Original Article

Routine addition of diffusion-weighted imaging to pediatric brain imaging with acute presentation: An initial experience

Shagufta Wahab, Rizwan Ahmad Khan[1], Shaista Siddiqui

Departments of Radiodiagnosis and [1]Pediatric Surgery, J. N. Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

Abstract

Context: A number of disorders affecting the pediatric brain pose a diagnostic challenge. Magnetic resonance imaging (MRI) is widely accepted as a sensitive technique for the diagnosis of ischemia, encephalitis, and leukodystrophies. Conventional MR sequences used in routine practice include T1-weighted (T1-W), T2-weighted, and fluid-attenuation inversion recovery (FLAIR) sequences. However usually, the presentation in small children is confusing and presents a diagnostic challenge even after the use of these various MR sequences requiring repeated MRI examinations. Detecting pathological changes occurring at microenvironment level is vital for early diagnosis, effective treatment, and obviating the need of repeated MRI.

Aims: The purpose of our study was to assess the additional role of diffusion-weighted imaging (DWI) in better detection of these various pathologies of brain.

Settings and Design: This was a prospective study.

Subjects and Methods: Thirty children of ages ranging from neonate to 12 years of age with various complaints of central nervous system involvement were evaluated with MRI brain within 72 h of initial clinical presentation. T1 and T2 spin-echo sequences FLAIR and postcontrast T1-W imaging were done. DWI was performed with echoplanar imaging using depth-resolved surface coil spectroscopy sequence. The lesions were evaluated on DWI and conventional sequences. The final diagnosis was established on the basis of clinical evaluation, electroencephalographic findings, imaging, cerebrospinal fluid analysis, serologic tests, and fatty acid evaluation in plasma assay.

Statistical Analysis Used: This was a descriptive study.

Results: The patients were divided into three groups. Group A included patients in whom DWI detected more lesions or showed a greater extent of lesions on apparent diffusion coefficient (ADC) map than conventional MRI. This group had 11 cases including 7 cases of ischemic encephalopathy, one case of adrenoleukodystrophy (ADL) showing increased extent of lesion with restricted diffusion at the advancing edge and 3 cases of viral encephalitis. In Group B, 12 cases had similar results in both DWI and conventional MRI imaging. Of these, 7 cases with no specific diagnosis and subsequent spontaneous recovery showed no lesion on both conventional and DWI; 5 cases showed equal extent and number of lesions on DWI; 1 case was diagnosed as ADL, 2 as viral encephalitis, and 2 as ischemic encephalopathy on final workup. In Group C, T2 and FLAIR showed more lesions than DWI and had 7 cases. 5 had normal ADC maps but 1–2 small hyperintense lesions on T2 and FLAIR imaging, while the remaining two diagnosed with ischemic encephalopathy had hyperintense areas on T2 and FLAIR sequences with associated ventricular enlargement

Address for correspondence: Dr. Rizwan Ahmad Khan, Kashana-E-Wahab, Street No 4, Iqra Colony, Aligarh, Uttar Pradesh, India.
E-mail: drrizwanahmadkhan@yahoo.co.in

Access this article online	
Quick Response Code:	Website: www.wajradiology.org
	DOI: 10.4103/wajr.wajr_27_17

How to cite this article: Wahab S, Khan RA, Siddiqui S. Routine addition of diffusion-weighted imaging to pediatric brain imaging with acute presentation: An initial experience. West Afr J Radiol 2018;25:15-20.

and cortical atrophy while DWI revealed them to be T2 shine through areas with increased ADC value focally. The 5 cases with hyperintensity on T2 and FLAIR, but normal ADC maps were labeled as nonspecific white matter hyperintensities. These children showed neither any progress of lesion nor any further clinical symptoms during the duration of study.

Conclusions: We concluded that DWI was more sensitive than the other MR sequences in detecting early pathological changes even in cases of viral encephalitis and leukodystrophy apart from ischemia. It was also helpful in delineating the area more accurately at the microscopic level. We were also able to rule out actual pathology from nonspecific hyperintensities on T2 and FLAIR in some cases on DWI.

