

CASE REPORT

MRI SPECTRUM OF X – LINKED ADRENOLEUKODYSTROPHY

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ABSTRACT: X-linked adrenoleukodystrophy is an inherited disorder of peroxisome metabolism which has a debilitating and often fatal course if untreated. Imaging plays an important role in diagnosis, characterizing and prognosticating these patients and several MR findings have been reported in the brain. We hereby discuss in detail the various MR imaging findings of this condition through presentation of a typical case. Most patients present late in disease with onset of severe neurological symptoms and then do not respond to most available treatment options. Thus, it is very important for physicians and radiologists alike to aware of this condition and its imaging findings so as to enable early diagnose of this condition, offering the best survival chances for the patient.

CASE REPORT: A 17-year-old male of poor socio-economic background presented with fever and decreased urine output for 2 days. The patient was ill for the last 4 to 5 years for which he was being treated symptomatically at home. At the age of about 13 years, he developed gradual difficulty in walking with stumbling gait. He was bed-ridden for the last one year and developed urinary incontinence over the last few months. Since last one year he had decreased response to commands and developed a staring gaze. He also had three episodes of seizures over the last two years for which he was receiving antiepileptics.

The patient was febrile at the time of this admission. The mother gave history of decreased oral intake for last 5 days. There was also decreased urine output for 2 days. On physical examination, the patient was conscious but not responding well to oral commands. However, he appeared to be well oriented in time and person and was able to communicate with his mother.

His blood pressure was low (96/56 mm Hg) at the time of admission. The other vital parameters were stable and examination of the respiratory and cardiovascular system did not reveal any

CASE REPORT

abnormality. Examination of the central nervous system revealed bilateral lower limb spasticity but the patient was able to move all four limbs. The deep tendon reflexes were normal in the upper limbs and brisk in the lower limbs. The plantar reflexes were up going in both lower limbs. The Routine blood investigations and electrolytes were normal. Blood sugar was normal. Lumbar puncture was also performed and CSF analysis revealed raised proteins (60mg/ml).

The patient was referred for an MRI scan, which was performed on a Seimens Avanto 1.5T scanner with a standard head matrix.

There was bilateral symmetric white matter involvement with relative sparing of the subcortical U-fibres, predominantly in the occipital lobes. The involved white matter appeared of low signal intensity on T1 weighted images and high signal intensity on T2 and FLAIR images, especially in the peritrigonal white matter on both sides. The corticospinal tracts and the deep white matter of both cerebral hemispheres also showed T2 hyperintensity. The involved areas showed patchy restriction on diffusion weighted images predominantly at the outer edges of the abnormal white matter. On contrast injection, 'leading edge enhancement' was noted involving the outer edges of the involved white matter in both cerebral hemispheres. MR Spectroscopy revealed decrease in N-acetyl aspartate (NAA) and increase in choline (Cho) levels as compared to the baseline creatine (Cr) along with peaks at 0.9 and 1.3 ppm, probably representing very long chain fatty acids. A diagnosis of adrenoleukodystrophy was proposed.

On further investigation, the patient had features of adrenal insufficiency. He had mildly increased skin pigmentation and weighed just 41 kgs. Examination of a sample of blood plasma revealed the presence of long chain fatty acids confirming the diagnosis of adrenoleukodystrophy.

The patient was put on corticosteroid therapy for adrenal insufficiency. However, not much improvement was noted. Urine examination showed numerous pus cells indicating a urinary tract infection (probably the cause of fever and presentation of the patient), which was treated with antibiotics.

DISCUSSION: Childhood Cerebral Adrenoleukodystrophy (CCALD) is an inherited disorder of Peroxisome metabolism involving impaired metabolism of very long chain fatty acids (VLCFA) which accumulate in the white matter of brain causing damage to the myelin and demyelination¹. The spinal cord may also be involved in a related condition called adrenomyeloneuropathy (AMN). Several different phenotypes of the disease are described and they differ due to different genes being involved.

VLCFAs are also deposited in the adrenal cortex causing adrenal insufficiency, which may produce an Addison's like picture, and in the Leydig cells of testes which may cause androgen deficiency.

CCALD usually affects preteen males and is the commonest form of X-linked adrenoleukodystrophy. The patient usually presents with behavioural abnormalities and difficulty in hearing, vision, gait and learning. Later, the CNS manifestations progress to spastic quadriplegia and maybe associated with urinary and bowel incontinence ultimately leading to a bed-ridden vegetative state². Adrenal insufficiency may cause bronze pigmentation of skin, fatigue, nausea and vomiting. This may also cause male pattern baldness in young adults. Death may occur in 2-5 years if bone marrow transplant is not done.

