00	00
201-250	05	00	00	02	01	00
>250	11	00	00	00	07	00
Total	**21**	**01**	**05**	**08**	**09**	**03**

In our study, 37.8% of PML cases had CD4 count under 100, 37.8% between 101-150 and 25.0% cases had CD4 count between 210-205. None of the cases had CD4 counts above 250.60% patients of Toxoplasmosis had CD4 count below 100. None of the patients had CD4 count more than 150.Single case of Cryptococcosis had CD4 count below 50.All three cases of lymphoma had their CD4 count below 150 with one case each in 0-50, 51-100 and 101-150.Among the cases of CNS Tuberculosis, maximum 52.4% (11/21) patients had CD4 counts above 250. Similarly, maximum number of patients with HIV encephalopathy i.e. 77.7% (07/09) had CD4 counts above 250.

Case 1: HIV encephalopathy

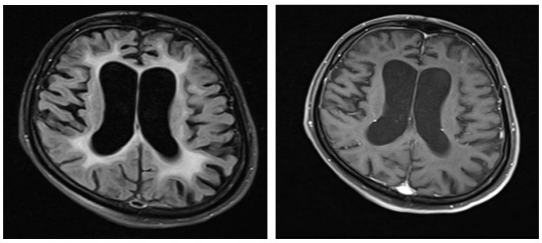

Figure 1: Flair axial**; Figure 2:** Post contrast T1 FAT SAT axial

Case 2: Progressive multifocal leukoencephalopathy

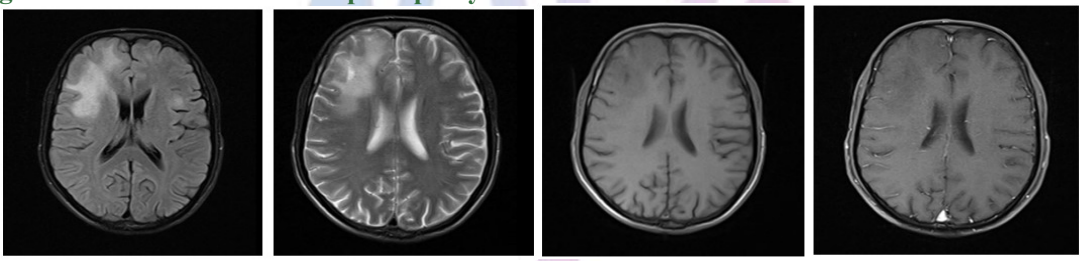

Figure 3: Flair axial **Figure 4:** T2WI axial **Figure 5:** T1WI axial **Figure 6:** Post contrast T1 axial

Case 3: Tuberculous meningitis with Vasculitic infarcts

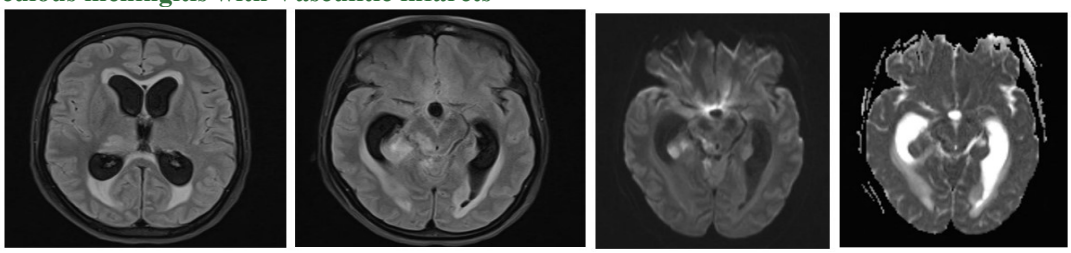

Figure 7: Flair axial **Figure 8:** Flair axial **Figure 9:** DWI **Figure 10:** ADC

