Imaging of CNS Infections with Clinico-pathological Correlation

Mandavee Ojha[1], Sameer R. Verma[2], Sonal Saran[3], Mukta Mital[4], Pradeep Bansal[5]

ABSTRACT

Introduction: CNS infections are an emerging health problem with poor prognosis if the treatment is not prompt and adequate. Thus, establishing a correct diagnosis is necessary to quickly start the appropriate treatment. This study was undertaken to study the etiology and the imaging spectrum of CNSI in and around western Uttar Pradesh in a tertiary health care set up and to correlate the neuro-imaging findings with clinic-pathological data.

Material and Methods: In this Prospective Observational study 80 patients clinically suspected of CNS infection were studied by CT/MRI and the neuro imaging findings were correlated with clinical and CSF findings.

Results: Based on clinical features, CSF findings, the treatment given and the response to treatment tuberculous infection (TBM) was most common infection (41.2%) followed by pyogenic meningitis (36.2%) and viral infection (22.5%). In 29 patients of pyogenic CNS infection most common imaging finding was leptomeningitis(62%) followed by pachymeningitis (31%), hydrocephalus (24.1%), abscess (6.8%), post vasculitic infarct(6.8%) and extra axial collection(6.8%). In 33 patients of tubercular CNS infection most common imaging finding was basal leptomeningitis (78.7%) followed by tuberculoma (72.7%), pachymeningitis (33.3%), hydrocephalus (27.2%), abscess (12.1%), post vasculitis infarct (12.1%) and spinal cord involvement in 1 (3%) patient. In the 18 viral CNS infection cases most common imaging finding was parenchymal hyperintensity on MRI or hypodensity on CT with/without peripheral vasogenic edema (94.4%) followed by leptomeningeal/pachymeningeal involvement (61.1%) and post vasculitis infarct (11.1%).

Conclusion: The sensitivity of neuroimaging in pyogenic CNS infection was 81.2% and specificity was 93.7% while sensitivity of neuroimaging in tubercular CNS infection was 88.8% and specificity was 97.8% and in viral CNS infection sensitivity was 84.2% and specificity was 96.7%. There was significant association (p value <0.05) of basal leptomeningitis and granulomas on imaging with tubercular infection and parenchymal signal changes with viral infections.

Keywords: Imaging, CNS Infections, Clinico-pathological Correlation

INTRODUCTION

Central nervous system infections are an emerging health problem with poor prognosis if the treatment is not adequate. Thus, establishing a correct diagnosis is necessary to quickly start the appropriate treatment. In 2004, the World Health Organization (WHO) reported about 350,000 deaths from meningoencephalitis (ME), with an approximate incidence of 700,000 cases worldwide.[1,2]

Radiology and pathology are inseparable at the time of understanding the phenomenon causing nervous system infections.[3] There are a wide range of neuroimaging findings in central nervous system (CNS) infections, often with considerable overlap, which makes determination of a specific diagnosis difficult. Correlation with laboratory tests, particularly cerebrospinal fluid (CSF) analysis, is considered to be essential in establishing a definitive diagnosis.[2]

MRI is the method of choice in the evaluation of patients with CNSI, but it is essential to assess images together with the patient's age, socioeconomic and immune status, as well as much clinical data as available. This technique helps to establish the presence of an infection, to rule out differential diagnoses, it is also essential to have a CSF study available and to know whether or not there is suspicion of an extra-neural focus of infection, as this contributes to an early diagnosis.[2] This study was undertaken to study the etiology and the imaging spectrum of CNSI in and around western Uttar Pradesh in a tertiary health care set up and to correlate the neuro-imaging findings with clinic-pathological data.

MATERIAL AND METHODS

This prospective observational study after approval from the institutional ethics committee, was conducted from 01st October 2016 to 30th June 2018 and included 80 patients with clinico-pathological findings suggestive of central nervous system infection, confirmed on neuro-imaging (MRI/CT) in the department of Radiodiagnosis and Imaging, Subharti Medical College, Meerut (U.P.). After taking informed written consent, relevant clinical history was taken, general and neurological examination findings, relevant laboratory investigations and CSF examination findings (wherever available) were noted and tabulated from available patient records. Patients were followed up clinically during their hospital stay for response or change in treatment and follow up imaging/lab investigations to reach final/conclusive diagnosis. Exclusion criteria: Pathologies mimicking central