CASE REPORT

MRI is the radiological investigation of choice to demonstrate the white matter involvement. The affected white matter usually includes the splenium of corpus callosum, peritrigonal white matter, corticospinal tracts, the fornical and commissural fibres and the visual and auditory pathways. The subcortical U-fibres are usually spared. The occipital and parietal lobes are affected first and frontal lobe affliction is uncommon in early stages. The affected white matter shows high signal intensity on T2 and FLAIR images³ and shows typical 'leading edge enhancement' at the outer edges of the abnormal white matter on post contrast scans⁴. Diffusion restriction is common and patchy, predominantly at the edges of the lesions indicating a progressive nature of the disease and ADC values in the involved areas maybe abnormal even in the absence of obvious T2 abnormality⁵. MR spectroscopy usually reveals decrease in NAA/Cr ratio and increase in Cho/Cr and ml (myoinositol)/Cr ratios consistent with demyelination⁶ and may reveal peaks between 0.9 and 2 ppm due to VLCFA macromolecules⁷.

The CSF may show raised proteins but most other routine investigations are usually normal. The diagnosis is usually confirmed by demonstrating long chain fatty acids in the plasma and urine. The disease is progressive and usually fatal. Hemopoietic stem cell transplant or bone marrow transplant probably offer the best chance of treatment but are effective only in asymptomatic children and those with early symptoms. Once advanced disease (especially neurological features) has set in, the chances of success of transplant are poor. Lorenzo oil (a mixture of glyceryl trioleate and glyceryl trierucate) and a diet low in VLCFAs are said to delay the progress of disease⁸ but have not been proven to be useful in reverting the neurological features and just normalize the blood VLCFA concentrations. In addition, steroid supplements may need to be given to counter associated adrenal and androgen deficiency. However, the outcome is poor. The best chance is to detect presymptomatic patients, especially those with a positive family history, and children with early symptoms by screening their blood for VLCFAs.

CONCLUSION: X-linked adrenoleukodystrophy is a debilitating and often fatal disease if untreated and most patients present late into the disease with onset of severe neurological symptoms. It is very important for physicians and radiologists alike be aware of this condition and its imaging findings so as to enable early diagnose of this condition, offering the best survival chances for the patient.

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CASE REPORT

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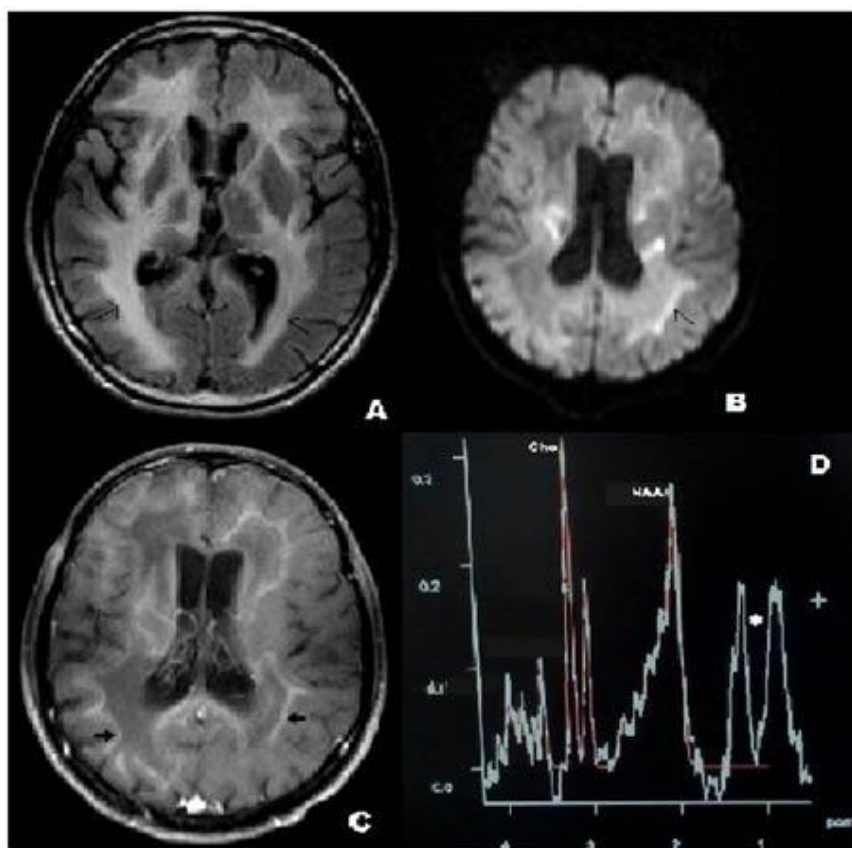


FIGURE LEGEND: MRI (1.5T, Head matrix) of the brain of a 17 year old male:(A)FLAIR axial showing bilateral symmetrical extensive white matter hyperintensity, predominantly affecting the occipital and parietal lobes.(B)Diffusion image at b value of 800 showing patchy restriction, predominantly at the outer edges of involved white matter.(C)Post Contrast T1 image showing leading edge enhancement of the involved white matter.(D)MR spectroscopy showing peaks at about 1 and 1.3 ppm probably representing VLCFA macromolecules in addition to decreased NAA and increased Cho representing demyelination.