

Radiological Quiz – Neuroradiology

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Ind J Radiol Imag 2006 16:1:139-141

A two and a half year old male child presented to our hospital with complaints of progressive spasticity, seizures and visual deficits.

Noncontrast T1W axial, T2W sagittal and TIRM axial images (Fig.1,2,3,4) are shown below. What is the diagnosis?

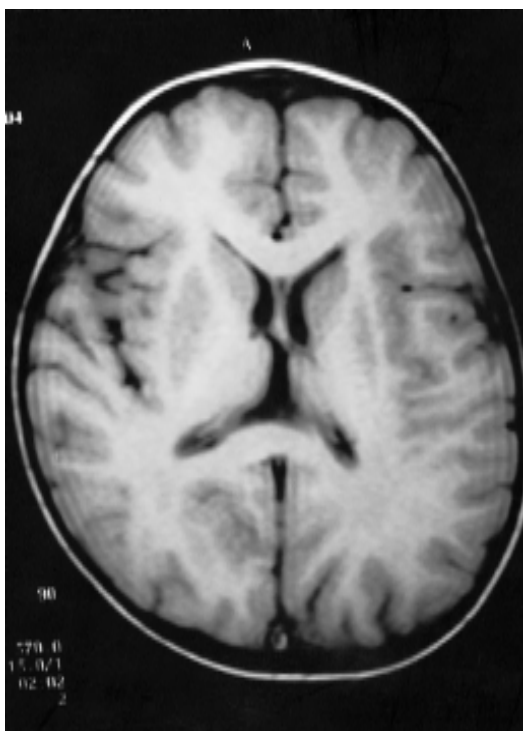


Fig 1

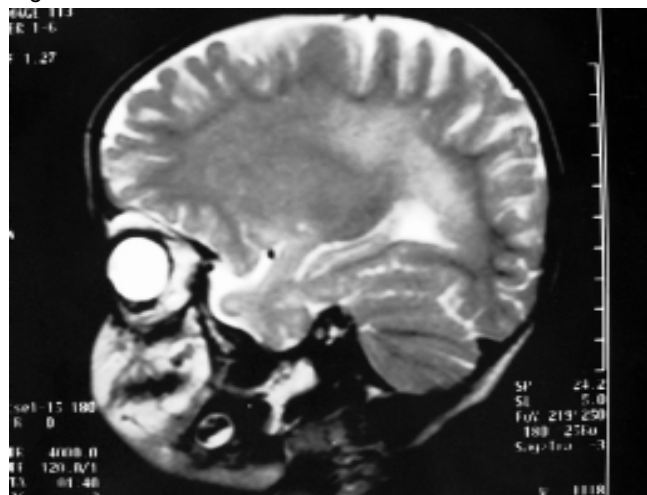


Fig 2

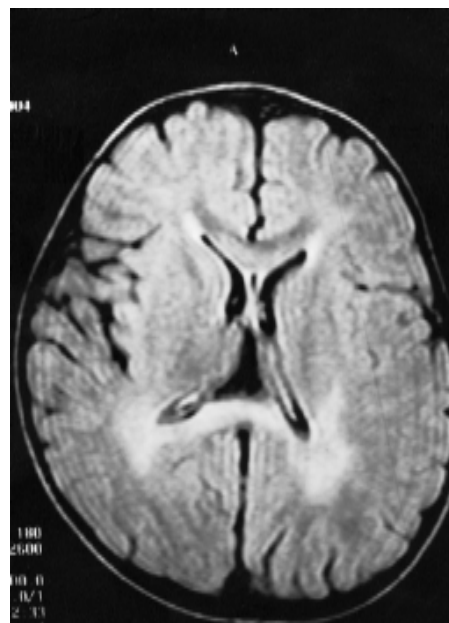


Fig 3

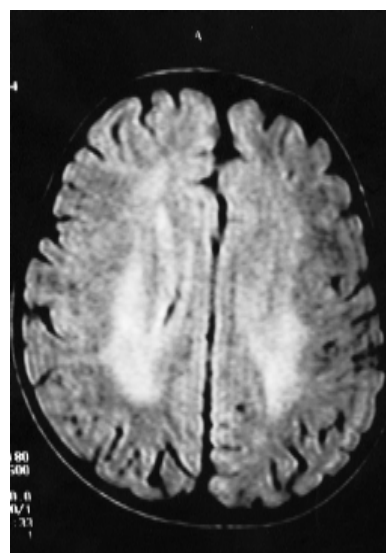


Fig 4

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Received on 11 April 2005; Accepted 12 December 2005

Radiological Diagnosis

ADRENOLEUKODYSTROPHY

MRI reveals symmetric hyperintensities involving bilateral posterior parietal and occipital areas and splenium of corpus callosum on T2W and TIRM sequences suggestive of adrenoleukodystrophy.

