Marie-Josée DURAN

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PubMed Results

Items 1 - 8 of 8

1. Mol Genet Metab. 2011 Nov 10. [Epub ahead of print]

Adrenoleukodystrophy in female heterozygotes: Underrecognized and undertreated.

Jangouk P, Zackowski KM, Naidu S, Raymond GV.

Source

Department of Neurology, Kennedy Krieger Institute, Research Fellow, Johns Hopkins School of Medicine, Baltimore MD, USA.

Abstract

X-linked adrenoleukodystrophy (X-ALD) is a neurodegenerative disease resulting from mutations in the gene ABCD1 and alterations in peroxisomal beta-oxidation of long chain fatty acids. As it has been frequently discussed, it manifests a wide range of phenotypes in male, with progressive myelopathy being the most common. Even though the gene is localized to the X-chromosome and a region subject to X-inactivation, female carriers still are affected significantly by this condition. It has been stated that between 20 and 50% of women who are carriers may manifest some symptoms and recent evidence has suggested the differences in disease manifestations and relative rates of progression between men and women. However there have been only limited studies specifically addressing this and to date there has been no comprehensive review discussing the different phenotypes in female carriers, as well as the differences in disease onset, progression, disability, nervous system pathology and neuroimaging patterns compared to affected males. This is of key importance as similarities and differences between genders

will assist in determining how best to target therapies in all affected individuals as opportunities for treatment present themselves. As will be further addressed in this review, we need to improve our understanding of the associations of emergent neuroimaging techniques to physical disability in this population. We reviewed the clinical presentations in the carrier population, the distinct disability profile and neuroimaging findings in order to put together pieces of this neglected segment in X-ALD and give direction to further studies.

PMID:
22112817
[PubMed - as supplied by publisher]
Related citations

2. Magn Reson Med. 2009 Jan;61(1):22-7.

Quantitative magnetization transfer characteristics of the human cervical spinal cord in vivo: application to adrenomyeloneuropathy.

Smith SA, Golay X, Fatemi A, Mahmood A, Raymond GV, Moser HW, van Zijl PC, Stanisz GJ.

Source

Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA. smith@mri.jhu.edu

Abstract

Magnetization transfer (MT) imaging has assessed myelin integrity in the brain and spinal cord; however, quantitative MT (qMT) has been confined to the brain or excised tissue. We characterized spinal cord tissue with qMT in vivo, and as a first application, qMT-derived metrics were examined in adults with the genetic disorder Adrenomyeloneuropathy (AMN). AMN is a progressive disease marked by demyelination of the white matter tracts of the cervical spinal cord, and a disease in which conventional MRI has been limited. MT data were acquired at 1.5 Tesla using 10 radiofrequency offsets at one power in the cervical cord at C2 in 6 healthy volunteers and 9 AMN patients. The data were fit to a two-pool MT model and the macromolecular fraction (M(ob)), macromolecular transverse relaxation time (T(2b)) and the rate of MT exchange (R) for lateral and dorsal column white matter and gray matter were calculated. M(ob) for healthy volunteers was: WM = 13.9 +/- 2.3%, GM = 7.9 +/- 1.5%. In AMN, dorsal column M(ob) was significantly decreased ($P < 0.03$). T(2b) for volunteers was: 9 +/- 2 micros and the rate of MT exchange (R) was: WM = 56 +/- 11 Hz, GM = 67 +/- 12 Hz. Neither T(2b) nor R showed significant differences between healthy and diseased cords. Comparisons are made between qMT, and conventional MT acquisitions.

PMCID: PMC2632947
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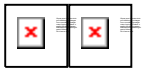
PMID:
19097204
[PubMed - indexed for MEDLINE]
Related citations



3. Arch Neurol. 2006 Jan;63(1):74-80.

Sensorimotor function and axonal integrity in adrenomyeloneuropathy.

Zackowski KM, Dubey P, Raymond GV, Mori S, Bastian AJ, Moser HW.

Source

Kennedy Krieger Institute, The Johns Hopkins University; Baltimore, MD 21205, USA.

Abstract

BACKGROUND:

Gait abnormalities and sensorimotor disturbances are principal defects in adrenomyeloneuropathy (AMN). However, to our knowledge, their association with overall impairment and neuroanatomical changes has not been defined.

