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SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY IN ADRENOLEUKODYSTROPHY*

A Case Report

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Adrenoleukodystrophy (ALD) is a genetic disorder leading to progressive dysfunction of the adrenal cortex and nervous system white matter. Accumulation of fatty acids in cerebral white matter results in some anatomical and functional changes which are detectable by imaging studies. Lately, single photon emission computed tomography (SPECT) has been suggested for evaluation of cerebral perfusion changes. In this report, magnetic resonance imaging (MRI) and SPECT neuroimaging of an eight-year-old boy with ALD are presented. SPECT revealed more extensive involvement than that demonstrated by MRI. Its role in early prediction of the extention of disease is stressed.

Key words: adrenoleukodystrophy, magnetic resonance imaging, SPECT neuroimaging.

Adrenoleukodystrophy (ALD) is an X-linked genetic disorder associated with the accumulation of saturated very long chain fatty acids (VLCFA) and progressive dysfunction of the adrenal cortex and nervous system white matter[1]. This accumulation of fatty acids is due to both impaired capacity to degrade them in peroxisomes, possibly related to a defective β oxidation system, and overproduction in microsomes[2,3]. Clinically, ALD is characterized by demyelination of the central nervous system and adrenal insufficiency. In ALD, deposition of fatty acids in cerebral white matter leads to some anatomical and functional changes which are detectable by imaging studies. While computed tomography (CT) and magnetic resonance imaging (MRI) studies domonstrate the anatomical changes, functional brain imaging techniques, positron emission tomography (PET) and signle photon emission computed tomography (SPECT) are gaining widespread use in revealing the characteristic images in childhood neurodegenerative diseases and inborn errors of metabolism[4].

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This report presents the anatomic and functional brain changes of an eight-year-old boy with ALD.

Case Report

An eight-year-old boy was admitted to our clinic for strabismus. His history revealed that he had difficulty with reading and writing during the previous month. Nervousness and some memory defects had also been noted. His parents were unrelated. One of his mother's brothers had died at the age of two years, cause unknown.

On physical examination he had nystagmus and reduced vision. Mild ataxia and positive Babinski sign on the right side were also noted. Contrast-enhanced CT demonstrated symmetrical, hypodense, inactive zones revealing involvement of the periventricular white matter in the posterior parietal and occipital lobes. MRI study showed symmetric increased signal intensity in the white matter of the parieto-occipital region (Fig. 1).

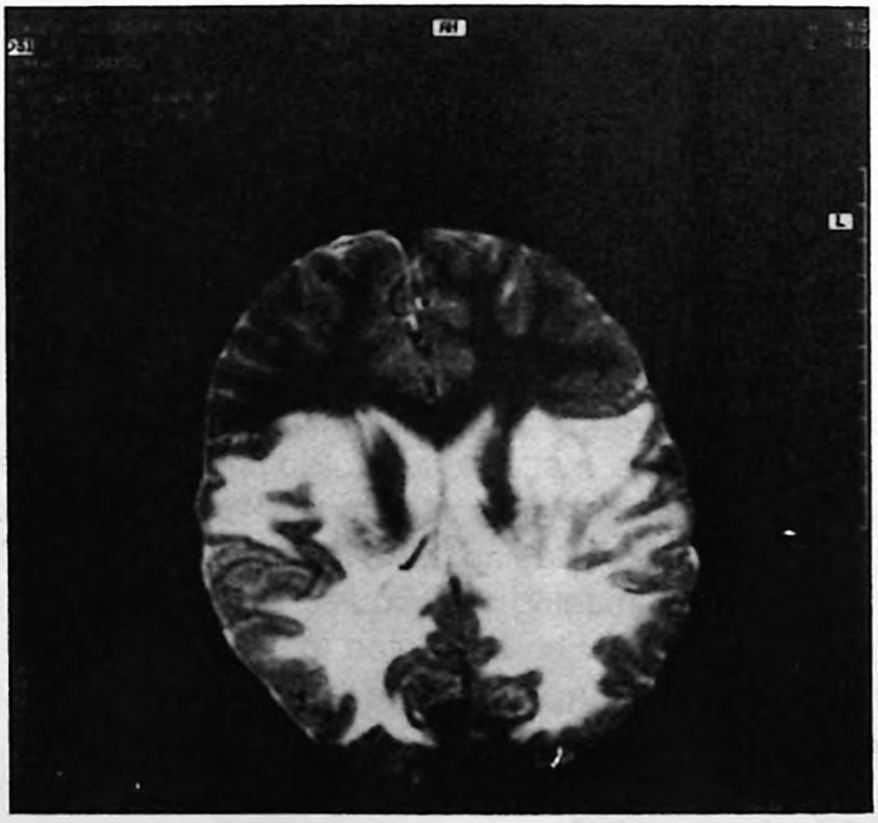

Fig. 1: High-intensity symmetrical signal of parieto-occipital white matter on MRI. The lateral and medial geniculate bodies, corpus callosum splenicum and lateral lemniscus were involved.

Baseline cortisol and ACTH values were 14 mg/dl and 94 pg/ml, respectively. After ACTH stimulation, the cortisol level (11 mg/dl) did not increase. Serum fatty acid analysis indicated a raised VLCFA level, with a ratio of C26:C22 = 0.065 and 0.074.

Four months after MRI imaging, SPECT was performed with intravenous injection of 6 mCi Tc99m HMPAO (Ceretec, Amersham International, UK). The radiopharmaceutical agent was administered to the child in a quiet and dimmed room, and 10 minutes later, 10 mg diazepam was injected intravenously for sedation. With high-resolution collimators, a three-headed gamma camera (GE/CGR neurocom, Horsholm, Denmark) was used for imaging. 128 images of 35 seconds duration in a 64 x 64 matrix were obtained over 360 degrees. Two pixel thick tomographic slices were reconstructed in the transaxial, coronal and sagittal planes. In the superior temporal and parietal cortices, the right occipital cortex, the right cerebellum and the left frontal cortex, markedly decreased blood flow was detected (Fig. 2).

