Quantitative DTI Assessment of Periventricular White Matter changes in Neonatal Meningitis

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Introduction: Meningitis is one of the most common and serious disorders of central nervous system infection in neonates characterized by inflammation of pia-arachnoid membrane with symptoms of lethargy, irritability, vomiting, and seizures.[1] Factors responsible for early onset of meningitis includes obstetric complications, prematurity, prolonged rupture of membranes, maternal infection and chorioamnionitis. Fatality rate associated with this disease can be as high as 20-30 %.[1] The major neuropathological consequence of bacterial neonatal meningitis is cerebral atrophy, manifested by loss of cerebral cortical neuron and loss of myelin in periventricular white matter.[2] The disorder fulminates in evolution but is amenable to therapeutic intervention; early diagnosis of neonatal meningitis followed by appropriate medical management can have a favorable effect on outcome. Till date definitive diagnosis of meningitis is dependent on examination and culture of cerebrospinal fluid (CSF). Although conventional magnetic resonance imaging (MRI) is more sensitive then computerized tomography (CT) to detect inflammatory vasculitis, it is insensitive to subtle changes in tissue microstructure.[3] Diffusion tensor imaging (DTI) characterizes the spatial properties of molecular diffusion that provides insights into white-matter microstructure. The aim of this study was to determine the role of DTI derived metrics in early detection of infection related white matter damage and to compare these measures with the clinical outcome of disease.

Materials and Methods: The present study was carried out on twelve-term babies (8 males and 4 females, mean age = 12.5 days) with neonatal meningitis and five term neonates with normal neurological examination, which served as control subjects. Diagnosis of meningitis was based on CSF examination. Neonates with congenital malformation, perinatal asphyxia, and intraventricular hemorrhage were excluded from this study. There was a gap of 3 days to 14 days (mean = 7.17 days) between the onset of symptoms and the imaging in all these cases.

Whole brain conventional MRI and DTI were acquired on a 1.5 Tesla GE MRI scanner using a standard quadrature head coil. DTI data was acquired using a single-shot echo planar dual spin echo sequence with ramp sampling. The acquisition parameters were: TR=8sec/TE=100ms/number of slice =30-34/slice thickness=3mm/interslice gap=0/FOV= 240mm/image matrix=256x256 (following zero-filling)/NEX=8/ diffusion weighting b-factor=700 s mm^{-2}. The DTI data were processed as described in detail elsewhere.[4] The DTI-derived maps were displayed and overlaid on images with different contrasts to facilitate the region-of-interest (ROI) placement. ROIs were placed on periventricular white matter of frontal (FWM), parietal (PWM), occipital (OWM) and temporal (TWM) lobes for fractional anisotropy (FA) and mean diffusivity (MD) quantification in these patients. To evaluate the regional differences in the DTI metrics between meningitis and healthy controls we used a student's independent t-test.

Results: On the basis of imaging findings, patients were classified into two groups: patients with normal (n = 5) and abnormal (n = 7) conventional imaging for the purpose of quantitative DTI. In patients with abnormal conventional imaging significant decrease in FA value was observed in all the periventricular white matter except left PWM as compared to controls. On comparing FA values between controls and patients with normal conventional imaging, significantly reduced FA was observed in right PWM, right OWM, and left OWM. Significantly reduced FA values were observed in right OWM, left OWM, and right TWM in patients with abnormal conventional imaging as compared to patients with normal imaging. Increased MD values were observed in periventricular white matter in 2 out of 7 patients with abnormal imaging. Whereas in rest 5 of the patients with abnormal imaging decreased MD values were observed in periventricular white matter as compared to controls. Out of seven patients with abnormal imaging 4 patients expired during hospital stay, 2 were lost to follow-up and 1 was clinically normal at the time of discharge.

Table 1: A summary of groups mean and standard deviation of the fractional anisotropy (FA) from the periventricular white matter region of brain collected from the 5 age/sex matched controls and 12 neonates with meningitis.

Region	a. Control (n=5)	b. Normal on conventional MRI (n=5)	c. Abnormal on conventional MRI (n=7)	p values
Right FWM	0.11 ± 0.34	0.09 ± 0.02	0.06 ± 0.01	pab = 0.27, pac = 0.03, pbc = 0.07
Left FWM	0.12 ± 0.03	0.09 ± 0.02	0.06 ± 0.03	pab = 0.12, pac = 0.03, pbc = 0.09
Right PWM	0.14 ± 0.03	0.09 ± 0.03	0.07 ± 0.03	pab = 0.03, pac = 0.01, pbc = 0.46
Left PWM	0.10 ± 0.01	0.10 ± 0.03	0.07 ± 0.03	pab = 0.99, pac = 0.07, pbc = 0.17
Right OWM	0.15 ± 0.03	0.10 ± 0.03	0.07 ± 0.02	pab = 0.04, pac = 0.00,pbc = 0.02
Left OWM	0.16 ± 0.04	0.11 ± 0.01	0.07 ± 0.02	pab = 0.02, pac = 0.00, pbc = 0.00
Right TWM	0.13 ± 0.01	0.12 ± 0.02	0.07 ± 0.03	pab = 0.45, pac = 0.00, pbc = 0.01
Left TWM	0.14 ± 0.03	0.12 ± 0.04	0.07 ± 0.02	pab = 0.16, pac = 0.00, pbc = 0.06

Discussion: Our finding of decreased FA, in abnormal as well as normal appearing periventricular white matter, in meningitic patients is consistent with previous neuropathological studies[5] and emphasizes the vulnerability of the periventricular white matter. Histologically there has been demonstration of neuronal loss in the deeper cortical layers and myelin loss in the periventricular region, with both areas showing gliosis.[5] Myelin sheaths limit the diffusion of water molecules in a directionally dependent fashion and provide obstacles to diffusion in white matter tracts. Therefore, demyelination and gliosis would be expected to decrease FA in periventricular white matter. High mortality among the patients with abnormal imaging shows significant decreased FA in these patients compared to the ones with normal conventional imaging suggesting more severe injury in these patients. Though in the patients with normal conventional imaging the short term clinical follow-up appears to be good, these may develop neurological sequlae in the long term like seizures, hearing deficits, learning and behavioral problems as described in the literature. We suggest that decreased FA values will improve assessment and prognosis of the extent of periventricular white matter injury in neonatal meningitis and this may help in prognosticating the disease outcome.

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