[1]PG Student, Department of Radiodiagnsosis, SMC, Meerut, [2]Professor, Department of Radiodiagnsosis, SMC, Meerut, [3]Assistant Professor, Department of Radiodiagnsosis, SMC, Meerut, [4]Professor, Department of Radiodiagnsosis, SMC, Meerut, [5]Associate Professor, Department of Radiodiagnsosis, SMC, Meerut, India

Corresponding author: Sameer R. Verma, Professor, Department of Radiodiagnsosis, Subharti Medical College, Swami Vivekanand Subharti University, NH-58, Meerut -250005 (UP), India

How to cite this article: Mandavee Ojha, Sameer R. Verma, Sonal Saran, Mukta Mital, Pradeep Bansal. Imaging of CNS infections with clinico-pathological correlation. International Journal of Contemporary Medical Research 2019;6(5):E6-E10.

DOI: http://dx.doi.org/10.21276/ijcmr.2019.6.5.23

nervous system infection. Patients lost to follow up or refusing consent to be part of study.

Technique: Requested neuro-imaging was done with prior explanation of the radiological investigation and informed written consent of the patient/relatives. CT was performed on Philips ingenuity core 128 multislice unit with axial, coronal and sagittal reconstructions of desired thickness of acquired data. CECT scans were performed after bolus injection of low osmolalaity non ionic iodinated contrast material (Iohexol 300mg/ml, dose: 1ml/kg). MRI scans were performed on 1.5T GE signa HDe 8 channel unit with acquisition of spin echo T1W, T2W, T2 Flair, SWI in desired planes and axial EPI- DWI and ADC maps. CEMRI was done post IV gadolinium (dose 0.1mmol/kg) injection with acquisition of TIW scans in three orthogonal planes. Imaging findings were evaluated and tabulated and correlated with the clinical findings and pathological findings (wherever available) subsequently.

Type of infection	Number of patients	Percentage
Tubercular	33	41.2
Pyogenic	29	36.2
Viral	18	22.5
Total	80	100

Table-1: Distribution of patients based on clinical and pathological findings and follow up of patient

Type of infection	Number of patients	Percentage
Tubercular	20	35.7
Pyogenic	18	32.1
viral	11	19.6
Non specific	7	12.5
Total	56	100

Table-2: Distribution of patients according to presenting CSF findings (available in 56 pts)

STATISTICAL ANALYSIS

Data were processed using SPSS version 21.0. Categorical data were processed using Chi-square test. Statistical analysis was performed using percentages and proportions. p values of less than 0.05 were considered as statistically significant.

RESULTS

Demographic distribution: The age ranges from 28 days old to 55 years in present study with majority (36.2%) of the patients being below 10 yrs of age. Out of 80 patients 42 were males and 38 females.

Clinical presentation: In most of the cases in our study, more than one symptoms and signs were present. The commonest symptom was fever in 92.5%, headache in 65%,vomiting in 58.7%, alteration of consciousness in 53.7%, seizure in 51.2% and neck stiffness in 45% cases.

Imaging findings: Based on clinical features, CSF findings, the treatment given and the response to treatment tubercular infection (TBM) was most common (41.2%) followed by acute bacterial/pyogenic infection (36.2%) and viral infection (22.5%) (Table 1).

According to CSF findings which was available in 56 patients tubecular infection was the most common (35.7% cases) followed by pyogenic (32.1%) and viral infections

Imaging parameter	Number of patients/percentage			p value	Significant
	Pyogenic (29)	Tubercular (33)	Viral (18)		
Basal leptomeningitis	8/28	26/78.7	2/11	0.018	Yes
Pachymeningitis	9/31	11/33.3	4/22.2	0.702	No
Parenchymal hyperintensity/hypodensity+/-peripheral vasogenic edema	4/13.7	9/2.7	15/83.3	0.000	Yes
Abscess	4/13.7	2/6	0	0.288	No
Hydrocephalus	7/24.1	16/48.4	0	0.001	Yes
Post vasculitis infarct	2/6.8	4/12.1	2/11.1	0.000	Yes
Extra axial collection	2/6.8	0	0/0	0.165	No
Granuloma(Tuberculoma)	NA	24/72.7	NA	0.000	Yes
Spinal cord involvement	0	1/3.0	0	0.486	No

