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Adrenoleukodystrophy: CT and MRI findings

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Abstract. A case of adrenoleukodystrophy (ALD) with CT and MRI findings is described. The CT scan showed low densities in the white matter of the parietal and occipital lobes. No calcifications were seen. Post-contrast CT showed an abnormal enhancement within the involved white matter. MRI showed changes of demyelination around the atria of the lateral ventricles bilaterally involving the posterior aspect of the cerebrum symmetrically. The posterior part of the posterior corpus callosum, splenium and pyramidal tracts also showed increased signal intensity. From a review of the literature, these findings are typical of the radiological changes seen in ALD. ALD can be diagnosed from typical history and biochemical changes as well as from CT and MRI findings.

Adrenoleukodystrophy (ALD) is a sex-linked metabolic encephalopathy of childhood in which the basic defect is an impaired capacity to degrade very long chain fatty acids, caused by a peroxisomal defect in beta-oxidation. The fatty acids thus accumulate, decreasing the stability of the myelin membrane and leading to the demyelination of the central nervous system. The adrenal cortex, testes, dermal and conjunctival nerve fascicles are also involved [1].

ALD occurs in three main forms [1, 2]. Neonatal ALD is an autosomal recessive disorder presenting with hypotonia, seizures and psychomotor retardation. It is usually of poor prognosis and is the rarest form. Childhood ALD, an X-linked recessive disorder, is the commonest form, characterized by behavioral disorders and dementia which usually precede adrenal insufficiency. The third form, adrenomyeloneuropathy (AMN), is a sex-linked disorder in young adults, usually presenting with paraparesis and Addison's disease. Those affected usually have siblings with ALD [3].

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ALD can easily be diagnosed without recourse to brain biopsy in view of the typical clinical features given above, including loss of hearing and visual impairment, the biochemical findings of adrenal insufficiency and the classic changes seen during brain imaging. This report documents the findings in a case of ALD, especially those seen on CT and MRI.

Case report

A 9-year-old Syrian boy developed loss of appetite, recurrent vague abdominal pains and recurrent vomiting with cutaneous pigmentations. His past medical history was non-contributory. His parents were not consanguineous and none of his relations had similar symptoms. After $1\frac{1}{2}$ years, he developed deteriorating vision, headaches, unsteady gait and impaired auditory discrimination. He then started to have severe behavioral problems and slurred speech. He had no seizures or loss of consciousness. The fundi were normal. Visual acuity and fields could not be successfully measured due to loss of cooperation.

Laboratory work-up showed normal blood count and electrolytes, cortisol levels: ranging from 7.0 μg/dl to 11.0 μg/dl (normal: 8–28 μg/dl) and after stimulation adrenocorticotropin (ACTH) showed a flat response consistent with primary adrenal insufficiency. His ACTH was elevated at 137 pg/l (normal: 20–80 pg/l), aldosterone level was low at < 4 ng/dl and plasma renin activity elevated at 8 mg/ml per hour (normal: 0.63–1.36 mg/ml per hour). Free fatty acids were 0.15 mmol/l (normal: 0.19–0.9 mmol/l). Addison's disease was diagnosed from the biochemical results and corticosteroid treatment was started.

CT brain scans showed low densities in the white matter of the parietal and occipital lobes. No calcifications were seen (Fig. 1). Post-contrast CT revealed an abnormal enhancement within the involved white matter (Fig. 2). The ventricular system and cerebellar hemispheres were normal.

MRI examination was performed with a high-field, 1.5-T Philips Gyroscan system. It showed demyelination around the atria of the lateral ventricles bilaterally, involving posterior aspects of the cerebrum symmetrically. The posterior part of the posterior corpus callosum, including the splenium and the middle and posterior parts of the pyramidal tracts, also showed increased signal intensity indicating demyelination (Fig. 3). There was an area of enhancement on the gadolinium-enhanced T2-weighted images within the demyelinated white matter representing a zone of active demyelination (Fig. 4).

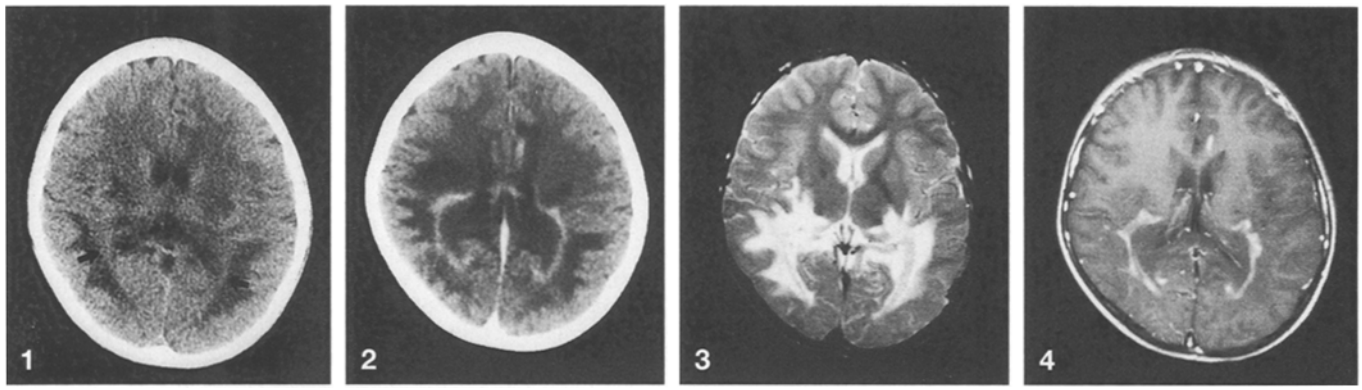

Fig. 1. Unenhanced CT of the brain showing increased low attenuation within the white matter of the parieto-occipital regions extending medially into the regions around the splenium. Note the isodense band within the low density areas *(arrows)*