OBJECTIVES:

To understand how sensorimotor impairments create mobility deficits and to analyze how these impairments are related to specific metrics of axonal integrity.

DESIGN:

Cross-sectional study assessing impairments, including vibration sensation, strength, spasticity, and global measures of walking and balance. Fractional anisotropy was measured to evaluate the integrity of the corresponding brainstem tracts.

PARTICIPANTS:

Men with AMN and healthy control subjects.

RESULTS:

Individuals with sensory loss only showed minimal walking deficits. Concomitant strength and sensory loss resulted in slower walking, with abnormal knee control; increased spasticity led to an exaggerated trunk motion and a knee-flexed (crouched) posture. Hip strength was an independent predictor of walking velocity in subjects with AMN. Subjects with sensory loss only had greater sway amplitudes during standing balance testing, which did not worsen with additional impairments. There were significant associations among sway amplitude, great toe vibration sense, and dorsal column fractional anisotropy. Brainstem fractional anisotropy in AMN was significantly negatively correlated with impairment, indicating that overall tract integrity is associated with sensorimotor abnormalities in AMN.

CONCLUSIONS:

Impairment measures capture specific abnormalities in walking and balance that can be used to direct rehabilitation therapy in AMN. Tract-specific magnetic resonance imaging metrics, such as fractional anisotropy (used herein to evaluate structure-function relationships), significantly reflect disease severity in AMN.

Free Article

PMID:
16401738

[PubMed - indexed for MEDLINE]
Related citations

4. Ann Neurol. 2005 Nov;58(5):758-66.

Diffusion tensor-based imaging reveals occult abnormalities in adrenomyeloneuropathy.

Dubey P, Fatemi A, Huang H, Nagae-Poetscher L, Wakana S, Barker PB, van Zijl P, Moser HW, Mori S, Raymond GV.

Source

Department of Neurogenetics and Functional Magnetic Resonance Imaging Kirby Center, Kennedy Krieger Institute, Baltimore, MD 21205, USA.

Abstract

"Pure" adrenomyeloneuropathy (AMN) is the noninflammatory myeloneuropathic variant of X-linked adrenoleukodystrophy, where the disease process appears to be restricted to spinal cord tracts and peripheral nerves. The absence of obvious brain involvement makes it distinct from the inflammatory cerebral phenotypes of X-linked adrenoleukodystrophy. However, some pure AMN patients later experience development of cerebral demyelination, but little is known about the extent of brain involvement in pure AMN patients who have normal brain magnetic resonance imaging. We used diffusion tensor imaging to investigate possible occult cerebral abnormalities in such pure AMN patients. Fractional anisotropy and trace were studied in three-dimensional reconstructions of white matter tracts commonly involved in cerebral phenotypes of X-linked adrenoleukodystrophy. Results demonstrated reduced fractional anisotropy and increased trace in bilateral corticospinal tracts and genu of corpus callosum ($p < 0.05$). Diffusion tensor imaging-based three-dimensional fiber tracking showed occult tract-specific cerebral microstructural abnormalities in pure AMN patients who had a normal conventional brain magnetic resonance image. Corticospinal tract abnormalities could reflect a centripetal extension of spinal cord long-tract distal axonopathy. Accompanying abnormalities in genu of corpus callosum indicate that the disease pathology in pure AMN may not be limited to spinal cord long tracts alone, although the involvement of the latter is most prominent and severe.

PMID:
16240348
[PubMed - indexed for MEDLINE]
Related citations

5. Neurology. 2005 May 24;64(10):1739-45.

Magnetization transfer MRI demonstrates spinal cord abnormalities in adrenomyeloneuropathy.

Fatemi A, Smith SA, Dubey P, Zackowski KM, Bastian AJ, van Zijl PC, Moser HW, Raymond GV, Golay X.

Source

Neurogenetics Research Center, Kennedy Krieger Institute, Department of Neurology, Johns Hopkins University, Baltimore, MD, USA.

Comment in

- Neurology. 2005 May 24;64(10):1677-8.

Abstract

BACKGROUND:

In adrenomyeloneuropathy (AMN) conventional MRI detects only spinal cord atrophy in the late stages.

