DYNAMIC SUSCEPTIBILITY CONTRAST MR PERFUSION IMAGING OF THE BRAIN IN X-LINKED ADRENOLEUKODYSTROPHY

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Background: X-linked Adrenoleukodystrophy (ALD) is a genetic disorder that leads to accumulation of very long-chain fatty acids in the brain, spinal cord and adrenal glands. The disorder manifests as inflammatory demyelination of the brain (cerebral ALD) or as non-inflammatory chronic axonopathy of the spinal chord (adrenomyeloneuropathy, AMN). Previous pathological studies have demonstrated a well-defined zonal pathology of white matter in cerebral ALD, with five different zones reflecting different pathological changes [1]. The purpose of this study is to provide a first assessment of perfusion abnormalities in patients with ALD and AMN as well as their relationship with conventional MRI findings.

Methods: Dynamic Susceptibility Contrast (DSC) MR perfusion was performed in 3 patients with cerebral ALD, 3 patients with AMN, 2 patients with asymptomatic ALD, and 2 normal controls using 1.5T MR units (GE and Siemens). MR perfusion data was post-processed using the nordicICE Perfusion module (NNL, Nordic Neurolab, Norway). Normalized CBV (nCBV) maps were obtained and co-registered with post contrast T1 and FLAIR images using this software and regions of interest within different well-defined areas of abnormal signal in the white matter were drawn and average nCBV values were measured.

Results: In cerebral ALD patients co-registration of post contrast T1 weighted and FLAIR images resulted in the segmentation of the white matter involvement in five different zones based on their signal characteristics: Zone A (central, FLAIR hyperintense, non enhancing), zone B (FLAIR hyperintense, with abnormal enhancement), zone C (FLAIR isointense, non enhancing, immediately outside zone B), zone D (FLAIR hyperintense, non enhancing, between zones C and E) and zone E (normal appearing white matter). DSC MR perfusion in symptomatic patients with ALD demonstrates a reproducible pattern of markedly decreased nCBV within zone A in comparison with normal controls (mean 0.38 ± 0.19; $p < 0.001$), relatively preserved to mildly increased nCBV in zones B and C (mean 0.9 ± 0.35 and 0.8 ± 0.19 respectively; $p > 0.05$), mild to moderately decreased nCBV in zone D (mean 0.55 ± 0.2; $p < 0.01$) and normal nCBV in zone E (mean 0.86 ± 0.12; $p > 0.05$). In asymptomatic ALD and symptomatic AMN patients, nCBV values were slightly but significantly decreased within the T2 hyperintense white matter abnormalities (mean 0.46 ± 0.21 and 0.58 ± 0.07 respectively; $p < 0.01$), without a defined zonal anatomy. nCBV values were uniform in normal controls without regional differences within the white matter (mean 0.94 ± 0.1).

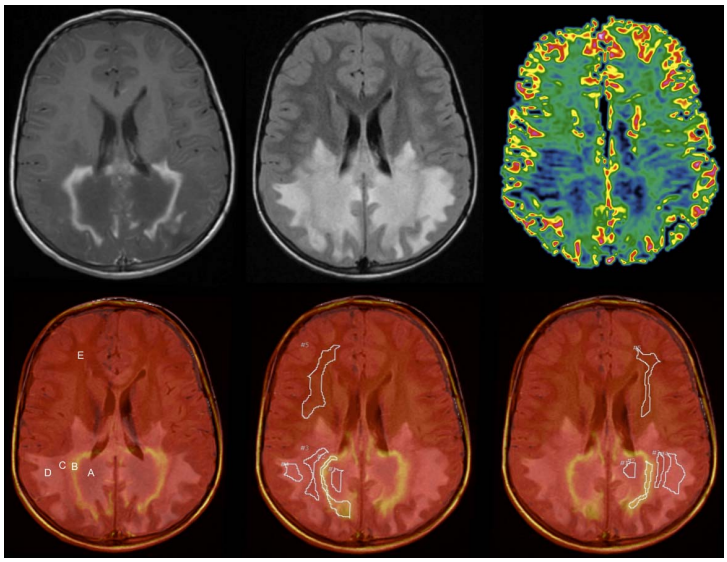

Figure. Nine-year-old male patient with symptomatic ALD. Post-contrast axial T1-weighted, FLAIR, nCBV map and fusion images (with regions of interest) are shown. Five different zones of involvement are noted in the white matter, with nCBV values markedly decreased within zone A, preserved to mildly increased values in zone B-C, slightly decreased in zone D and normal values in zone E.

Conclusion: Zonal abnormalities of brain MR perfusion were found in patients with cerebral ALD but not AMN or asymptomatic ALD patients. The novel observation of in vivo brain MR perfusion abnormalities corresponds to the known zonal pathology on autopsy of cerebral ALD patients. This finding may assist in predicting disease progression [2], selecting candidates for bone marrow transplantation and elucidating the pathophysiology of inflammatory demyelination in ALD.

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References:

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