Keywords: Diffusion-weighted imaging, pediatric, white matter diseases

INTRODUCTION

A wide variety of disorders may affect the neonatal and pediatric brain-inherited, congenital and acquired, and usually, the presentation in small children is similar and confusing, posing a diagnostic challenge. Establishing a specific diagnosis is often delayed at great financial costs. Magnetic resonance imaging (MRI) is widely accepted as a sensitive technique for the diagnosis of ischemia, encephalitis, and leukodystrophies and is very useful for detecting changes not seen by any other modality even a computed tomography (CT) scan.[1,2] Conventional MR sequences used in routine practice include T1-weighted (T1-W), T2-weighted (T2-W), and fluid-attenuation inversion recovery (FLAIR) sequences.[3] Diffusion-weighted imaging (DWI) has become an important tool in the evaluation of a variety of disorders of brain in children. It is based on variation in the diffusion of water molecules in the presence of an applied magnetic gradient to produce contrast.

The purpose of our study was to assess the role of DWI in the visualization of various pathologies of brain in children with acute presentation and compared with conventional MRI in a group of 30 children ranging from neonate to 12 years of age undergoing MR examination for various complaints.

SUBJECTS AND METHODS

Thirty children of age ranging from neonate to 12 years of age from March 2014 to May 2016 were evaluated for imaging findings on conventional MRI and diffusion-weighted sequences. The inclusion criteria were central nervous system symptoms such as fever, unconsciousness, motor or sensory deficit, bowel bladder involvement, and visual or speech impairment, with MRI performed within 72 h of initial clinical presentation. All patients with allergy to MRI contrast, previously established diagnosis, brain tumor, or bacterial meningitis on initial workup were excluded from the study. The final diagnosis was established on the basis of clinical evaluation, electroencephalographic findings, imaging, cerebrospinal fluid analysis, serologic tests, and fatty acid evaluation in plasma assay. Viral encephalitis was diagnosed in 5 cases, ischemic insult to brain in 11 cases, and adrenoleukodystrophy (ADL) in 2 cases. 12 children were found to be normal by all investigations and had a spontaneous recovery within a day or two of MR examination. MR examination was performed on a 1.5-T superconducting system (Magnetom Avanto Siemens), using a head coil. MR examination included T1-W spin-echo images, T2-W spin-echo images, and FLAIR images routinely obtained in the axial plane. Additional T1-W imaging after intravenous administration of Gadolinium contrast agent was also done. DWI was performed with echoplanar imaging using depth-resolved surface coil spectroscopy sequence. The b values were 0, 500 and 1,000 s/mm^2, with diffusion gradients applied in the three orthogonal directions. Image evaluation was done by two radiologists with >3 years' experience in MRI. The conspicuity of the lesions on DWI was compared with images obtained on conventional sequences. Data obtained were tabulated and statistically analyzed.

RESULTS

Of 30 children, 18 were male and 12 female (M:F = 1.5:1). Age range was from neonate to 12 years of age with mean age 4.6 years ± 3.7. Ishemic encephalopathy was more common in neonates and early infancy while other two disease entities were more common in children beyond 1 year of age. After image interpretation and final diagnosis, the patients were divided into three groups. Group A included patients in whom DWI detected more lesions or showed a greater extent of lesions on apparent diffusion coefficient (ADC) map than conventional MRI, Group B where both diffusion-weighted and conventional MRI imaging yielded similar results and Group C where DWI did not show any evidence of restricted diffusion while conventional imaging showed some abnormalities [Table 1].

Group A showed 11 cases. These included 7 cases of ischemic encephalopathy, out of which 4 were completely normal on conventional MRI (T1, T2 and FLAIR) imaging but showed areas of restricted diffusion on ADC map [Figure 1]

Table 1: Summary of MRI findinings

	Group A	Group B	Group C
Ischemic Encephalopathy (*n*)	7	2	2
Adrenoleukodystrophy (*n*)	1	1	-
Viral encephalitis (*n*)	3	2	-
No specific diagnosis with spontaneous recovery (*n*)		7	5 (DWI Normal with FLAIR abnormal small foci)
Total (n)	11	12	7

and 3 cases of hypoxic ischemic encephalopathy showed increased number of lesions on DWI than were detected by routine MRI protocol. 1 case of ADL showed increased extent of lesion with restricted diffusion at the advancing edge [Figure 2] and 3 cases of viral encephalitis showed increased number and extent of lesion [Figure 3].