Table-3: Imaging analysis of cases with pyogenic infection(n=29) and tubercular infection(n=33) and viral infection (n=18) of central nervous system

Study and year	Sensitivity / Specificity for CNS TB	Sensitivity / Specificity for CNS pyogenic	Sensitivity / Specificity for CNS Viral
Present study	88.8/97.8	81.2/93.7	84.2/96.7
Kumar R(2015)[3]	88.5/100	14.2/96.9	26.6/88.8
Granerod et al(2016)[4]	-	-	81/100
Mei-Ling Sharon TAI et al (2017)[5]	89/95.6	-	-
Dongfeng Zhang(2017)(MRI+CSF)[6]	62.46/80.35	24.75/75.36	68.71/76.96
Oliviera CRet al (2014) (MRI +CSF)[7]		81.3/100	

Table-4: Comparison of present study with various other studies

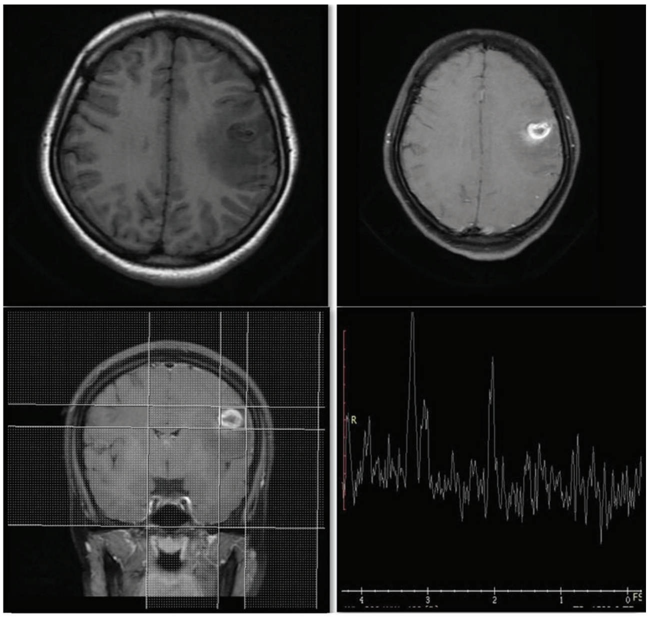

Fig 1:Axial preconstrastT1/post contrast T1 axial and Cor T1C+/MRS: showing thick conglomerated ring enhancing lesion with perilesional vasogenic edema seen in left parietal region, cortical and subcortical in location. MRS shows elevated choline, decreased creatinine and NAA peaks, Choline/creatine>1with small lipid peak at 1.2-1.4ppm suggestive of conglomerated tuberculomas

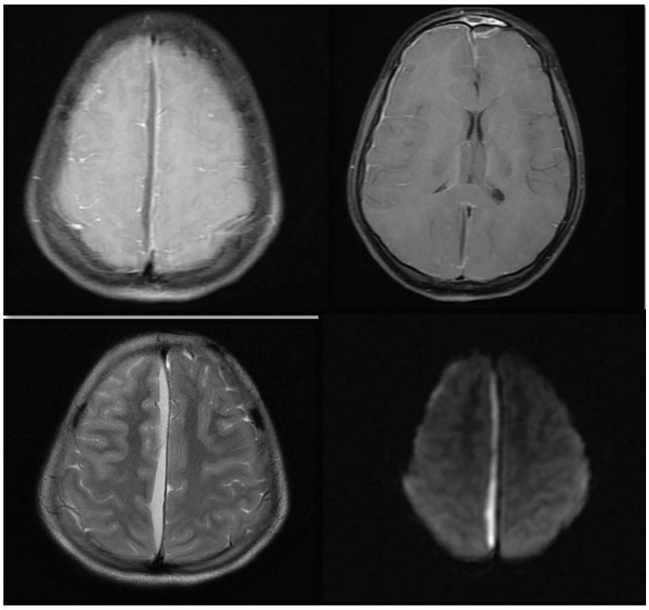

Fig 2: Axial T1C+/T2/DWI: showing an extra axial collection along falx cerebri on right side with mild shaggy peripheral enhancement and restriction on DWI. Thin extra axial collection showing similar enhancement characteristic is noted along left cerebral convexity. Subdural empyema in right parafalcine region and left epidural empyema along cerebral convexity in case of pyogenic CNSI

(19.6%) while CSF findings were nonspecific in seven cases (Table 2).

