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ABSTRACT

Introduction: India has a very large burden of people living with HIV infections. All the systems in the body tend to be affected by the HIV virus, but the central nervous systems affection is involved very early in the disease as the virus is neurotropic. There is a wide spectrum of central nervous system diseases occurring in AIDS patients. The purpose of our study was to detect, characterize and compare various CT and MRI findings in central nervous system diseases in PLHIV and correlate it with CD4+ counts.

Material and Methods: The study was carried out on 98 patients who were HIV positive and had Central nervous system complaints. CT and MRI were performed on all the patients included in the study and the findings were compared for both the studies.

Results: In our study 25.5% cases were normal on CT and 8.2% by were normal on MRI. The most common final diagnosis in our study group was CNS Tuberculosis detected in 31.6% of cases, followed by AIDS dementia complex in 15.4% cases, cerebrovascular complications in 10.2% cases, Toxoplasmosis in 9.2% cases each.

Conclusion: Although CT and MRI both can be used for the work up of PLHIV MRI should be used as the first line investigation for radiological work up of a PLHIV patient presenting with neurological symptoms and CT should be used only when there is a contra indication to MRI.

Keywords: CT, MRI, HIV Encephalopathy

INTRODUCTION

AIDS was first reported in 1981 and in 1984 human immunodeficiency virus was identified as the causative agent. In India the first case was reported by Christian Medical College, Vellore in 1986. The HIV belongs to a subset of retroviruses called lentiviruses (or slow viruses), which means that there is an interval between the initial infection and the onset of symptoms. Upon entering the bloodstream, HIV infects the CD4+ T cells and begins to replicate rapidly. In the more advanced stages of HIV infection, acquired immunodeficiency syndrome (AIDS) develops. The total number of people living with HIV (PLHIV) in India is estimated at 21.17 lacs in 2015 as per the NACO report¹. HIV is a neurotropic virus, so in the early course of infection that enters the central nervous system (CNS). HIV crosses the intact blood-brain barrier, and the virus has been cultured from the brain, nerve, and cerebrospinal fluid of patients at all stages of disease. This virus infects the cells of the monocyte-macrophage lineage, and the indirect effects on macrophage activation are implicated as a cause of nervous system injury in HIV infection.

In 10%–20% of patients neurologic disease is the first manifestation of symptomatic HIV infection. Diseases occurring in brain in HIV patients are:

- 1. Primary effects of HIV: AIDS Dementia complex HIV encephalopathy HIV meningoencephalitis
- 2. Opportunistic infection:

Progressive multifocal leukoencephalopathy CMV encephalitis Herpes encephalitis Toxoplasmosis Cryptococcosis Bacterial and fungal abscesses Neurosyphilis Meningitis-Tubercular HIV meningoencephalitis Cryptococcal Ventriculitis

3. Neoplasm

Primary CNS lymphoma CNS glioma

4. Vasculitis

5. Immune reconstitution inflammatory syndrome.

Differential diagnosis of neurological disease processes in PLHIV patients is difficult as the clinical symptoms are often non specific. Hence CT and MRI are often used. The purpose of our study was to detect, characterize and compare various CT and MRI findings in central nervous system diseases in PLHIV and correlate it with CD4+ counts.

MATERIAL AND METHODS

This was a prospective observational study carried out on 98 HIV infected patients who attended the OPD and wards at Sassoon General Hospitals' from October 2013 to August 2015 and presented with symptoms of CNS involvement after approval from the ethical committee of Sassoon General Hospital. Patients were enrolled in the study only after their informed consent.

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Inclusion Criteria: Patients were included in the study after their HIV status was confirmed by ELISA or Western Blot test and CD4+ count was recorded.

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.

Risk involved: Adverse drug reaction due to contrast agent (gadolinium) and (iopamidol) used in MRI and CT respectively.

Study Protocol

Equipment used

For CT examination 64 rows 128 slice CT scanner of Siemens

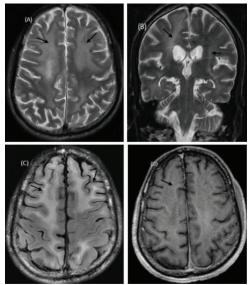
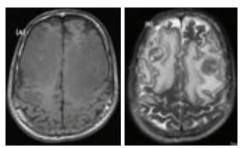


Figure-1: A, B) Axial and coronal T2W MR images showing bilateral asymmetrical sub cortical white matter hyper intensities (black arrow), C) Axial FLAIR image showing bilateral asymmetric sub cortical white matter hyper intensities with involvement of U fiber (black arrow), D) Post contrast axial image showing no enhancement - Progressive Multifocal Leucoencephalopathy (PML)



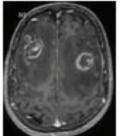


Figure-2: Showing multiple ring enhancing lesions with edema - Neurotuberculosis (Caseating Granuloma)

make Model name Somatom Definition AS + Configure was used.

