Section: Radiodiagnosis

Original Research Article

MRI SPECTRUM OF NEURO-IMAGING FINDINGS IN HIV POSITIVE CHILDREN & ITS CORRELATION WITH CD4 COUNTS

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ABSTRACT

Background: Neurological complications are common in paediatric HIV patients, with neuro-imaging playing a crucial role in early detection and management. This study aims to evaluate the spectrum of MRI neuro-imaging findings in HIV-positive children and correlate these findings with their CD4 counts.

Materials and Methods: A Cross sectional descriptive study was conducted in the Department of Radiodiagnosis, of an urban tertiary care teaching hospital. The study included thirty consecutively enrolled HIV infected children up to 15 years of age having neurological manifestations, attending paediatric OPD as well as those admitted to the paediatric ward at this tertiary care hospital from Dec 2021 till Nov 2023.

Results: None of the children were less than 01 year of age in our study. In 21 (70 %) cases, there were T2 and FLAIR hyperintense white matter lesions noted suggestive of HIV encephalopathy. Out of these 21 cases, 11 (52.3 %) patients had white matter lesions in periventricular location, 6 (28.5 %) in deep white matter and 4 (19 %) in both periventricular and deep white matter. 15 (71.4%) out of these patients diagnosed as HIV encephalopathy had associated cerebral atrophy. Out of total 30 cases studied, only two patients (6.6 %) had focal intra-cranial lesions and only one (3.3 %) patient had chronic ischemic infarct in left MCA territory with ectasia of M1 segment of right middle cerebral artery. Both the patients with focal intra-cranial lesions were diagnosed as tuberculomas based on imaging findings, CSF studies and serological markers. Patients with HIV encephalopathy presented with varied neurological manifestations & were more commonly associated with severe degree of immune suppression as indicated by low CD4 counts. This association was found to be statistically significant (as indicated by p value of <0.05 in Fisher exact test).

Conclusion: This study highlights the range of neurological abnormalities in HIV-positive children and emphasizes the association between lower CD4 counts and more pronounced MRI findings. Early detection of these abnormalities in children with declining CD4 levels could aid in timely clinical interventions and improve the management of neurological complications in paediatric HIV.

Keywords: HIV-positive children, Neuro-imaging, Magnetic Resonance Imaging (MRI), CD4 counts.

INTRODUCTION

Human Immunodeficiency Virus (HIV) remains a significant global health challenge, particularly in paediatric populations, where it can have severe and lasting effects. Children infected with HIV often present with a wide array of systemic complications, with neurological manifestations being among the most debilitating.[1] These neurological issues can arise due to direct viral invasion of the central nervous system (CNS), opportunistic infections, or as a consequence of immune suppression due to the progressive decline in CD4 counts.[2]

Magnetic Resonance Imaging (MRI) is a crucial non-invasive investigation modality for detecting CNS abnormalities in HIV-positive children, offering insights into the spectrum of neurological changes. As HIV-related immunosuppression advances, children become more prone to neurodevelopmental delays, cognitive dysfunction and progressive neurological impairment, all of which can be visualized on MRI. Furthermore, CD4 counts serve as a critical marker of immune function in HIV patients, with lower counts correlating with greater vulnerability to opportunistic infections as well as neurological damage.[3,4]

Paediatric HIV is a unique subset of the global HIV epidemic, presenting with distinct clinical challenges due to the developing immune systems of children.[5] Without adequate treatment, HIV can lead to significant immunodeficiency, as reflected by a progressive decline in CD4 T-lymphocytes. CD4 counts are a well-established surrogate marker for immune function and disease progression in HIV-infected individuals. In children, a reduction in CD4 counts has been associated with an increased risk of systemic infections and CNS involvement.[6]

Neurological involvement in HIV-positive children is multifactorial, resulting from direct HIV encephalopathy, or from opportunistic infections like toxoplasmosis, in addition to other CNS pathologies, like progressive multifocal leukoencephalopathy. These conditions can lead to a wide range of structural changes in the brain, including white matter abnormalities, cerebral atrophy, and calcifications. MRI, being the most sensitive imaging modality for detecting CNS abnormalities, provides critical information that can help in diagnosis and management of these conditions.[7]

This study aims to explore the spectrum of neuro-imaging findings in HIV-positive children, correlating MRI abnormalities with CD4 counts to enhance our understanding of the relationship between immune suppression and CNS involvement. Understanding this relationship can assist in the early detection of neurological complications, potentially guiding therapeutic interventions and improving the quality of life for these children.

MATERIALS AND METHODS

A Cross sectional descriptive study was conducted in the Department of Radiodiagnosis, of an urban tertiary care teaching hospital. The study included thirty consecutively enrolled HIV infected children up to 15 years of age having neurological manifestations, attending paediatric OPD and those admitted to the paediatric ward at this tertiary care institute from Dec 2021 till Nov 2023.