Group B included 12 cases in which 7 cases showed no lesion on both conventional and DWI. These cases also recovered spontaneously within 2–3 days without any specific diagnosis. 5 other cases also showed equal extent and number of lesions, of these 5, 1 case was diagnosed as ADL, 2 as viral encephalitis and 2 as ischemic

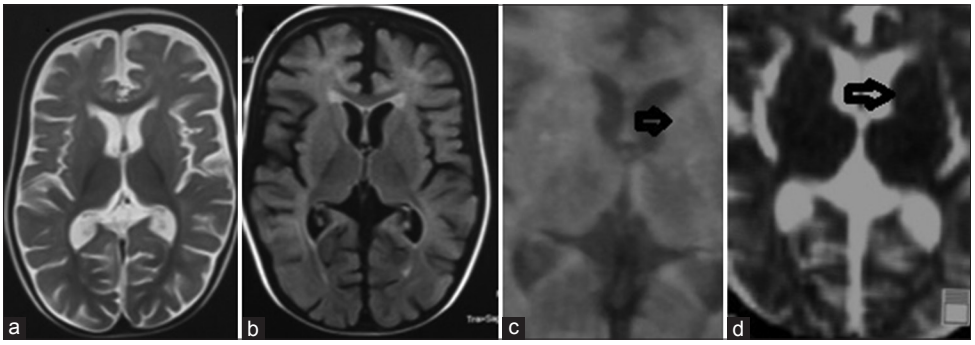

Figure 1: (a and b) T2 and fluid-attenuated inversion recovery image showing completely normal findings while (c and d) DWI and ADC map revealed small areas of restricted diffusion in left basal ganglia(black arrows)

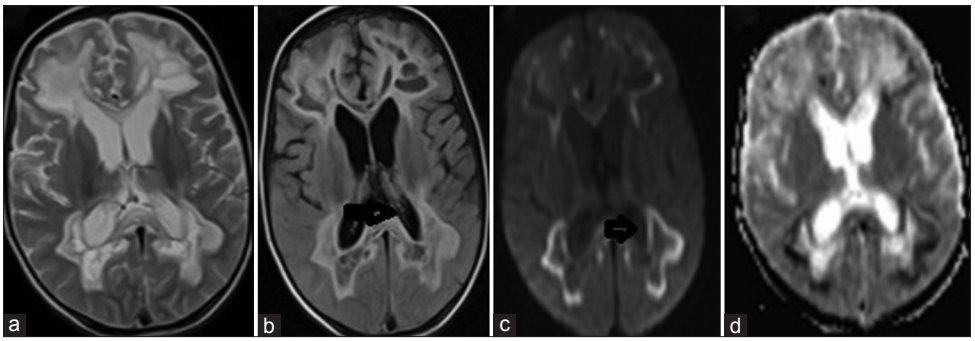

Figure 2: (c and d) Diffusion-weighted imaging and apparent diffusion coefficient map showing advancing edge with clear restriction of diffusion beyond the extent of lesion seen on T2 and fluid-attenuation inversion recovery (a and b) in a 1.5-year-child with adrenoleukodystrophy (black arrows)

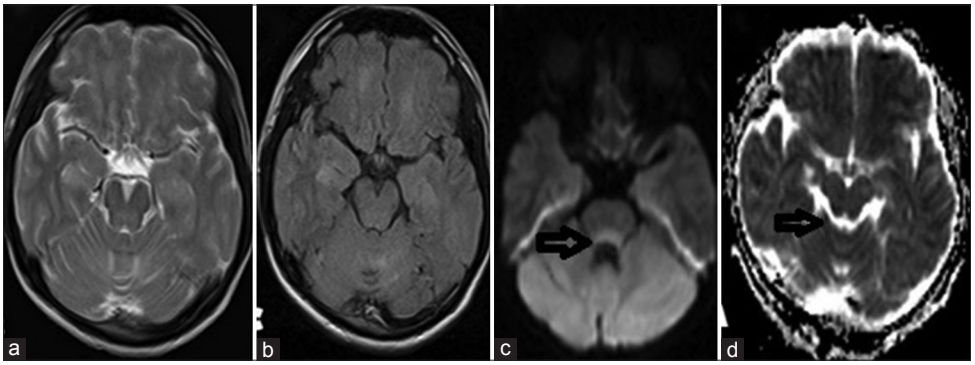

Figure 3: (c and d) Diffusion-weighted imaging and apparent diffusion coefficient map showing small focal areas of restricted diffusion in midbrain (black arrow) while no significant abnormality is detected on T2 or fluid-attenuation inversion recovery (a and b) in a case of viral encephalitis

encephalopathy on further workup. Group C had 7 cases in which 5 had normal ADC maps, but 1–2 small lesions on FLAIR imaging [Figure 4]. These children also did not have any specific diagnosis. The remaining two cases had diagnosis of ischemic encephalopathy with diffusion imaging showing T2 shine through effect with increased ADC focally [Figure 5].

