Increased Cortical Fractional Anisotropy is a marker of Infection in meningitis patients associated with Brain Abscess

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Introduction: Bacteria cause severe infections which may involve one or more intracranial compartments producing brain abscesses, meningitis, sub-dural and extra-dural empyema. Early diagnosis and aggressive therapy helps to reduce morbidity and mortality. These abscesses have been reported to account for 1-2 and up to 8% of all intracranial space-occupying lesions in patients in developed and developing countries, respectively (1) Mortality rate of bacterial meningitis 3 to 20% (*N meningitides* the lowest and *S. pneumoniae* the highest). Diffusion tensor imaging (DTI) provides information about microstructural organization measured through fractional anisotropy (FA) and mean diffusivity (MD). DTI of brain abscess (BA) has shown high FA in the cavity and it has been suggested that expression of various cell adhesion molecules on inflammatory cells is responsible for their orientation along the principle eigen vector in the abscess cavity (2). In this study we report similar change in the cortical regions as well as in abscess cavity of the patients of bacterial meningitis associated with brain abscess, suggestive of presence of inflammatory cells that clumps with the help of cell adhesion molecules resulting in to increase FA through similar mechanism as in the case of BA.

Material and Methods: Ten patients of meningitis associated with brain abscess (7 males, median age = 18 years) were included in this study. For the purpose of comparison 10 age/sex matched controls were also included in our study. Informed consent for carrying out the study was obtained from both controls and patients or their nearest kin. The inclusion criteria for the initial diagnosis were based on biochemical examination by applying pus and CSF in to separate BACTEC plus aerobic/anaerobic media (Becton Dickinson Co., Sparks, MD, USA) to isolate aerobic, facultative anaerobic and anaerobic bacteria for the identification of etiologic agents as well as conventional MR (magnetic resonance) imaging (3) including diffusion weighted imaging (DWI), in vivo proton MR spectroscopy and post-contrast T1 imaging. The etiological agents obtained through culture media were same in both pus as well as CSF. Conventional MR imaging and DTI were acquired on a 1.5 Tesla MR scanner using standard quadrature birdcage head coil. DTI data were 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=34-36/with contiguous 3 mm slice thickness/FOV=240mm/image matrix=256×256 (following zero-filling)/NEX=8/diffusion weighting b-factor=1000 s mm^{-2}. The DTI data were processed as described elsewhere (4). For the purpose of quantitative analysis free hand region of interest (ROI)s of variable size depending upon the abscess lesion were placed in BA cavity and elliptical ROIs of 2×4 pixels were placed in the cortical regions with maximal contrast enhancement (Fig 1F). The cortical ROIs were positioned on the DWI images (b = 1000) to ensure the absence of CSF contamination. Student's independent t test was performed using Package for Social Sciences (SPSS, version 12.0, SPSS Inc, Chicago, USA). P value less then 0.05 was considered as statistically significant.

Results: Among 10 cases, 8 patients had a BA with ventricular rupture, and 2 had associated sub-dural collection. Post contrast T1-weighted images showed rim enhancement of lesion with abnormal meningeal enhancement in all the cases. The microorganisms cultured were S. aureus (n = 1), anaerobic streptococci (n = 3), Bacteroids (n = 1), Gram negative bacilli (Enterobacter clocae) (n = 1) and mixed (n = 1). In the remaining three patients, CSF/pus culture did not show any microorganisms, and was termed as sterile. Significantly increased FA (p=0.00) values with no change in MD values (p=0.10) in cortical region (maximal enhancement) were observed in patient group (FA=0.11±0.02, MD=1.11±0.15) as compared to healthy controls (FA=0.07±0.01, MD=1.08±0.15). In the abscess cavity FA values (0.28±0.04) comparable to white matter were observed in all cases.

Discussion: There is a general agreement that FA represents white matter tracts integrity. But few groups have shown non-white matter causes of increased FA (5,6). Once bacteria gains access to the CNS, they elicit an acute inflammatory response. Leukocyte recruitment to inflammatory sites (brain parenchyma/sub-arachnoid space) consists of a complex series of interactions mediated by cell adhesion molecules expressed on the surface of inflammatory and endothelial cells (7). Our results of increased FA in cortical region and BA cavity are in line with previous results (2). That showed increased FA values in pyogenic BA cavity and it has been suggested that expression of various cell adhesion molecules on inflammatory cells is responsible for their orientation on principal eigen vector in the abscess cavity (2). This is suggested that high FA in BA cavity in comparison to cortical region in patients is due to the greater concentration of inflammatory cells in BA cavity as compared to sub-arachnoid space. Inflammatory cells clump through cell adhesion molecules providing restriction in water movement and resulting in high FA values in both cavity and cortical region. As on MRI cortex can not be differentiated from pia-arachnoid, the oriented inflammatory cells arranged in the pia-arachnoid interface give a psudo-impression of high FA values in the cerebral cortex. Our results suggest that the presence of aggregated inflammatory cells due to the response of bacterial antigen inside the abscess cavity as well as in sub-arachnoid space is responsible for high FA in abscess cavity and cortical region respectively. Noninvasive monitoring of inflammatory course using DTI in bacterial pathologies may be of value in improving the understanding of therapeutic response over time.

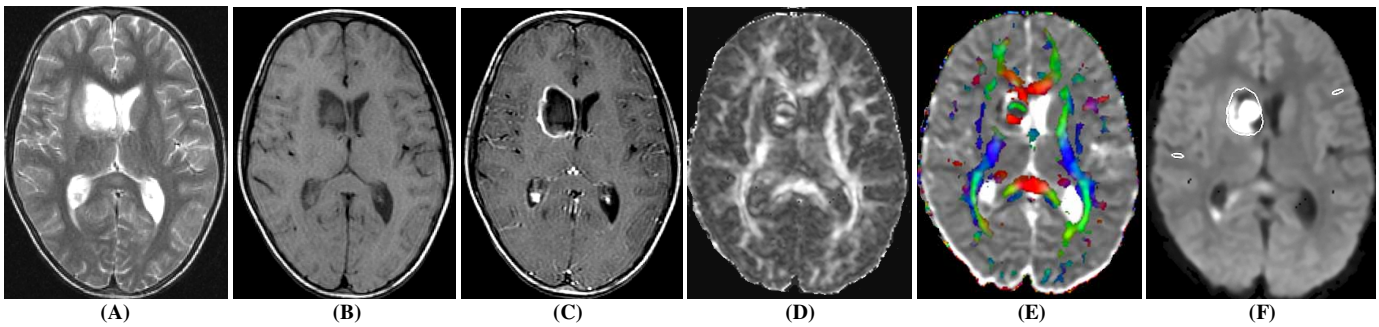

Figure1: A 24-years-old male with right ear discharge and brain abscess with intraventricular rupture. T2 image (A) through the lateral ventricles shows hyperintensity in the right periventricular region. Corresponding T1 image (B) shows the lesion as hypointense that displays rim as well as meningeal enhancement on post contrast T1image (C). FA map (D) shows areas of high FA values in the cavity mixed with intervening low FA values. Color modulated FA maps fused with D_{av} map shows (E) orientation in the abscess cavity similar to what is observed in the oriented white matter. DW image (F) show restricted diffusion in the cavity. The elliptical and free hand ROIs placed on DWI image (F) on cortical region as well as abscess cavity that was co-registered with figures 1A-E to get uncontaminated values of FA and MD.

References:

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