Inclusion Criteria

- Paediatric HIV positive patients with age < 15 Years, With Neurological Manifestations

Exclusion Criteria

- Patients who have contraindication to MR imaging such as claustrophobia, cochlear implants and pacemaker.
- Asymptomatic patients were not included.

Sample size

Total of 30 HIV infected children were included in the study. The study did not have any therapeutic implications; however, clearance from the ethical committee was obtained. Written informed consent was obtained.

Methodology

1. A detailed history was obtained from the patients, parents or care giver which included the mode of infection, duration of infection, details of HAART, opportunistic infections complicating the disease and past history of any major illness. Clinical details regarding type, duration and severity of neurological symptoms were recorded
2. Neurological examination was done according to the presenting complaint.
3. All subjects underwent following examinations
   a) CD4 counts
   b) MR imaging of the brain
4. Depending on the clinical presentations and imaging findings, additional tests were done which included CSF studies (biochemical, India Ink preparation, culture), Serological tests for antibody titres including IgG anti-toxoplasma antibodies, Mantoux test and chest radiograph.

Imaging evaluation

All cases underwent MRI brain with 1.5 Tesla MRI scanner (Philips Achieva 1.5 Tesla). Various sequences were used which included axial T1, axial T2, FLAIR axial, DWI with corresponding ADC maps and GRE axial sequence. At the end of aforementioned sequences, the patients were administered 0.1 mmol/kg of IV Gadopentetate dimeglumine following which an axial T1WI and 3D Gradient sequences were performed.

After image acquisition, following aspects were studied

a) Presence and distribution of T2 and FLAIR hyperintense and T1 hypointense lesions in white matter in periventricular location deep white matter
b) Involvement of the juxta-cortical U-fibres

c) Involvement of the corpus callosum.
d) Presence of sulcal widening and ventricular dilatation.
e) Dilatation / ectasia / aneurysm of the intracranial vessels.
f) Presence of infarct(s).
g) Presence of any focal lesion.
h) Any foci of restricted diffusion or susceptibility artifacts
i) Post contrast enhancement, of any focal lesion, enhancement of the meninges or the cisterns.

Statistical Analysis

Data was presented as mean ± standard deviation (SD) for descriptive data. All calculations were done using the SPSS software version 24 for Windows. P value < 0.05 was considered significant.

RESULTS

The patients were divided based on the CDC classification (Centres for disease classification, Atlanta), into less than 1 year, 1-5 years and > 6 years age groups as the normal range of CD4 counts and degree of immune suppression differ based on the child's age. There was no child less than 01 year of age in our study. The mean CD4 count was 447 in patients 1-5 years old and 429 in the patients > 6 years of age.

27 out of 30 paediatric patients in our study had acquired the infection perinatally (vertical transmission). None of the patients had transmission via transfusion or sexual route of infection. In three patients, the route of transmission was not known.

There were T2 and FLAIR hyperintense white matter lesions noted in 21 (70 %) of cases. In 21 (70 %) cases, there were T2 and FLAIR hyperintense white matter lesions noted suggestive of HIV encephalopathy. Out of these 21 cases, 11 (52.3 %) patients had white matter lesions in periventricular location, 6 (28.5 %) in deep white matter and 4 (19 %) in both periventricular and deep white matter. 15 (71.4%) out of these patients diagnosed as HIV encephalopathy had associated cerebral atrophy. Out of total 30 cases studied, only two patients (6.6 %) had focal intra-cranial lesions and only one (3.3 %) patient had chronic ischemic infarct in left MCA territory with ectasia of M1 segment of right middle cerebral artery. Both the patients with focal intra-cranial lesions were diagnosed as tuberculomas based on imaging findings, CSF studies and serological markers. One patient also had a single focus of T2 and FLAIR hyperintensity in the frontal region in the juxta-cortical white matter along with bilaterally symmetrical periventricular and deep white matter lesions. No involvement of the corpus callosum was seen in the study population. [Table 1]

White matter lesions were commonly associated with behavioural changes, developmental delay, hyperreflexia, hypertonia and language impairment. The ventricular dilatation and sulcal widening were commonly associated with behavioural abnormalities, language impairment and hyperreflexia. However no statistically significant association was found, by using the Fisher's exact test. [Table 2]

The most common diagnosis in our study was HIV encephalopathy which was seen in 21 patients (70 %) (Fig 1). 15 out of these 21 patients also had associated cerebral atrophy (Fig 2). These patients presented with varied neurological manifestations and were more commonly associated with severe degree of immune suppression as indicated by low CD4 counts with statistically significant association (as indicated by p value of <0.05 in Fisher exact test). [Table 3]