OBJECTIVE:

To apply a magnetization transfer-weighted (MTw) imaging to patients with AMN and AMN-like syndrome in order to visualize and quantitatively assess the pathology of white matter tracts in the cervical spinal cord.

METHODS:

MTw studies were conducted in nine men with AMN, eight symptomatic heterozygous women, and 10 age- and sex-matched controls and compared to the Expanded Disability Status Scale (EDSS) and quantitative tests of vibratory sense and postural sway. MTw data sets were obtained at the level of C1 to C3 using a three-dimensional gradient echo acquisition technique, these images were then standardized between subjects by using the in-slice CSF signal as a normalization reference, allowing a quantitative assessment of the MTw signal.

RESULTS:

In contrast to conventional MRI, MTw images showed signal hyperintensities in the lateral and dorsal columns of all patients. The MT signal quantified in the dorsal column showed significant differences between patients with AMN, X-linked adrenoleukodystrophy heterozygotes, and controls. MT hyperintensity in the dorsal column correlated with EDSS, vibratory sense, and postural sway.

CONCLUSION:

Magnetization transfer-weighted imaging is a sensitive modality for the visual and quantitative assessment of spinal cord pathology in adrenomyeloneuropathy, and is a potential tool for evaluation of new therapies.

PMID:
15911801
[PubMed - indexed for MEDLINE]

Related citations

6. Neurology. 2005 Jan 25;64(2):304-10.

Spectroscopic evidence of cerebral axonopathy in patients with "pure" adrenomyeloneuropathy.

Dubey P, Fatemi A, Barker PB, Degaonkar M, Troeger M, Zackowski K, Bastian A, Smith SA, Pomper

MG, Moser HW, Raymond GV.

Source

Departments of Neurogenetics, Kennedy Krieger Institute, Johns Hopkins University, Baltimore, MD, USA.

Abstract

BACKGROUND:

Adrenomyeloneuropathy (AMN) is the adult variant of X-linked adrenoleukodystrophy. The disease pathology is usually limited to spinal cord and peripheral nerves, and when this is the case, it is referred to as "pure" AMN. Histopathology shows cerebral involvement even in pure AMN; however, not much is known about the nature, extent, and clinical relevance of these findings.

OBJECTIVE:

To investigate brain involvement in AMN patients with normal MRI, employing multislice MR spectroscopic imaging.

METHODS:

Twelve men with pure AMN were compared with 19 age-matched healthy volunteers. Metabolite ratios (N-acetylaspartate [NAA]/choline [Cho], NAA/creatine [Cr], and Cho/Cr) were measured from seven brain regions. Global metabolite ratios were generated as an average of these seven regional ratios. The Expanded Disability Status Scale (EDSS) was used for neurologic evaluation.

RESULTS:

The patients with AMN showed reduced global NAA/Cho (AMN 1.40 +/- 0.16 vs controls 1.75 +/- 0.34; p = 0.003)) and global NAA/Cr (AMN 2.32 +/- 0.13 vs controls 2.62 +/- 0.43; p = 0.03). Regionally, NAA/Cho was lowered in the internal capsule (AMN 1.30 +/- 0.20 vs controls 1.69 +/- 0.37; p = 0.002) and in parieto-occipital white matter (AMN 1.45 +/- 0.19 vs controls 1.78 +/- 0.55; p = 0.04). NAA/Cr was lowered in parieto-occipital white matter (AMN 2.34 +/- 0.31 vs controls 2.83 +/- 0.71; p = 0.04). EDSS demonstrated an inverse association with global NAA/Cr (r = -0.65, p = 0.02) and NAA/Cr in centrum semiovale (r = -0.73, p = 0.006) and in parieto-occipital white matter (r = -0.64, p = 0.02). Cho/Cr was not significantly elevated.

CONCLUSIONS:

(1)H-MR spectroscopic imaging is able to detect biochemical abnormalities suggestive of axonal damage even in the brains of patients with pure adrenomyeloneuropathy. The axonopathy is most prominent in internal capsule and parieto-occipital white matter and may contribute to clinical disability.

PMID:
15668429
[PubMed - indexed for MEDLINE]

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7. Neurology. 2003 Apr 22;60(8):1301-7.

MRI and proton MRSI in women heterozygous for X-linked

adrenoleukodystrophy.