For MRI 1.5 Tesla machine of GE make model name – Signa Hdxt MRI was used.

Patients were first subjected to contrast enhanced CT examination and the MRI was done the next day. The CT and MRI findings were evaluated by authors 1 and 2.

CT scan was done first with the patient in supine position and External auditory meatus was the first part to enter the gantry of the equipment. The end position of the scan was the top of the skull vault. Reconstructions were then carried out in axial, sagittal and coronal planes. All patients were given 30-50cc of 300mg% non ionic contrast medium (Iopamidol) by hand injection/pressure injector through the patent antecubital vein IV access. Scanning was done both immediately after injection of the contrast material, followed by a second scan using same parameters after a delay of 5 minutes. The acquired data was then reconstructed in medium smooth kernel using the cerebral algorithm.

MRI (figure 1,2)

Coil: Standard head coil/head angiography coil with centering around superior orbital ridge.

FOV: 22x26. Matrix: 512x512.

The slice thickness was 3 to 5mm

Gadolinium: DTPA is used as the contrast media.Dose-0.1 mmol/kg.

Brain accessed in axial, sagittal and coronal planes. Sequences:

DWI, ADC, T1- Axial, T2-Axial, T2- FLAIR, GRE.

POST CONTRAST T1- Axial /Sagittal / Coronal.

MR Spectroscopy in required cases.

MR Angiography and MR Venography were used when required.

(Drugs: Gadolinium contrast agent. Sedation was used in case of uncooperative and pediatric patients. A stand by Anaestheologist was present throughout the procedure.)

STATISTICAL ANALYSIS

The final diagnosis was made after considering clinical

| Diagnosis | CT (%) | MRI (%) | | | |
|--|--------|---------|--|--|--|
| Normal | 25.5 | 8.2 | | | |
| ADC | 13.3 | 15.4 | | | |
| CNS Tuberculosis | 21.4 | 31.6 | | | |
| Toxoplasmosis | 6.1 | 9.2 | | | |
| PML | 4.1 | 5.1 | | | |
| Cerebritis | 3.1 | 5.1 | | | |
| Cryptococcosis | 1 | 3.1 | | | |
| Herpes Zoster | 0 | 1 | | | |
| Isolated meningitis | 3.1 | 5.1 | | | |
| CVC | 6.1 | 10.2 | | | |
| Lymphoma | 1 | 2.0 | | | |
| Glioma | 1 | 1 | | | |
| Indeterminate | 13.3 | 1 | | | |
| Others | 1 | 2 | | | |
| Total | 100% | 100% | | | |
| Table-1: Comparison of detection of Diseases on CT and MRI | | | | | |

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| Diagnosis | Sensitivity | | Specificity | | PPV | | NPV | |
|---------------------|----------------|------------------|------------------|---------------|----------------|--------------|-----------------|-------|
| | СТ | MRI | СТ | MRI | СТ | MRI | СТ | MRI |
| ADC | 80 | 100 | 98.8 | 100 | 92.3 | 100 | 96.5 | 100 |
| CNS TB | 67.7 | 96.7 | 100 | 98.7 | 100 | 96.7 | 87 | 98.7 |
| Toxoplasmosis | 55.5 | 88.8 | 98.8 | 98.8 | 83.3 | 88.8 | 95.7 | 98.8 |
| PML | 80 | 100 | 100 | 100 | 100 | 100 | 98.4 | 100 |
| CVC | 60 | 100 | 100 | 100 | 100 | 100 | 95.6 | 100 |
| Cerebritis | 60 | 100 | 100 | 100 | 100 | 100 | 97.9 | 100 |
| Crypto | 33.3 | 100 | 100 | 100 | 100 | 100 | 97.9 | 100 |
| Isolated meningitis | 40 | 80 | 98.9 | 98.9 | 66.7 | 80 | 96.8 | 98.9 |
| Neoplasm | 50 | 75 | 100 | 94 | 100 | 100 | 98 | 99 |
| Table-2: Sho | ws the Sensiti | vity, Specificit | ty, Positive (Pl | PV) and Negat | ive predictive | values (NPV) | of various find | lings |

features, laboratory investigations, and radiological findings. Confirmatory histopathological findings were available in some cases. P values and Sensitivity, Specificity, Positive and Negative Predictive Values were calculated to compare the findings as seen on CT and MRI.