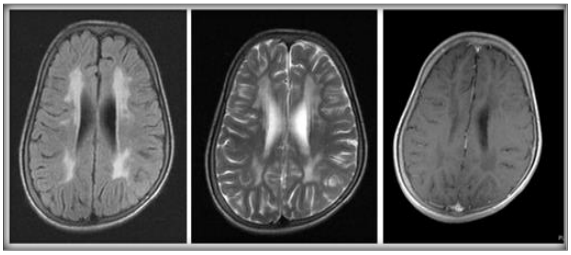

Figure 1: HIV encephalopathy: 11 yrs old boy (CD4 count = 193/µL) with behavioural abnormalities showed multiple, discrete, T2 and FLAIR hyperintense foci in bilateral periventricular and deep white matter in the frontal and parietal lobes without any abnormal enhancement on post contrast images.

A rarer diagnosis of HIV arteriopathy was encountered in only one patient who presented with chronic infarct in left MCA territory. On imaging there was ectasia of right middle cerebral artery (M1 segment) (Fig 3). This patient's CD4 count was 165/µL. Also noted were associated white matter changes as seen in other patients with HIV encephalopathy.

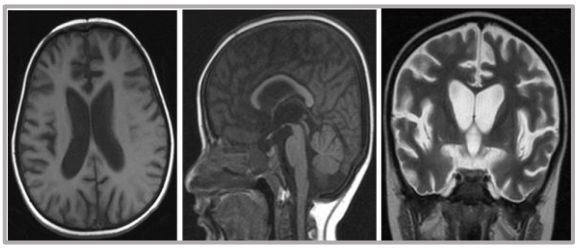

Figure 2: Diffuse cerebral atrophy: 9 years old boy (CD4 count = 459/µL) with history of language difficulties and poor academic performance. T1 axial and sagittal and T2 coronal images of brain showed symmetrical widening of sulcal spaces and cisterns bilaterally with ventricular dilatation. No focal lesion was seen in the brain.

Focal ring enhancing lesions were seen in two patients. Both of these patients had presented with seizures. CD4 counts in these patients at the time of imaging were 472 / µL and 612 / µL respectively. Based on the imaging findings, CSF studies and serological tests these patients were diagnosed as tuberculomas. (Fig 4).

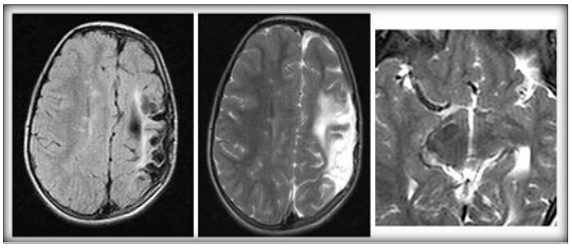

Figure 3: HIV arteriopathy: 8 years old male child who suffered paralysis of right side of body 05 years back, with partial recovery over a period of several months. FLAIR and T2 axial sections of brain showed chronic infarct in left middle cerebral artery territory with fusiform ectasia of the M1 segment of right MCA (zoomed image). In addition, patient also had multiple T2 & FLAIR hyperintense foci in the deep white matter on right side.

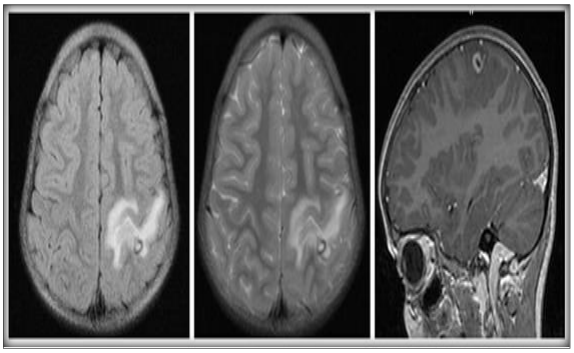

Figure 4: Tuberculoma: 8 years old girl (CD4 count = 472/µL) with history of two episodes of GTCS, revealed ring enhancing lesion in the left parietal lobe with central hyperintense signal on T2 & FLAIR along with T2 hypointense rim & Perilesional edema.