DISCUSSION

MRI is an investigation of choice in the diagnostic workup of wide variety of acute neurological conditions in children such as infection, ischemia, or leukodystrophies.[2-4] Since diagnostic workup of these patients is often very costly and complicated, early diagnosis makes a large difference not only in the management and prognosis of these patients but it also reduces the financial and emotional burden of the parents and the caregivers. CT may show nondescript hypodensities, but it is much less sensitive than MRI. Routine MR sequences include T1-W, T2-W, and FLAIR imaging to identify abnormal areas. MRI shows encephalitic, ischemic, and ADL lesions as areas with prolonged T1 and T2 relaxation times, appearing hypointense on T1-W and hyperintense on T2-W images. FLAIR imaging is more sensitive than T2-W sequences in detecting these lesions making them more obvious.[3,4] The differential involvement of brain matter makes the diagnosis possible. In neonatal hypoxic ischemic encephalopathy, T1 and T2 images within 24 h may be normal with findings only on DWI. Even DWI performed within 24 h may reveal lesser extent of lesion than actual insult and hence should be repeated at 2–4 days.[5,6] By day 2 in neonates, hyperintensity on both T1-W and T2-W images in thalami, caudate nucleus, posterior putamen, and corticospinal tracts may develop due to paramagnetic effects of free radicals, hemorrhage, or calcification.[5,6] At the end of first week, DWI "pseudonormalize" when findings are most obvious on conventional T1-W and T2-W and FLAIR images. In the chronic stage of injury, if children present with seizures as in our study where one child presented at 6 months and another at 1.5 years of age, atrophy of the injured structures will be seen along with T2 hyperintensity, particularly in the peritrigonal, watershed zones thalami, and basal ganglia. Associated enlargement of ventricles and cortical atrophy are also seen. These 2 cases did not show any restricted diffusion on ADC. MRI in herpes encephalitis shows hypointensity on T1, hyperintensity on T2 in the medial temporal and the inferior frontal lobes.[5] Bilateral T2 hyperintense and T1 hypointense thalamic lesions, especially hemorrhagic, are characteristic of Japanese encephalitis. However, occasionally temporal lobe involvement could be seen in patients of Japanese encephalitis.[7]

MRI findings in ADL consist of bilateral symmetric involvement of the parieto-occipital white matter,

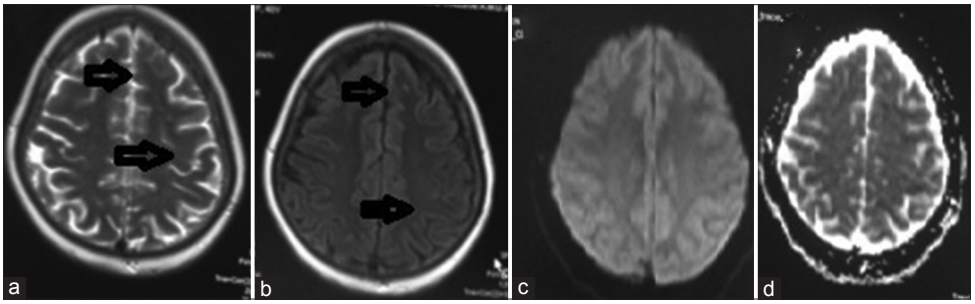

Figure 4: (a and b) T2 and fluid-attenuation inversion recovery images showing small foci of non specific white matter hyperintensities in left cerebral hemisphere. The area appears normal on diffusion-weighted imaging and apparent diffusion coefficient map (c and d)