Fatemi A, Barker PB, Uluğ AM, Nagae-Poetscher LM, Beauchamp NJ, Moser AB, Raymond GV, Moser HW, Naidu S.

Source

Kennedy Krieger Institute, Johns Hopkins Medical Institutions, Baltimore, MD 21287, USA. barker@mri.jhu.edu

Abstract

OBJECTIVE:

To utilize neuroimaging procedures to assess the extent of cerebral involvement in female subjects heterozygous for X-linked adrenoleukodystrophy (X-ALD).

METHODS:

Brain MRI studies were performed in 76 female subjects heterozygous for X-ALD (mean age 43 years, range 8 to 75 years). Sixty-five had clinical evidence of spinal cord involvement resembling that in males with adrenomyeloneuropathy (AMN), two had clinical evidence of cerebral involvement, and nine showed no neurologic abnormality. Readers blinded to clinical findings further analyzed abnormal MRI studies. In eight women whose MRI results were normal, four-slice long echo time MRS imaging (MRSI) studies were performed and compared to those of eight age-matched controls.

RESULTS:

MRI results were normal in 65 subjects and abnormal in 11. In eight of the latter group, the MRI changes were judged to be due to causes other than X-ALD. Lesions were attributed to X-ALD in the remaining three. Two of these patients had lesions that resembled those in male patients with cerebral X-ALD. In one patient with a mild AMN-like syndrome, brain MRI abnormalities were confined to the corticospinal tract. When compared to those of controls, MRSI studies in eight female patients with normal results on brain MRI showed a significant reduction of N-acetylaspartate/creatine and N-acetylaspartate/choline ratios in the internal capsule and corticospinal projection fibers. The N-acetylaspartate/choline ratio was significantly reduced in the parieto-occipital white matter and the choline/creatine ratio was significantly increased in the frontal white matter.

CONCLUSION:

Brain involvement demonstrable by MRI is rare in female subjects heterozygous for X-ALD, including those who have clinical evidence of spinal cord involvement. Nevertheless, N-acetylaspartate levels are reduced in the corticospinal projection fibers in female subjects with normal results on MRI, suggesting axonal dysfunction.

PMID:
12707433
[PubMed - indexed for MEDLINE]

Related citations

8. Ann Neurol. 2001 Feb;49(2):186-94.

Evolution of phenotypes in adult male patients with X-linked adrenoleukodystrophy.

van Geel BM, Bezman L, Loes DJ, Moser HW, Raymond GV.

Source

Department of Neurology, Kennedy Krieger Institute, Johns Hopkins University, Baltimore, MD 21205, USA.

Abstract

Our objective was to study the phenotype evolution of X-linked adrenoleukodystrophy (X-ALD) and the relation between axonal degeneration and cerebral demyelination. Although different X-ALD phenotypes are recognized, little is known about their evolution. Neuropathological and electrophysiological studies have shown that X-ALD is a disease with mixed features of axonal degeneration, leading to myeloneuropathy, and a severe inflammatory reaction in the cerebral white matter, resulting in demyelination. Retrospectively, 129 men with X-ALD were studied who were 1) at least 20 years presently or at the time of death, and 2) regularly monitored. Phenotype assignments were made at diagnosis and at present, or at death, using medical history and findings of neurological examination. Handicap was studied with the modified Rankin scale, and cerebral abnormalities with the X-ALD MRI severity (Loes) score. The mean follow-up interval was 10.1 +/- 5.0 years. Among 32 patients neurologically asymptomatic at diagnosis, 16 (50%) developed neurological deficits. Among 68 adrenomyeloneuropathy (AMN) patients initially without clinical brain involvement, 13 (19%) additionally developed cerebral demyelination. In a subset of 60 AMN patients, a moderate handicap evolved over a period of 16.2 +/- 8.9 years. Among 13 AMN patients with additional definite or probable cerebral involvement at diagnosis, eight died and one remained in a vegetative state. Most of the 16 patients with the cerebral phenotypes deteriorated. There is a high risk for adult neurologically asymptomatic patients to develop neurological deficits and for AMN patients to develop cerebral demyelination. Axonal degeneration and cerebral demyelination emerge in X-ALD independently of each other. This may have implications for the phenotype classification, the search for modifying factors, and the development and evaluation of new therapies.

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11220738
[PubMed - indexed for MEDLINE]

Related citations