In this study in the 29 patients of pyogenic CNS infection, most common imaging finding was leptomeningitis (62%) followed by pachymeningitis (31%), hydrocephalus (24.1%), abscess (13.7%), post vasculitis infarct (6.8%) and extra axial collection(6.8%). The sensitivity of neuroimaging in pyogenic CNS infection was 81.2% and specificity was 93.7%. Among the 33 patients of tubercular CNS infection most common imaging finding was basal leptomeningitis

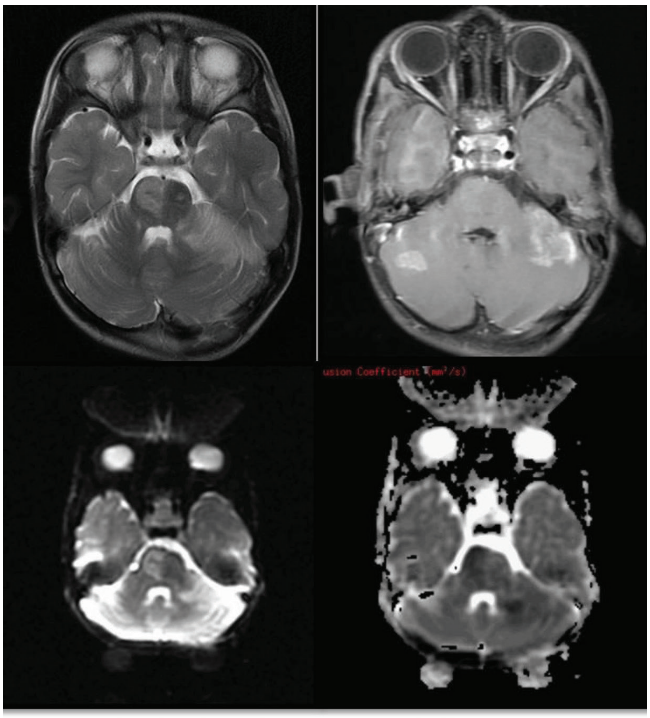

Fig 3: Axial T2/T1C/DWI/ADC: showing multifocal patchy areas of altered signal changes appearing hyperintense on T2/FLAIR noted involving pons, bilateral cerebellar hemispheres and left cerebellar peduncle. These areas show faintly restricted diffusion on DWI with corresponding defect on ADC. Case of viral CNSI

(78.7%) followed by granuloma (tuberculoma) (72.7%), pachymeningitis (33.3%), hydrocephalus (27.2%), abscess (6%), post vasculitis infarct (12.1%) and spinal cord involvement in 1(3%) patient.

p value was less than 0.05, for the following neuroimaging findings: basal leptomeningitis, parenchymal hyperintensity/hypodensity+/- peripheral vasogenic edema and granuloma(tuberculoma), while it was above 0.05, for findings like pachymeningitis, abscess and extra axial collections probably because of small sample size. (Table 3)

DISCUSSION

As shown in results, in the present study tubercular infection (TBM) was most common(41.2%), followed by pyogenic meningitis (36.2%) and viral infection (22.5%) which is similar to Kumar Raju et al[3] study in which they observed Tuberculous infection (TBM) was most common infection (33%) followed by pyogenic meningitis(27%), encephalitis(22%), NCC(13%) and brain abscess (5%).

The sensitivity of neuroimaging in pyogenic CNS infection was 81.2% and specificity was 93.7%. The sensitivity of neuroimaging in tubercular CNS infection was 88.8% and specificity was 97.8%. The sensitivity of neuroimaging in viral CNS infection was 84.2% and specificity was 96.7%. The results are nearly similar to Kumar Raju[3] study which showed that in TBM sensitivity of basal enhancement and tuberculoma were 84.4% and 39.1% respectively while specificity of both were found to 100%. In pyogenic meningitis the specificity of subdural effusion was 96.9% but sensitivity was only 14.2%. Granerod et al[4] found the overall sensitivity of neuroimaging for viral CNS infection to be 80%, while specificity was more than 95% with PPV of 100% and NPV of more than 90%,[8,5] which is also nearly similar to our study. Similar results are stated by Mei-Ling Sharon TAI et al[5] that the sensitivity of the imaging features for diagnosis of TBM was 88.9% and the specificity was 95.6%. Dongfeng Zhang[6] also found that sensitivity of MRI in combination with cerebrospinal fluid analysis in diagnosing tubercular meningitis, viral meningitis and cryptococcal meningitis was higher than that in diagnosing purulent meningitis which correlates with our study. (Table 4)

Neuro-imaging analysis of pyogenic CNS infections

In our study out of 29 patients of pyogenic CNS infection most common imaging finding was leptomeningitis (62%) followed by pachymeningitis (31%), hydrocephalus (24.1%) and abscess(13.7%), post vasculitis infarct(6.8%) and extra axial collection(6.8%).