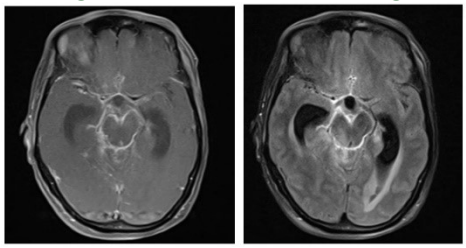

Figure 11: Post contrast T1 FAT SAT**; Figure 12:** Post contrast flair

Case 4: Tubercular abscess

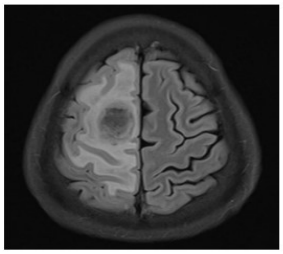
Figure 13: Flair axial

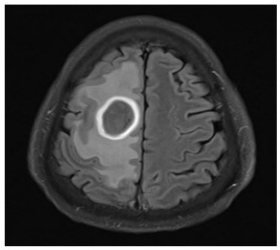
Figure 14: Post contrast flair axial

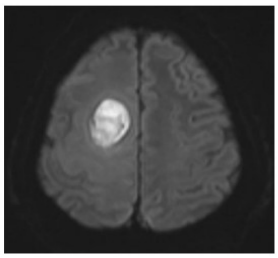
Figure 15: DWI

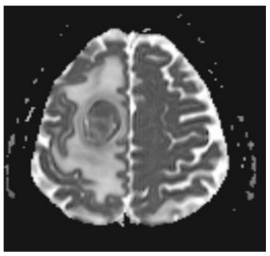
Figure 16: ADC

Case 5: Tuberculomas with tubercular meningitis and arachnoiditis

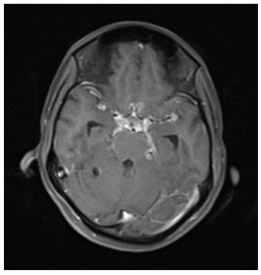
Figure 17: Post contrast T1W1 axial

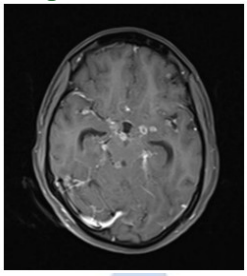
Figure 18: Post contrast T1W1 axial

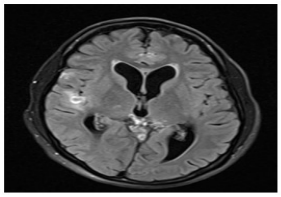
Figure 19: Post contrast flaire axial

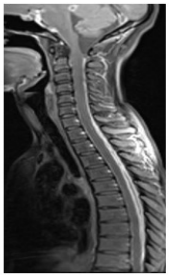
Figure 20: Spine post contrast T1 fat sat sagittal

