Evolution of Brain Edema in Experimental Pneumococcal Meningitis

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Introduction

The development of brain edema is believed to be a fundamental contributory factor leading to morbidity and complications in bacterial meningitis. The changes in brain water distribution during the course of disease have, to our knowledge, not yet been fully elucidated. Knowledge of the dynamic development of edema and changes in the characteristics of edema during the course of disease are essential to the understanding of meningitis and its treatment.

Results:

Cortex ADC values in rats with meningitis differed significantly from controls in the study interval from 6-48 hours (Kruskal-Wallis test p=0.0033). A significant increase in ADC values in the brain cortex was found between 12 and 30 hours in infected rats compared to the controls (Mann Whitney p=0.049) whereas cortex ADC values between 36 and 42 hours were significantly decreased in the infected rats compared to controls (Mann Whitney p=0.049). Among infected rats ADC values were significantly decreased from 30 to 36 hours (Mann Whitney p=0.015). The significant changes in ADC values in rats with meningitis were associated with highly significant differences in clinical and neurological scores (Mann Whitney p<0.001). The diagnosis of hydrocephalus was more frequent in rats with low ADC values (36-42h) compared to the previous time points (1/12 versus 6/8, Fisher’s exact test p=0.0044).

Conclusion:

Brain cortex ADC values in experimental meningitis change over time reflecting edema formation. In the early stages of meningitis, increased brain ADC values are most likely due to vasogenic edema. The late finding of decreased ADC values suggests the formation of cytotoxic edema or compression of cortical tissue as a result of ventricular expansion due to hydrocephalus. This study suggests that the measurement of ADC could support the staging of the disease in the clinic.

Materials and Methods:

Wistar male rats (ca. 280g) were injected intracisternally with 30µl of a suspension containing 1 x 10⁵ CFU/ml of a Streptococcus pneumoniae serotype 3 strain (n=29) or on equal volume of saline (control group, n=13). T1W, T2W, quantitative diffusion (along the z-axis), dynamic contrast enhanced MRI and post contrast T1W images were obtained at 6, 12, 24, 30, 36, 42 and 48 hours after inoculation using a Varian SISCO 4.7T imaging system. Prior to imaging a thorough clinical and neurological assessment of each rat was performed. ADC maps were calculated from images acquired with b-values of 0, 185, 740 and 1665 s/mm². Regions of interest were drawn around the cortex of each hemisphere in three brain slices. After imaging rats were euthanized and brains perfused with paraformaldehyde for histopathology. Matched histopathological sections were obtained.

Figure 1: Changes in cortex ADC values with time

Figure 2: T2W images showing hydrocephalus together with matching histological slices in the three slices used to select the ROIs

Figure 3: Matched histological (a & c) and MR sections showing an example of localized vessel- and tissue damage. Note the decreased T2W signal intensity (b) and decreased ADC value (d) in the affected area (arrowed).