Temporal Changes in Brain Water Diffusivity in Neonatal Meningitis

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Introduction: Meningitis is an illness with potentially devastating consequences in neonates. Neonatal meningitis characterized by inflammation of pia-arachnoid membrane often has non-specific signs with symptoms of lethargy, irritability, vomiting, and seizures. Meningitis during the first few weeks of life poses a particular hazard with high mortality and a considerable risk of permanent damage to survivors in developing brain (1). In a recent diffusion tensor imaging study demonstrated abnormalities in periventricular white matter regions even in the absence of any abnormality on conventional imaging (2). Periventricular white matter of neonatal brain is known to be vulnerable to oxidative and hypoxic/ischemic injury secondary to neuro-infections. Diffusion imaging has proved to be a valuable clinical tool in the assessment of hypoxic-ischemic injury. In the transition from acute to sub-acute and chronic stroke, first apparent diffusion coefficient (ADC) decreases in acute phase then renormalizes and subsequently increases (3). The aim of this study was to demonstrate the hypoxic ischemic changes if any in brain parenchyma of neonatal meningitis on diffusion weighted imaging (DWI).

Materials and Methods: The present study was carried out on 45 term babies [30 males, mean age = 14.2 days] with neonatal meningitis and 10 age/sex matched controls. The diagnosis of bacterial meningitis was based on clinical manifestations, meningeal enhancement on post contrast T1 images as well as biochemical analysis of CSF. The microorganisms cultured were E. coli (n=20), S. pneumoniae (n=8) and Group B streptococcus (n=7). In the remaining 10 patients CSF was termed sterile. The patients were treated with standard antibiotics protocol for neonatal meningitis. 25 neonates with meningitis had repeat imaging after 3 weeks of antibiotic treatment. Of the remaining 20 patients, 13 died and other 7 subjects were lost for follow up. There was a gap of 2 to 15 days (mean = 5.9 days) between the onset of symptoms and the imaging in all these cases. Whole brain conventional MRI (T2, T1) and DWI were performed on a 1.5-Tesla GE MRI system. Fast spin echo T2 imaging along with DWI was performed in the axial plane by using a single shot EPI-SE pulse sequence with: TR/TE= 10.5 s/ 110 ms, FOV = 24 cm, NEX= 2, slice thickness =3 mm, interslice gap= 0, matrix size of 128×128. Diffusion sensitizing gradients were applied sequentially along the three orthogonal directions with diffusion sensitivity of b =0 and 1000 s/mm^2 with ramp sampling on. An in-house software generate ADC maps from the DW images (b=0 and 1000 s/mm^2). Post-contrast T1 images were also obtained in patients, after injecting Gadodiamide (Gd-DTPA-BMA, Omniscan, Amersham Health, Oslo, Norway) intravenously at a dose of 0.1 mmol/ kg- body weight.

Results: Abnormal meningeal enhancement on post contrast T1 images was noted in all the neonates with clinically diagnosed bacterial meningitis (n=45). On follow-up MRI studies in 25 neonates, after 3 weeks of antibiotic treatment meningial enhancement though less intense than before treatment, was observed in 15 neonates.
Imaging at first study: Eleven neonates (24.4 %) with meningitis at the time of first MRI showed no obvious abnormality on T2, T1, and ADC map. Rest of the 34 neonates showed some evidence of cerebral injury on imaging at the time of first study. The lesions appeared iso to hypo-intense on T2-weighted images, hyperintense on T1-weighted images, and showed low ADC values [$(0.64\pm0.08)\times10^{-3}$ mm^2/sec] on ADC map in the cortex, periventricular, and subcortical white matter regions in sixteen patients (35.6 %) compared to controls [$(0.97\pm0.10)\times10^{-3}$ mm^2/sec]. Thirteen patients (29 %) showed low ADC values [$(0.74\pm0.09)\times10^{-3}$ mm^2/sec] with normal conventional imaging in periventricular/subventricular white matter, cortical and deep gray matter. Remaining 5 patients (11 %) showed multiple bilateral brain abscesses as a secondary consequence of meningitis.
Imaging at second study: No abnormalities were observed at the time of second study in patients with normal imaging. In patients with abnormal T1/T2 and ADC map T1/T2 abnormalities were persisted on second study; however ADC map showed high ADC values [$(1.27\pm0.08)\times10^{-3}$ mm^2/sec] in those regions. The abnormalities visible on ADC map at the baseline study in patients with low ADC values with normal T1/T2 imaging the abnormalities were detected subsequently on T1 images with no change in ADC values at follow-up study.

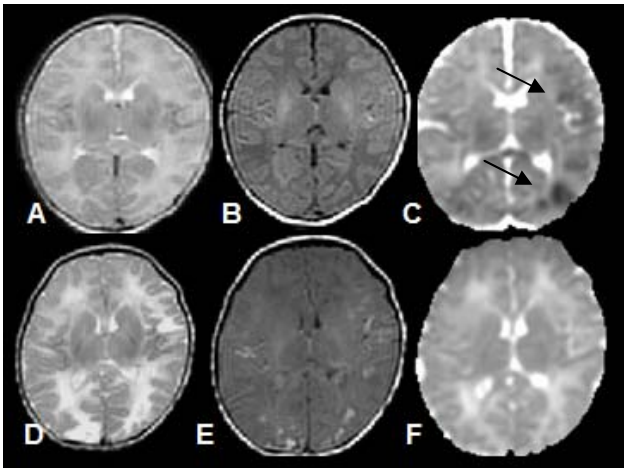

Figure1: (A-C) 9-day-old neonate with bacterial meningitis. T2 (A), and T1 (B)-weighted images shows no evidence of parenchymal injury. ADC (C) map shows reduced MD in splenium, bilateral subcortical white and grey matter regions (arrow). (D-F) Follow-up MRI of the same patient,after 3 weeks of antibiotic treatment. T2-weighted (D) image at the same level as in first study appears normal; however T1-weighted (E) image shows multiple bilateral hyperintensities in the regions showing low ADC (C) on 1st study. ADC map (F) shows phenomenon of pseudo-normalization on follow-up study.

Figure 1

Discussion: Focal ischemia has been observed in humans and experimental animals with bacterial meningitis as a consequence of vasculitis (4). Vasculitis in the small subarachnoid vessels results in thrombotic obstruction of vessels and decreased cerebral perfusion pressure leading to focal ischemic lesions. ADC values are the most sensitive measure for detecting acute ischemia. DWI studies show that diffusion parameters decreases in the acute stage, "pseudonormalize" in the subacute stage (7 days), and increase in the chronic stage of neonatal hypoxic-ischemic injury. The progressive change in ADC values from low to subsequently high values during the acute and subacute stage of disease is suggestive of hypoxia related injury in neonatal meningitis that may be responsible for long term neurological sequelae in the long term like seizures, hearing deficits, learning and behavioral problems as described in the literature (5).

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