Case 6: Toxoplasmosis

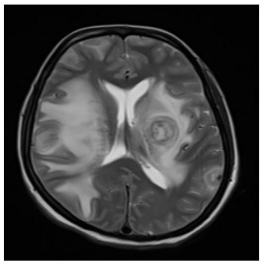
Figure 21: T2WI axial

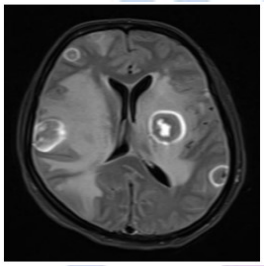
Figure 22: Post Contrast flair axial

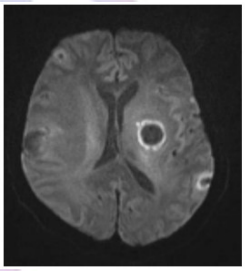
Figure 23: DWI

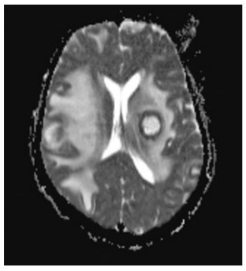
Figure 24: ADC

Case 7: Cryptococcosis

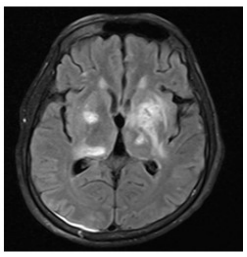
Figure 25: Flair axial

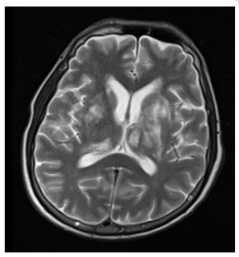
Figure 26: T2W1 axial

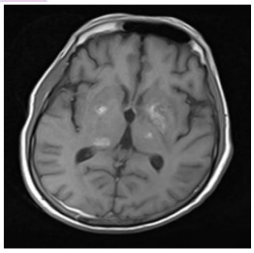
Figure 27: T1WI axial

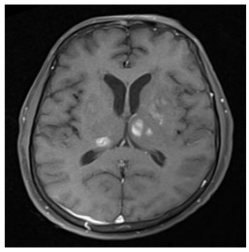
Figure 28: Post contrast T1WI

Case 8: Primary CNS lymphoma

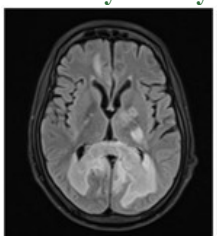
Figure 29: Flair axial FAT SAT axial

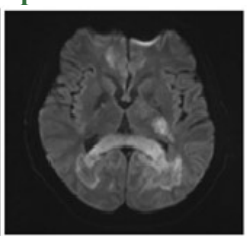
Figure 30: DWI flair axial

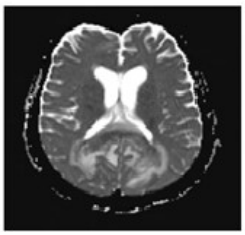
Figure 31: ADC

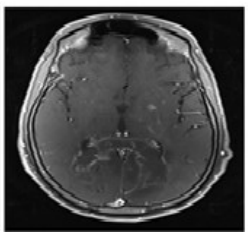
Figure 32: Post contrast T1

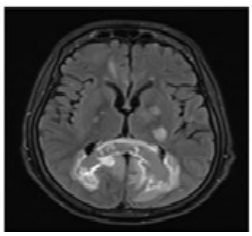
Figure 33: Post contrast

DISCUSSION

This was a cross sectional descriptive study carried out in the Department of Radiodiagnosis at a Tertiary care teaching Institution in Mumbai,India wherein 60 seropositive patients who presented with neurological complains underwent MRI and the imaging findings studied. Most common age group was found to be more than 40 years with 51.6 % of the total study population followed by the age group of 21-40 years which accounted for 45%. Males were affected more commonly than females. Male: Female ratio in patients with neurological involvement is 1.86:1. The most common presenting symptom on admission was fever (41.6%) followed by altered sensorium (33.3%), headache and stroke in 26.6% patients each,dementia (20%) ,convulsions (6.6%) and vomiting found in 6% patients. HIV induced primary neurological illness were present in 25% cases, while opportunistic infections were seen in 60 % cases. Most common opportunistic infection in HIV was Tuberculosis which was present in 58.3% (21/36) cases followed by PML 22%, Toxoplasmosis 14 % and fungal infections 6%. Cryptococcosis was found in only one patient out of total 60 patients. Primary CNS Lymphoma was found in 5% cases. In comparison to previous Indian studies done by HM Rana *et al.* [9] in 2011, Sharma SR *et al.*[14] in 2017 and S Pawar *et al.* [15] in 2017, our study showed higher percentage of CNS manifestations due to primary effects of HIV (HIV associated Dementia) as well as Progressive Multifocal leukoencephalopathy (PML). The percentage involvement of Neurotuberculosis was nearly the same. There were lesser cases of fungal pathologies in our study. No case of Neurosyphilis was encountered. When compared to Non Indian studies by Sokolska *et al.* [20]and Berhe *et al.* [21], our study showed lower incidence of Toxoplasmosis and fungal infections and higher incidences of Neurotuberculosis. However, the Percentage involvement of HIV associated dementia is quite comparable. CNS Tuberculosis was the overall most common pathology in our study accounting to 35.0% i.e 21/60 cases. Out of 21 patients with CNS TB, 10 (47.6%) patients demonstrated cisternal/ meningeal enhancement. 10 (47.6%) patients showed enhancing parenchymal lesions and tuberculomas and 03 (14.7 %) had tubercular abscesses. Communicating hydrocephalus was present in 08 (38%) of 21. Vasculitic infarcts were seen in 05 (23.8%) cases. Additional findings of arachnoiditis (1/21) and tubercular spondylodiscitis with para vertebral abscesses (2/21) were also appreciated in few cases. The spectrum of CNS tuberculosis in HIV patients seen in our study is comparable to multiple previous studies like Sarosh *et al.* [23] Michelle Whiteman *et al.* [24.] The imaging findings in cases of Toxoplasmosis ,Progressive multifocal leukoencephalopathy, CNS lymphoma ,HIV encephalopathy and fungal infections in our study were in concordance with previous studies done by Miguel J *et al.,* Enting *et al.* [25], Mark *et al.* [26,] Johnson *et al.* [27]keerati hongsakul *et al.* [28] and M.Judith Donovan [22] Out of 60 patients, 6 % (10/60) showed meningitis. All the cases of meningitis were associated with CNS tuberculosis. We did not come across aseptic meningitis or meningitis due to other opportunistic infections. In our study 11 (18.3 %) patients had imaging feature suggestive of Infarct. Five patients had infarct secondary to tuberculosis infection.In another five patients etiology of infarct was not clearly established but these patients had no other risk factors such as hypertension, diabetes, hyperlipidemia or smoking. In this particular group in absence of obvious etiological factors and after ruling out other predisposing factors to CV stroke, presumed diagnosis of HIV Vasculopathy was considered. However Possibility of infarcts secondary to other infection like CMV, varicella-zoster virus, previous sub clinical CNS infection or fungal infection were not ruled out. The etiology of vasculopathy in HIV-infected individuals has been widely debated, and is probably multifactorial. For practical purposes HIV vasculopathy may be classified as HIV-related vasculitis. Single case with subacute infarct showed mild irregularity of ipsilateral MCA on MR angiography. On deeper probe into the history,the patient gave history of chronic smoking and hypertension. Our study is comparable to study done by M.D. Connor *et al.* [29] , Brent Tipping *et al.* [30] and Alaka Deshpande *et al.* [31].

SUMMARY AND CONCLUSION

Tuberculosis is still the most common CNS pathology encountered in HIV/AIDS in India while there is rising trend in the cases of HIV induced primary neurological illness.Imaging findings of different brain pathologies may overlap but certain imaging characteristics and location of the lesions may favour a particular diagnosis. Nonetheless correlation with clinical history and other laboratory parameters are instrumental along with imaging. MRI is an excellent means of detection and characterization of brain lesions in Acquired Immunodeficiency Syndrome (AIDS) and should be considered as one of the first line investigations in a seropositive patient with neurological complains, in absence of any contraindication.

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