RESULTS

The mean age in our study was 35.3 with a range from 2 years to 71 years. 63.3% were males and 36.7% were females. There was no imaging abnormality in 25.5% of the cases on CT and 8.2% on MRI. The most common abnormality detected on CT as well as MRI was opportunistic infections (38.8% on CT and 60.1% on MRI). The next common abnormality detected was generalized cerebral atrophy (13.3% on CT and 15.4% on MRI). Detection of ADC did not differ significantly between CT and MRI; however there was a significant difference between CT and MRI noted in case of HIVE and PML (P value< 0.05).

CVC were seen in 6.1% cases on CT and 10.2% cases on MRI with cerebral infarction being the most common cerebrovascular complication. In our study 13.3% of lesions had indeterminate findings on CT like non enhancing or poorly enhancing lesions with/ without mass effect. But on MRI evaluation and correlation with other lab data they turned out to be opportunistic infections like Tuberculosis/ Toxoplasmosis. These patients had CD4+ counts less than 100. Cryptococcosis was seen in 1% cases on CT and 3% cases on MRI.

Neoplasms were detected in 2% cases on CT and 4% on MRI. Lymphoma was the most common neoplasm followed by glioma. Cerebritis was seen in 5.1% cases and there was no significant difference in CT and MRI in detection. There was a significant correlation between CD4+ counts and CT and MRI findings (p value 0.001) (table-1).

Amongst the opportunistic infections Tuberculosis was the most common etiology.

In Toxoplasmosis CT was better than MRI in picking up non enhancing hypodensities and hemorrhage (P value of 0.002 and 0.028 respectively) (table-2).

DISCUSSION

HIV virus due to its capability of synthesizing reverse transcriptase enzyme targets lymphocytes (CD4+) affecting the immune system adversely. Hence CNS is infected early in the course of the disease. The neurologic problems in such

patients may be either primary to the pathogenic processes of HIV infection or secondary to opportunistic infections or neoplasm³.

Diseases occurring in brain in HIV patients are classified as follows $\!\!\!^4$

- 1. Primary effects of HIV: This includes ADC, HIVE, etc.
- 2. Opportunistic infections
- 3. Neoplasms
- 4. Vasculitis and complications like infarcts.
- 5. Immune reconstitution inflammatory syndrome (IRIS)

Tuberculosis was the commonest CNS infection among AIDS patients similar to the findings of M. L. Patel^{1,5}. In our study the findings of Toxoplasmosis were similar to other workers⁶. The only differentiating feature was that in our study CT was more sensitive than detecting non enhancing hypodensities and hemorrhage. We came across 3.1% cases of Crypto coccosis which was better detected on MRI than CT similar to the study of Vincent P Mathew et al⁷. As in the study of Mercader-Sobreques JM et al MRI was better in picking up HIVE lesions⁸.

Opportunistic infections, primary effect of HIV, neoplasms had mean CD4+ counts below 200 cells/ μ L. Cerebro vascular complications had mean CD4 count above 200 cells/ μ L and those with normal MRI had mean CD4 count above 500 cells/ μ L.

Limitations of our study: Small sample size and lack of availability of final histopathological diagnoses are the limitations of our study.

CONCLUSION

As both the modalities CT and MRI are available in most hospitals one will always be in dilemma – Which modality to use? From our study we have concluded that MRI is superior to CT in evaluating CNS problems of PLHIV patients. At the same time one should be aware that in the early stages of the disease MRI may prove indefinite in a few cases. Secondly on routine sequences calcified granulomas may be confused with chronic blood products. CT scores over MR in these areas and has the added advantage of speed. Hence MRI should be used as the first investigation for radiological work up of a PLHIV patient presenting with CNS symptoms and CT should be used only when there is a contra indication or unavailability of MRI. Due to constraints of space only MRI images of lesions have been represented. AIDS: Acquired Immune Deficiency Syndrome, CT: Computed Tomography, MRI: Magnetic Resonance Imaging, PML: Progressive Multifocal Leukoencephalopathy, HIVE: HIV Encephalopathy, ADC: AIDS Dementia Complex, CNS: Central Nervous System, CVC: Cerebro vascular complications

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