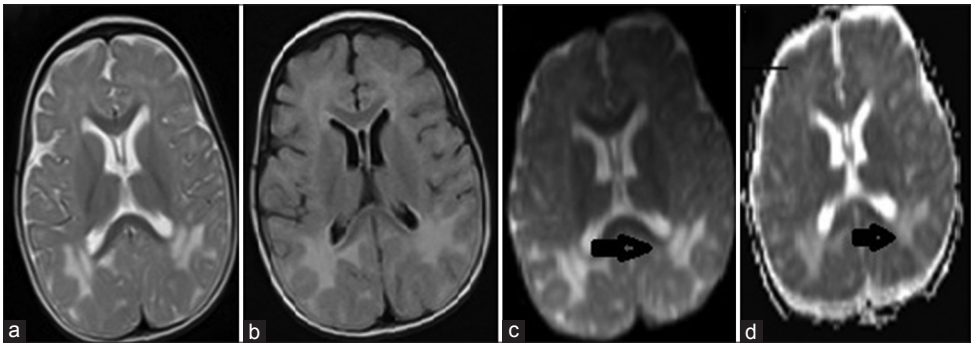

Figure 5: (c and d) Diffusion-weighted imaging and apparent diffusion coefficient map showing lesser extent of involvement and T2 shine through areas in a case of ischemic encephalopathy in a Group C patient. These areas appear bright on T2 & FLAIR images (a and b)

corpus callosum, visual and acoustic corticospinal tract, and cerebellar peduncles with classical sparing of cortex and subcortical U fibers. In one of our cases, gadolinium-enhanced T1-W MRI, the white matter lesions, in the parieto-occipital periventricular area, showed peripheral enhancement corresponding to region of active inflammatory demyelination.[6,8] Inspite of the great sensitivity of MRI, changes at microscopic level as in early stages of these diseases may not be detected by conventional T1, T2, and FLAIR imaging. The appearance on DWI may be related to pathologic changes that occur at cellular and cellular microenvironment level. The purpose of our study was to evaluate the utility of adding DWI in routine protocol to detect these early pathological changes in not only cerebral ischemia but also other conditions as encephalitis and white matter disorders.

Cytotoxic edema that leads to restricted diffusion and low ADC appears as hyperintense lesions on DWI in early ischemia. This probable mechanism also occurs in encephalitic lesions in cortical gray matter neurons and deep white matter in ADL.[9,10] There were 4 cases of ischemia that were found to be normal on conventional sequences. However, 3 cases of ischemic encephalopathy, 1 case of ADL and 3 cases of viral encephalitis showed increased extent of lesion on diffusion-weighted protocol. The earliest MRI abnormalities in these cases of increased signal on DWI and restricted diffusion on ADC map correspond to the pathophysiological change of cytotoxic edema. All these patients were evaluated within 72 h of symptom onset and represented acute changes. The one case of ADL was 1½ years of age with first episode of seizure and was brought within 24 h. On T1, T2, and FLAIR imaging, involvement of parieto-occipital and basifrontal white matter was noted with subtle peripheral edge enhancement on post contrast T1-W imaging. On DW imaging, restricted diffusion was seen at the advancing edge in parieto-occipital and basifrontal regions, i.e., increased extent beyond the borders seen on T2 and FLAIR. Earliest microscopic pathological changes were noted only in DW imaging. The affected area was only subtly detected on post contrast imaging and was not seen on T2 sequence. Viral encephalitis cases in Group 1 also showed small areas of restricted diffusion on ADC in temporal lobes, midbrain, and thalami. In subacute stages, the components of vasculitis and perivascular cuffing diminish, diffusion restriction decreases with interstitial collection of fluid and ADC starts to increase. At this stage, T2-W imaging and FLAIR imaging become more sensitive.[8,11] As in cerebral ischemia, in addition to providing early information that may not be available on conventional MRI sequences, DWI can allow discrimination of cytotoxic edema from vasogenic edema in encephalitis and also ADL lesions and coupled with other sequences can help in the differentiation from the other diseases and disorders.[8,11] Signal intensity on DWI is affected by water diffusibility and the intrinsic T2 properties of the brain area evaluated, so the hyperintense appearance of lesions on DWI may result from a combination of these factors. Of 30 patients evaluated, 12 were in Group B where T2, FLAIR, and DWI detected equal number of lesions. Of these, 7 cases with spontaneous recovery had no specific diagnosis showed no lesion on both conventional and DWI and 5 cases showed equal extent and number of lesions on DWI, 1 - ADL, 2 - viral encephalitis, 2 - ischemic encephalopathy. Group C where T2 and FLAIR showed more lesions had 7 cases in which 5 had normal ADC maps but 1–2 small hyperintense lesions on T2 and FLAIR imaging.[12,13] These areas appeared white on DWI but on ADC map did not show any restriction of diffusion. Thus, these were probably T2 shine through effects. Since no final diagnosis was established and the patients also recovered completely in 2–3 days – these were labeled as nonspecific white matter hyperintensities. At the time of writing the results (i.e. 6 months since presentation), no further complaints were noted in the follow-up. The role of DWI in ruling out actual pathology from these nonspecific hyperintensities on T2 and FLAIR also needs to be further evaluated in a larger cohort. Two other similar cases, one infant aged 6 months and another aged 1.5 years had final diagnosis of ischemic encephalopathy with delayed milestones. The areas in these patients were bright on T2 and FLAIR sequences with associated ventricular enlargement and cortical atrophy while DWI revealed them to be T2 shine through areas with increased ADC value focally. These were probably areas of gliosis from old ischemic insult but had presented late in children with neonatal ischemic encephalopathy which went unrecognized at the time of initial presentation.[13,14]