Basal serum cortisol levels were slightly less than normal. The diagnosis was confirmed by demonstration of elevated levels of very low chain fatty acids (VLCFAs) in plasma

Adrenoleukodystrophy (ALD) is a hereditary peroxisomal disorder that affects the white matter of the central nervous system (CNS), adrenal cortex and testes (1). It is usually an X-linked recessive disorder with an incidence of 1:50,000. The gene defect in X-linked ALD is located in Xq28, the terminal segment of the long arm of the X chromosome (2). This gene normally encodes for a peroxisomal membrane protein called ALD-P. The genetic defect results in accumulation of saturated VLCFAs. This accumulation causes demyelination of white matter in the CNS, adrenocortical insufficiency and testicular disorders.

The different phenotype forms include cerebral ALD, adrenomyeloneuropathy (AMN) and primary adrenocortical insufficiency without CNS involvement (2). The cerebral form is further subdivided into childhood, adolescent and adult types. The childhood cerebral type manifests most commonly between the ages of 4 and 8 years and is characterized by rapid progressive demyelination of the CNS and adrenal insufficiency. Clinical features include progressive dementia, blindness, deafness and spastic quadriplegia, leading to a vegetative state within 2 years. The less common adolescent and adult forms present after the age of 10 years with similar but less rapidly progressive neurological and neurocognitive deficits. In most cases, bilateral demyelination of white matter is seen involving the parieto-occipital areas extending across the corpus callosum, but lesions can also appear in the frontal white matter. Three pathological zones called Schaumburg's zones are described in the affected white matter. Zone A is a central burned out zone of scarring with gliosis and scattered astrocytes. The adjacent zone B contains numerous perivascular inflammatory cells and is characterized by demyelination. The outermost zone C is characterized by ongoing demyelination with active destruction of myelin sheaths but with a lack of perivascular inflammatory cells (3).

The most common phenotype is AMN and these patients typically present in the third or fourth decade with progressive spastic paraplegia, sphincter disturbances, peripheral neuropathy and ataxia. It involves mainly the

spinal cord and peripheral nerves but 35% patients with AMN subsequently develop cerebral demyelination. Primary adrenocortical insufficiency with no neurological deficits may be seen in a minority of patients.

The laboratory diagnosis of ALD depends upon the demonstration of increased levels of VLCFAs in plasma and fibroblast cultures. Mutation analysis is the most reliable method for heterozygote identification. Reliable methods for prenatal screening are available. Systematic screening for at-risk family is also recommended because it identifies affected males at a stage when therapy has the greatest chance of success and allows for accurate identification of heterozygotes (4).

On plain CT, ALD characteristically shows symmetric confluent low density areas in the parieto-occipital regions, adjacent to the trigone of the lateral ventricles and continuous across the midline via the splenium of the corpus callosum (5).

MRI imaging is a powerful tool for early detection of CNS abnormalities, distinguishing active demyelination from gliosis and monitoring disease progression in ALD. In cerebral ALD, three patterns are described on MRI imaging. The most common pattern (80%) is characterized by confluent T1 and T2 prolongation of the deep parieto-occipital white matter, splenium and posterior body of corpus callosum, visual pathway, auditory pathway and cortico-spinal tracts. The second pattern (15%) is characterized by similar changes involving the deep anterior frontal white matter, genu and anterior body of the corpus callosum, frontopontine tract, and deep white matter of the cerebellum. Projectional white matter fibres are involved in the third pattern (5%) (2). Characteristic contrast enhancement patterns are seen involving the periphery of the involved white matter corresponding to zone B on CT and T1 weighted MRI images. The enhancement is attributed to the breakdown of blood-brain barrier resulting from an auto-immune or cytokine mediated immune process and may be useful in predicting the natural history of the disease (1). Follow up MRI typically shows central to peripheral progression with cortical gray matter involvement and focal and generalized brain atrophy late in the disease (2). Magnetization transfer MR imaging can differentiate regions of early demyelination from regions of irreversible white matter destruction and can help quantify disease burden, gauge progression of disease and monitor effects of therapy. Diffusion weighted MR imaging may provide a sensitive marker for early white matter injury in ALD. Elevation of choline containing compounds to total creatinine ratio and

reduction of N-acetyl-L-aspartate to total creatinine ratio is seen in affected areas on MR spectroscopy. The elevation of the choline peak is most pronounced in regions of active demyelination while the reduction in N-acetyl-L-aspartate is most pronounced in regions of axonal loss and gliosis (2).

In AMN, MRI often shows no abnormality. Infrequently spinal cord atrophy and T2 hyperintensity may be present.

Therapeutic options include adrenal steroid replacement therapy for all patients with adrenal insufficiency. Bone marrow transplant benefits boys and adolescents with early brain involvement, and patients in this category should be searched for by MRI screening at 6-12 months interval. Lorenzo's oil appears to have a preventive effect in boys who are less than 6 years old, are neurologically asymptomatic and have a normal MRI, and is recommended for this group (4). Other therapies being investigated include lovastatin, 4- phenylbutyrate and retroviral transfer of the ALD gene into CD34+ cells of patients.

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