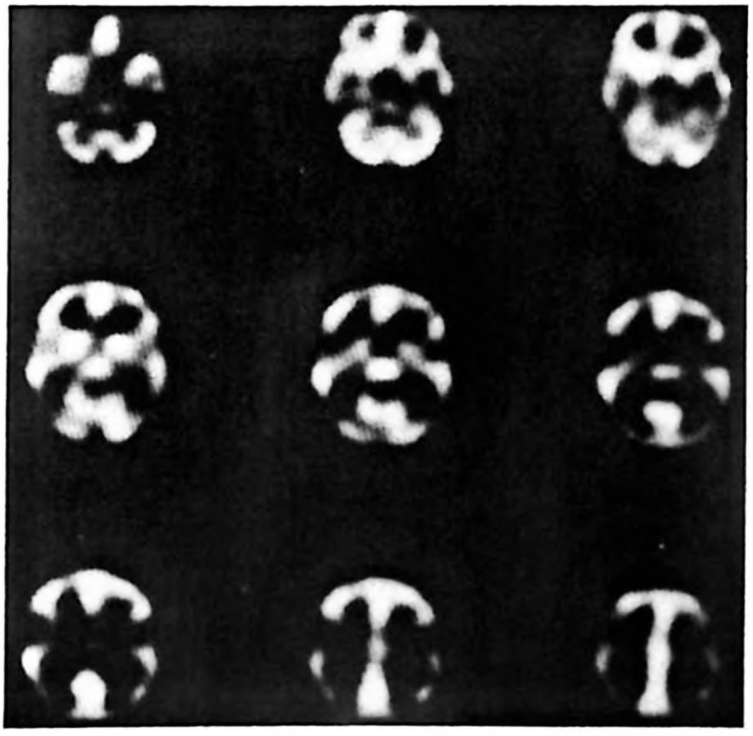

Fig. 2: Markedly decreased blood flow in superior temporal and parietal cortices, right occipital cortex, right cerebellum and left frontal cortex in SPECT.

During the following weeks, the patient's neurologic status rapidly deteriorated, and as of this writing he had great difficulty in swallowing and walking.

Discussion

Clinical and laboratory findings and imaging studies led to the diagnosis of ALD. Serum fatty acid analysis also confirm this neurodegenerative disorder. Although adrenal insufficiency was not apparent clinically, test results indicated the failure of increase in the baseline cortisol value in response to ACTH stimulation.

In ALD patients, characteristic changes have been described in imaging studies. Mostly symmetric lesions involving the periventricular white matter in the posterior parietal and occipital lobes and then advancing to the temporal and frontal lobes

are detectable with CT and MRI studies. Noncontrast CT scans show hypodensities in these regions. After the injection of contrast material, it accumulates adjacent and anterior to the hypodense lesions. This zone corresponds to the zones of intense perivascular lymphocytic infiltration where the blood-brain barrier breaks down. MRI identifies the normal and abnormal white matter more clearly than CT and may even demonstrate abnormalities missed by CT[5].

Lately, SPECT neuroimaging has had an important and expanding role in evaluating physiologic changes in regional cerebral perfusion[6]. In the literature, the number of SPECT studies in ALD is limited. A previous case report of a PET study in ALD showed decreased cerebral blood flow and glucose uptake in the gray matter at the occipital, temporal and posterior parietal cortex[7]. In another report, Tc99m HMPAO SPECT revealed the same regional distribution of decreased blood flow in the posterior cerebral areas as in the PET study, and one recent report showed that brain blood flow was remarkably decreased[8,9]. The demyelinating process of the nerve fibers decreases the neuronal output from the related cortical areas. Decreased cortical metabolism results in decreased perfusion due to the metabolic coupling of glucose utilization and blood flow[10]. In our case, though on MRI the lesions were confined to the parietooccipital region, SPECT demonstrated more extensive cortical hypoperfusion. Additionally, the right cerebellum and left frontal cortices showed decreased perfusion, which may be due to corticocerebellar diaschisis. The lesions in SPECT were more extended than those in MRI. Scattered neuronal loss and mild gliosis in the gray matter has been reported by histopathology in ALD[9]. MRI and CT showed no gray matter involvement, and no histopathologic examination of gray matter is present in our case. SPECT might have revealed a true gray-matter abnormality as well. Our patient's ataxia could be explained by cerebellar hypoperfusion. The degree of functional impairment seemed to correlate better with the SPECT results. Deterioration of the patient's status in the following weeks, provided a clue for possibility of predicting the disease progression by SPECT, when perfusion defects were more extensive than shown on MRI. It may be concluded that SPECT abnormalities precede MRI changes and symptoms, and this may give the earliest indication of the presence of cerebral involvement.

Treatment with glyceryl trierucate and glyceryl trioleate oils combined with dietary restriction of VLCFA leads to a reduction in plasma VLCFA levels, though very limited evidence exists regarding its clinical benefit[11,12]. Dietaray restrictions are recommended for patients with rapidly progressive ALD. Patients who show early cerebral involvement or early signs of progression are considered candidates for bone marrow transplantation[13]. Since therapeutic approaches are based on the extent of the disease, SPECT seems to be of great importance in selecting therapeutic options and follow-up.

This report stresses the indications for SPECT neuroimaging in ALD. Utilization of SPECT in making an early diagnosis, prediciting the prognosis and selecting the therapy, which itself is under intensive investigation, should be encouraged by other studies.

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