Fig. 2. Enhanced CT showing marked enhancement, the so-called "garland appearance", within the white matter of the parieto-occipital regions, areas identical with the isodense band seen in Fig. 1. Enhancement is also noted in the medial aspects of the white matter around the anterior aspect of the lateral ventricles

Fig. 3. T2-weighted MRI image showing very intense signals within the entire white matter of both parieto-occipital lobes extending into the posterior part of both internal capsules and thalamus. A curvilinear band of relatively low signal intensity is seen within the white matter, corresponding to the high intensity signals in Fig. 4.

Fig. 4. MRI scan with T2 proton-density-weighted images showing high intensity signals within the white matter around the ventricular atria an appearance similar to those in Fig. 2. Note the intense signal in the left cingulate gyrus

Although a brain biopsy was not performed, a diagnosis of ALD was made on the strength of the typical history and biochemical changes, as well as the CT and MRI findings which were also typical.

Discussion

CT and MR are promising diagnostic techniques in the appraisal of ALD, firstly, in depicting the global anatomy of areas of involvement and secondly, in pinpointing areas of active demyelination.

In 1976, Duda and Huttenlocher first described CT findings in ALD when bilateral hypodensities of the white matter of the parietal and occipital lobes were seen on CT scan [4]. A review of CT findings shows that the typical pattern was of large symmetrical contiguous or confluent low-density lesions with enhancement in the involved white matter, usually in the occipito-parietal and parieto-temporal lobes with subsequent involvement of or spread to the frontal lobes, the midbrain and the pons. The external and internal capsules and the corpus callosum are usually involved. Involvement of the geniculate bodies, visual and auditory pathways is also common [4–9].

Di Chiro et al. described a pattern on CT scans in which there was no hypodensity in the posterior white matter but marked contrast enhancement in areas such as the internal capsule, corona radiata, and cerebral peduncles, which they termed type II [5]. Dubois et al. also noted the typical hypodensity of the peri-atrial white matter with pathological enhancement of the centrum ovale, corpus callosum, internal capsule, cerebral penduncles and pons [6]. Kumar et al. noted that in the terminal disease specific white matter tracts, global radiations, basal ganglia and thalami are involved [10], while cerebral atrophy may be the only change in older patients [11].

Other previously reported atypical findings include unilateral involvement, white matter calcifications, mass effects, and involvement of the frontal lobe, cerebellum and other areas of the CNS [5, 9, 10, 12]. It is presumed that these forms represent phenotypic variants and/or various stages in the temporal evolution of the disease complex with the disease starting bilaterally in the occipital region and spreading outward and forward as a confluent lesion whilst sparing the subcortical unmyelinated fibers [2].

Contrast enhancement occurs within, adjacent to, or anterior to the abnormally hypodense deep white matter of the parieto-occipital complex [10]. It is quite often circumferential giving the so-called "garland appearance" [7]. These areas represent zones of focal blood-brain barrier, corresponding to regions of active demyelination. Our case appears typical, with typical enhancement and extension into the posterior aspect of the internal capsule, basal ganglia, thalami and geniculate bodies.

MRI studies usually show prolongation of the T1 and T2 images of the white matter. Inversion recovery scans may commonly show low signal enhancement with gadolinium. The areas of involvement are similar to those seen on CT but with better detail, extent and resolution.

Enhancement areas seen on contrast-enhanced CT images depict regions of active demyelination (Fig. 2). It is these active areas which show up as high-intensity regions on enhanced T2-weighted MRI images (Fig. 4). Not only do non-enhanced T2-weighted images show areas of demyelination but also the active regions within these areas show relatively low intensity signals. Contrast enhancement is therefore essential both on MRI and CT in mapping out areas of active demyelination more so when one notes that the areas of active demyelination are seen as isodense or non-enhanced CT images (Fig. 1).

MRI has a high sensitivity in demonstrating white matter disease and in identifying in detail the anatomical sites of involvement. In our case the changes seen on MRI were also typical. However, the involvement of the corpus callosum and pyramidal tract seen by MRI were not seen on CT [11]. MRI was the first modality to demonstrate visual and auditory structural disease in ALD [11]. Similarly, it has been used to demonstrate cervical and thoracic cord involvement due to cortico-spinal and spinocerebellar tract degeneration in the ALD-AMIN complex [3]. However, calcifications are poorly demonstrated on MRI, being better visualized on CT [10]. Correlating histological data with MRI images has shown that the gadolinium DTPA enhancing zone in the middle of the lesions corresponds to an area of very active inflammation. This region encircles an inner gliotic area where the destructive process has "burnt out" and where calcification may be seen. The outer region corresponds to a zone of active demyelination with partial loss of myelin [2].

There are many white matter diseases to be excluded in the differential diagnosis of ALD. However, this disease of young children, especially males, has a characteristic pattern of symmetrical high signal in the white matter posteriorly, and is usually associated with adrenal dysfunction. The disease is relentlessly progressive and severe brain atrophy results.

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