Regarding leptomeningeal enhancement in pyogenic infection the result is similar to the study done by Oliveira CR et al[7] regarding MRI findings in 75 CSF bacterial culture positive infants showing leptomeningeal enhancement to be the most common finding present in 57% of the cases. Pachymeningeal enhancement was seen in 9(31%) patients. The paucity of pachymeningeal enhancement in pyogenic meningitis observed in our study correlates well with the study by Kioumehr F et al[8] involving 83 patients with meningeal enhancement on MR scans. Pachymeningeal enhancements observed by them were attributed to proven cases of meningeal carcinomatosis (83% of cases) and in 100% of the reactive cases (due to trauma, shunt, surgery). In contrast all the cases of infectious meningitis and 78% cases of the chemical meningitis subgroups had leptomeningeal enhancement.

Vasculitic infarcts were seen in 2 (6.8%) of our patients. Chang et al[9] observed in their study that cerebral infarction patients accounted for 10% of bacterial meningitis cases. Associated hydrocephalous was seen in 7(24%) patients in our study. These findings correlate well the study of Wang KW et al[10] in 136 adult patients with culture-proven bacterial meningitis who found that twenty-eight patients had hydrocephalus, accounting for 21% (28/136) of the episodes. Hoever Kasanmoentalib ES et al[11] who studied the occurrence of hydrocephalous in 577 cases of community acquired bacterial meningitis, the occurrence of hydrocephalous was seen in only 5% cases. Extra axial collection (subdural empyema) was seen in 2(6.8%) of our patients. Though the prevalence of subdural empyema was low in our study, yet it is one of the strong indicators of bacterial meningitis as is evident by the large cohort study by Jim KK et al[12] showing the occurrence of subdural empyema in 1034 cases of bacterial meningitis over a period of 5 years and it's prevalence to be 2.7% (28 cases). They discussed that although rare, subdural empyema must be considered in patients with community-acquired bacterial meningitis and otitis / sinusitis, focal neurologic deficits, or epileptic seizures.

Neuro-imaging analysis in tubercular CNS infections

Out of 33 patients of tubercular CNS infection most common imaging finding was basal leptomeningitis(78.7%) followed by tuberculoma (72.7%), pachymeningitis (33.3%), hydrocephalus(27.2%) and abscess(12.1%) and post vasculitis infarct(12.1%). These findings are consistent with the study by Uysal G et al[13] in which they found meningeal enhancement present in up to 90% of cases and considered it to be the most sensitive feature of tubercular meningitis. Similar results were also interpreted by Andronikou S et al[14] who showed sensitivity of basal enhancement to be as high as 89% in making the diagnosis of tubercular meningitis. Tuberculoma was found in 24 (72.7%) patients which is not in agreement with Kumar Raju et al[3] study in which tuberculoma was found in 25% of the patients.

Hydrocephalous was seen in 16 (48.4%) of our patients. The incidence, predictive factors and the impact of hydrocephalous in tubercular meningitis was studied by Raut T et al[15] who in his study of 80 patients with tuberculous meningitis showed that 52(65%) had hydrocephalus at presentation. Our findings are also similar to Larry E. Davis et al[16] community-based study which analyzed 54 patients with definite or probable tuberculous meningitis and observed ventricular dilatation on CT or MRI in 52% of patients

Vasculitic infarcts were found in 4 (12.1%) of our patients, which differs from Tai et al[5] study which showed that cerebral infarction was seen in 67% of tuberculous meningitis patients

Neuro-imaging Analysis in Viral CNS infections

In our study parenchymal hyperintensity on MRI or hypodensity on CT with/without peripheral vasogenic edema was seen in 83.3%.which is similar to Kumar Raju et al[3] study who observed that hypodense lesion in medial portion of temporal lobe on CT scan was present in 81.2% cases of encephalitis. Post vasculitis infarct was noted in 11.1% patients whereas in Gupta et al[17] study 6.6% patients had infarcts

CONCLUSION

As discussed we found neuro-imaging accurate in early diagnosis and categorization of CNS infections with high sensitivity and specificity. There was significant association (p value <0.05) of basal leptomeningitis and granulomas on imaging with tubercular infection and parenchymal signal changes with viral infections. This study has inherent disadvantage of small sample size and hence a larger study is warranted for corroboration of our findings.