CONCLUSION

Through this study, we concluded that DWI was more sensitive than the other MR sequences in detecting early pathological changes in children with neurological diseases including viral encephalitis and leukodystrophy apart from ischemia. Since it was helpful in delineating the pathology more accurately even at the microscopic level, we were also able to rule out actual pathology from nonspecific hyperintensities on T2 and FLAIR in few cases on DWI. This possibility and potential of DWI need to be further evaluated in a larger cohort. However, there are two major limitations of this study: We could not directly compare the imaging findings and the pathologic findings, and the study sample had limited number of patients. In conclusion, we

consider that the addition of DWI to the routine imaging protocol in most of the pathologies of brain in children is necessary in a wide variety of disorders apart from ischemia as it detects early lesions more effectively and also rules out nonspecific spots of hyperintensities on T2 and FLAIR.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Wedeen VJ, Hagmann P, Tseng WY, Reese TG, Weisskoff RM. Mapping complex tissue architecture with diffusion spectrum magnetic resonance imaging. Magn Reson Med 2005;54:1377-86.
2. Sahin T, Bozgeyik Z, Menzilcioglu MS, Citil S, Erbay MF. Importance of Diffusion weighted magnetic resonance imaging in evaluation of the treatment efficacy in multiple sclerosis patients with acute attacks. Pol J Radiol 2015;80:544-8.
3. Van der Knaap MS, Valk J. Magnetic Resonance of Myelination and Myelin Disorders. 3rd ed. Berlin: Springer; 2005. p. 141-3.
4. Tuch DS, Reese TG, Wiegell MR, Wedeen VJ. Diffusion MRI of complex neural architecture. Neuron 2003;40:885-95.
5. Kamran S, Bener AB, Alper D, Bakshi R. Role of fluid-attenuated inversion recovery in the diagnosis of meningitis: Comparison with contrast-enhanced magnetic resonance imaging. J Comput Assist Tomogr 2004;28:68-72.
6. Rutherford M, Counsell S, Allsop J, Boardman J, Kapellou O, Larkman D, *et al*. Diffusion-weighted magnetic resonance imaging in term perinatal brain injury: A comparison with site of lesion and time from birth. Pediatrics 2004;114:1004-14.
7. Prakash M, Kumar S, Gupta RK. Diffusion-weighted MR imaging in Japanese encephalitis. J Comput Assist Tomogr 2004;28:756-61.
8. Bajaj M, Mody S, Natarajan G. Clinical and neuroimaging findings in neonatal herpes simplex virus infection. J Pediatr 2014;165:404-7.e1.
9. McCabe K, Tyler K, Tanabe J. Diffusion-weighted MRI abnormalities as a clue to the diagnosis of herpes simplex encephalitis. Neurology 2003;61:1015-6.
10. Bladowska J, Kulej D, Biel A, Zimny A, Kalwak K, Owoc-Lempach J, *et al*. The role of MR imaging in the assessment of clinical outcomes in children with X-linked adrenoleukodystrophy after allogeneic haematopoietic stem cell transplantation. Pol J Radiol 2015;80:181-90.
11. Soares BP, Provenzale JM. Imaging of Herpesvirus Infections of the CNS. AJR Am J Roentgenol 2016;206:39-48.
12. Küker W, Nägele T, Schmidt F, Heckl S, Herrlinger U. Diffusion-weighted MRI in herpes simplex encephalitis: A report of three cases. Neuroradiology 2004;46:122-5.
13. Hafezi W, Hoerr V. *In vivo* visualization of encephalitic lesions in herpes simplex virus type 1 (HSV-1) infected mice by magnetic resonance imaging (MRI). Methods Mol Biol 2013;1064:253-65.
14. Jain R, Deveikis J, Hickenbottom S, Mukherji SK. Varicella-zoster vasculitis presenting with intracranial hemorrhage. AJNR Am J Neuroradiol 2003;24:971-4.