Table 1: Age wise distribution of patients and their CD4 counts

	Age (< 6 years)	Age (≥ 6 years)	CD4 Count (< 6 years)	CD4 Count (≥ 6 years)
Number	5	25	5	25
Mean	4.08	9.22	447.40	429.00
Median	3.67	8.50	292.00	394.00
Std. Deviation	1.06	2.21	263.04	253.27
Range	2.58	8.67	594.00	698.00
Minimum	3.17	6.25	212.00	107.00
Maximum	5.75	14.92	806.00	805.00

Table 2: Correlation of MR findings with clinical features

	Ventricular dilatation & sulcal widening			White Matter Lesions		
	N=30	Present (n=15)	p-value	N=30	Present (n=21)	p-value
Ataxia	1	0	0.467	1	1	1.00
Behavioural changes	7	4	1.00	7	4	1.00
Developmental delay	2	2	0.485	2	2	1.06
Headache	2	0	0.503	2	0	0.064
Hyperreflexia	4	2	1.00	4	4	0.272
Hypertonia	4	2	1.00	4	4	0.55
Language Impairment	5	3	1.00	5	4	1.06
Loss of Milestone	2	2	1.00	1	1	1.00
Seizure	3	0	0.089	3	1	0.146

Table 3: Correlation of the CD4 count with the diagnosis

Diagnosis	CD4 count category			p-value
	For age > 6 yrs			
	<200	200-499	>500	
	For age 1-5 yrs			
	<500	500-999	>1000	
HIV Arteriopathy*	1*	-	-	
HIV Encephalopathy	11	7	2	0.047
Tuberculoma	-	1	1	
Normal	-	-	7	0.025
Total	12	8	10	0.673

*Patient also had additional features of HIV encephalopathy, however for statistical purpose, patient was counted under HIV arteriopathy.

DISCUSSION

Our study describes the neuro-imaging findings in symptomatic HIV positive children (less than 15 years of age) enrolled over a period of 02 years, from 2021 to 2023. The majority of children with neurological abnormalities presented with HIV encephalopathy in 21 patients (70%) in the form of white matter lesions in all of them with or without ventricular enlargement and/or sulcal widening. Neurological abnormalities, predominantly language impairment, behavioural changes, developmental delay and motor symptoms were detected in the affected children.

On imaging, scattered or confluent white matter lesions are typically seen within the periventricular

white matter and centrum semiovale. They are usually underestimated on CT and are best demonstrated on MRI, as low signal on T1 weighted sequences and high signal on T2 weighted sequences.[8] The changes are secondary to direct involvement of the brain by HIV, resulting in areas of demyelination and gliosis.[9,10] HIV encephalopathy does not result in mass effect and no post contrast enhancement is found. If either of these findings is present, another diagnosis must be considered.[10]

Slightly higher incidence of HIV encephalopathy in our study can be explained by the fact that our study included only symptomatic patients presenting with neurological manifestations. These patients had bilateral and symmetrical T2 and FLAIR hyperintense lesions in the periventricular and deep white matter (predominantly involving the fronto-parietal regions). No restriction of diffusion or foci of susceptibility artifacts were noted in these lesions. No post contrast enhancement was noted in these white matter lesions. The corpus callosum was not involved.

One patient had a single focus of T2 and FLAIR hyperintensity in the frontal region in the juxta-cortical white matter, involving the U fibres with associated bilaterally symmetrical periventricular and deep white matter lesions, without any mass effect or post contrast enhancement, suggestive of HIV encephalopathy. There was no feature to suggest progressive multifocal leukoencephalopathy. This finding of involvement of focal involvement of juxta-cortical white matter could not be explained.

Arnhem et al,[11] reported ventricular enlargement & sulcal widening (29%) along with white matter lesions (38%) in HIV-1 infected children presenting with abnormal neurologic examinations including language impairment (22%), abnormal muscle tone (hyper/hypotonia) (14%) and delay in reaching developmental milestones (12%). White matter lesions in this study were positively correlated with HIV-1 viral load levels.

Kaufmann et al,[12] reported CT and MRI findings in 29 HIV positive children with neurological abnormalities. They reported cerebral atrophy (in 25 children), basal ganglia calcification (10 children), periventricular frontal white matter calcification (four children), cerebellar calcification (one child), white matter low attenuation areas (two children), intracranial hemorrhage (three children) and cerebral infarction (one child). MR abnormalities noted in this study were cerebral atrophy (four children), areas of high signal intensity in white matter (four children), and loss of normal posterior pituitary high signal intensity (one child). Focal intracranial infections were unusual and neoplastic lesions were not found in the study.

However, some studies have reported considerable incidence of focal lesions and opportunistic infections in HIV positive children. Kumar A and Gupta S in their study on focal brain lesions in HIV infected children in India,[13] reported 9 (9.4%) cases from among the 96 cases who had a CT scan done for suspected focal brain pathology based on their clinical presentation. Four patients had solitary lesions (44%) and 5 (56 %) patients had multiple lesions.

CONCLUSION

HIV encephalopathy in the form of cerebral atrophy with periventricular and deep white matter lesions was the most common abnormality seen neuro-radiologically in our study of HIV-infected children which showed significant association with low CD4 counts. Apart from 02 patients with tuberculoma, other opportunistic infections like cerebral toxoplasmosis, cryptococcal infection and progressive multifocal leukoencephalopathy (caused by JC virus) were not encountered in our study.

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