REFERENCES

1. Sgarbi N. Central nervous system infections: New diagnostic tools. Rev. Argent. Radiol. 2015;79:12-31.
2. Zee CS, Geng D, Go JL,Kim P, Ahmadi J, Segall HD. Cerebral Infections and Inflammation. In: Haaga JR, Boll D.CT and MRI Imaging of the whole body 5th ed. Dogra V, Forsting M, Gilkeson R, Ha KH, Sundaram M, editors. St. Louis:Mosby;2009:145-182.
3. Kumar R, Kumari P, Verma N. Evaluation of neuroimaging studies in CNS infections and its correlation with clinical presentation in children in

Bihar. International journal of medical and applied sciences.2015;4:224-229
4. Granerod J, Davies NW, Mukonoweshuro W, Mehta A, Das K, Lim M, et al. Neuroimaging in encephalitis: analysis of imaging findings and interobserver agreement. Clin Radiol. 2016;71:1050–8.
5. Tai MS, Viswanathan S, Rahmat K, Nor HM, Kadir KA, Goh KJ, et al. Cerebral infarction pattern in tuberculous meningitis.Sci Rep.2016;6:38802.
6. Zhang D.Values of magnetic Resonance imaging and Cerebrospinal fluid analysis in the diagnosis of Central Nervous System associated infectious diseases. Pak J Med Sci.2017; 33: 1065–1069.
7. Kastrup O, Wanke I, Maschke M. Neuroimaging of infections. NeuroRx. 2005; 2: 324-332.
8. Kioumehr F, Dadsetan MR, Feldman N, Mathison G, Moosavi H, Rooholamini SA, et al. Postcontrast MRI of cranial meninges: leptomeningitis versus pachymeningitis. J Comput Assist Tomogr.1995;19:713-20.
9. Chang CJ, Chang WN, Huang LT, Chang YC, Huang SC, Hung PL, et al. Cerebral infarction in perinatal and childhood bacterial meningitis. QJM. 2003;96:755-62
10. Wang KW, Chang WN, Chang HW, Wang HC, Lu CH. Clinical relevance of hydrocephalus in bacterial meningitis in adults. Surg Neurol. 2005;64:61-5.
11. Kasanmoentalib ES, Brouwer MC, van der Ende A, van de Beek D. Hydrocephalus in adults with community-acquired bacterial meningitis. Neurology. 2010;75:918-23.
12. Jim KK, Brouwer MC, van der Ende A, van de Beek D. Subdural empyema in bacterial meningitis. Neurology. 2012;79:2133-9.
13. Uysal G, Köse G, Güven A, Diren B. Magnetic resonance imaging in diagnosis of childhood central nervous system tuberculosis. Infection. 2001;29:148-53.
14. Andronikou S, Smith B, Hatherhill M, Douis H, Wilmshurt J. Definitive neuroradiological diagnostic features of tuberculous meningitis in children. Pediatr Radiol. 2004;34:876-85.
15. Raut T, Garg RK, Jain A, Verma R, Singh MK, Malhotra HS, et al. Hydrocephalus in tuberculous meningitis: Incidence, its predictive factors and impact on the prognosis. J Infect 2013;66:330-7.
16. Davis LE, Rastogi KR, Lambert LC, Skipper BJ. Tuberculous meningitis in the southwest United States: A community based study.Neurology.1993;43:1775.
17. Gupta K, Banerjee A, Saggar K, Ahluwalia A, Saggar K. A prospective study of magnetic resonance imaging patterns of central nervous system infections in pediatric age group and young adults and their clinico-biochemical correlation. J Pediatr Neurosci. 2016; 11: 46–51.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 25-03-2019; **Accepted:** 17-04-2019; **Published:** 19-05-2019