Proton spectroscopy and imaging at 3T in Ataxia Telangiectasia

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Introduction: Ataxia Telangiectasia (A-T) is an autosomal recessive disorder caused by a defect on chromosome 11. Typical clinical features include cerebellar ataxia, abnormal clusters of blood vessels in the eyes and skin (telangiectasia) and immune system deficiency. A-T patients are also at increased risk of developing cancer, due to reduced ability to repair DNA damage caused by ionising radiation. This study sought to characterise the imaging and proton spectroscopic appearances of A-T at 3T.

Methods: The study group comprised 12 patients with known A-T (7 male, 5 female; mean age=31.8 years) and 11 age-matched controls (6 male, 5 female; mean age =32.9 years). All subjects underwent imaging at 3T (Intera, Philips Medical Systems, Holland). T2-weighted images were acquired using an axial turbo spin echo technique (TR=3000 ms, TE=80ms, α=90°) and T2*-weighted images were acquired using a fast field echo technique (TE=18ms, TR=1144ms, α=18°). A consensus, qualitative evaluation of cerebellar atrophy was made by 2 experienced raters (normal, mild, moderate, severe). Proton spectra were acquired using a PRESS (TR=2000ms, TE=144ms, 256 averages) technique from (i) a 2x1x1cm^3 single voxel placed in the dentate region of right cerebellar white matter and (ii) a 2x2x2cm^3 voxel placed in the right peritrigonal parieto-occipital white matter (POWM). Results are expressed as the ratios of the areas under the 3 prominent resonances due to N-acetyl-aspartate (NAA), choline (Cho) and creatine (Cr). Statistical analysis was performed using a non-parametric Mann-Whitney U-test.

Results: All 12 A-T patients demonstrated severe cerebellar atrophy. Three of the controls had mild atrophy whilst the remaining 7 were normal. Four A-T patients had capillary telangiectasia best depicted on T2*-weighted imaging (2 solitary, 2 multiple). Example multiple telangiectasias are demonstrated in figures 1a & b.

Fig.1a T2-weighted image from an A-T patient.

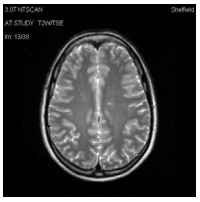
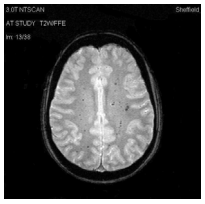


Fig. 1b Corresponding T2*-weighted image.



Spectra from 3 A-T patients were unusable; thus the results from 9 controls were matched to the remaining patients for statistical analysis. Figures 2a and 2b show sample spectra from an A-T patient for the POWM and cerebellum.

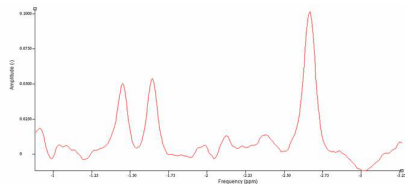


Fig. 2a Sample A-T spectrum from POWM.

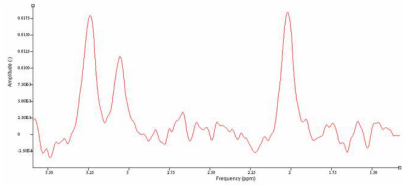


Fig. 2a Sample A-T spectrum from dentate region of the cerebellum.

Fig. 3a cerebellum NAA/Cho.

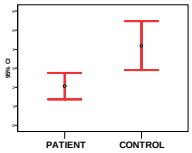
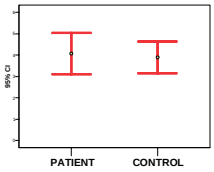


Fig. 3b POWM NAA/Cho.



Significantly lower cerebellar NAA/Cho (P=0.002, fig 3a) and higher cerebellar Cho/Cr (p=0.008) were observed in the A-T compared to control groups. No significant differences were found in cerebellar NA/Cr or in any of the metabolite ratios from POWM (fig3b).

Discussion: Histological studies of the cerebellum show loss of purkinje and granule cells and small telangiectasias within white matter. The present study documents the imaging appearances of telangiectasia in the studied cohort. Unsurprisingly, the presence of capillary telangiectasias are best depicted on T2*-weighted imaging. The spectroscopic results imply an increase in the cerebellar Cho signal at TE=144ms in patients with A-T. As in acute demyelination, this may be indicative of active membrane breakdown, suggesting that the atrophy demonstrated on imaging is an ongoing process. Other ataxias (for example gluten-related ataxia, abstract submitted to this conference) often show abnormalities in the NAA resonance at 2.02ppm and the lack of similar significant abnormality in A-T suggests a discriminatory role for proton spectroscopy.