Adrenoleukodystrophy: Case Report

Pages with reference to book, From 110 To 112

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Introduction

Adrenoleukodystrophy (ALD) is an X-linked neurodegenerative disorder associated with progressive central demyelination and adrenal insufficiency[1]. It was first described by Siemerling and Creutzfeldt[2] in 1923 as "bronzed sclerosing encephalomyelitis. In 1970, Biaw[3] assigned the now generally used term adrenoleukodystrophy. It is believed to be peroxisomal disease and biochemically characterized by the accumulation of very long chain saturated fatty acids (VLCFA) especially hexacosanoic acid (C26:0) and tetracosanoic acid (C24:0) because of deficiency of acyl CoA synthetase[4]. ALD gene has been mapped to the q28 segment of the X-chromosome, close to G6PD. haemophilia A and colour blindness[1-6]. The clinical phenotype of X-iinked ALD varies widely from no central nervous system involvement to rapidly progressive neurological disorder which is fatal in early childhood or as a slowly progressive paraparesis in older children or even in adults. Childhood cerebral type is the most common type and age of onset is generally between 4 to 10 years of age, progressing rapidly to vegetative state and death within 2 years[5]. The initial clinical features are mainly behaviour abnormalities, poor school performance. loss of memory, gait distutbances. visual and hearing difficulties. The adult type (adrenomyeloneuropathy) has a chronic course dominated by myelopathy and peripheral neuropathy[4]. At the time of onset of neurological symptoms, about 20% have features of adrenal insufficiencyb. Twelve to 40% of carriers show some degree of neurological abnormalities[1]. Neonatal ALD, inherited as autosomal recessive, is a quite different clinical entity.
The earliest changes seen on computed tomogram (CT) scan are bilateral hypodensities located in the white matter of parieto- occipital lobes[7]. As the disease progresses, demyelination extends to the frontal lobe, Magnetic resonance imaging (MRI) is more sensitive and allows precise definition of white matter lesions. It can distinctly differentiate between normal and abnormal white matter and detects lesions in subcortical white matter, medulla oblongata, pons, geniculate bodies, lateral lemniscus and colliculus which are not seen on CT scan[8]. Preclinical lesions of white matter can also be demonstrated on MRI in ALD patients[9]. Electroencephalogram (EEG) in ALL) shows irregular high amplitude slow waves, dominant in posterior regions with normal rhythmic activity in paracentral areas[10]. Measurement of VLCFA in plasma by gas-liquid chromatography is rapid and sensitive method of diagnosis". Prenatal diagnosis of ALD can be made by determining C26:0 concentrations in amniocytes and chorionic villus cells. Heterozygotes (carriers) are detected by measurement of VLCFA in plasma and skin fibroblasts[11]. At present no therapy is available for ALD, although, strategies such as dietary restrictions of VLCFA, use of clofibrate or carnitine, gammaglobulins, replacement of adrenal hormones and plasma exchange have been tried". Dietary supplement with Lorenzo's oil containing erucic acid and oleic acid have shown inconsistent results[5,11]. There are reports of successful bone marrow transplants in very early stage of the disease[12].

Case Report

A 10 years old boy from northern Pakistan was referred to Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad, because of gradual loss of milestones. He was born normally after fuilterm uneventful pregnancy. Apgar score is not known, however, parents said that there was no

problem during and afterbirth. His weight and head circumference were average (exact measurements flot known). He acquired his motor milestones and speech at appropriate age. Eight months ago, he complained of progressive weakness of legs, walking difficulty and frequent falls. Four months ago, he developed hearing problem and slurred speech. There is history of occasional headaches ofvanable degree since several months. There is no history of fits, visual difficulties or vomiting. One yearago, he was treatedfor meningitis in the referring hospital and recovered without any neurological sequelae. Parents are reiatea ana otner man patient, nave rour neaitny cmiaren (2 males, 2 females) between the ages of 12 and 2 years.

On physical examination, patient was of appropriate weight and heightwith moderately impaired intelligence, poor attention but cooperative and obeyed simple commands. He had slow, unsteady gait, dysarthric speech and poor finger coordination. Tone was moderately increased in upper and lower limbs. Deep tendon reflexes were brisk with anide clonus and bilateral extensor plantars. Pupils were round arid reacting to light. Fundoscopic examination was normal. There was no abnormal pigmentation of skin.

Results of routine blood count, serum electrolytes, sugar, calcium, urea, creatinine, liver function tests, cerebrospinal fluid and urine analysis were normal. Serum cortisolwas also within normal limits.

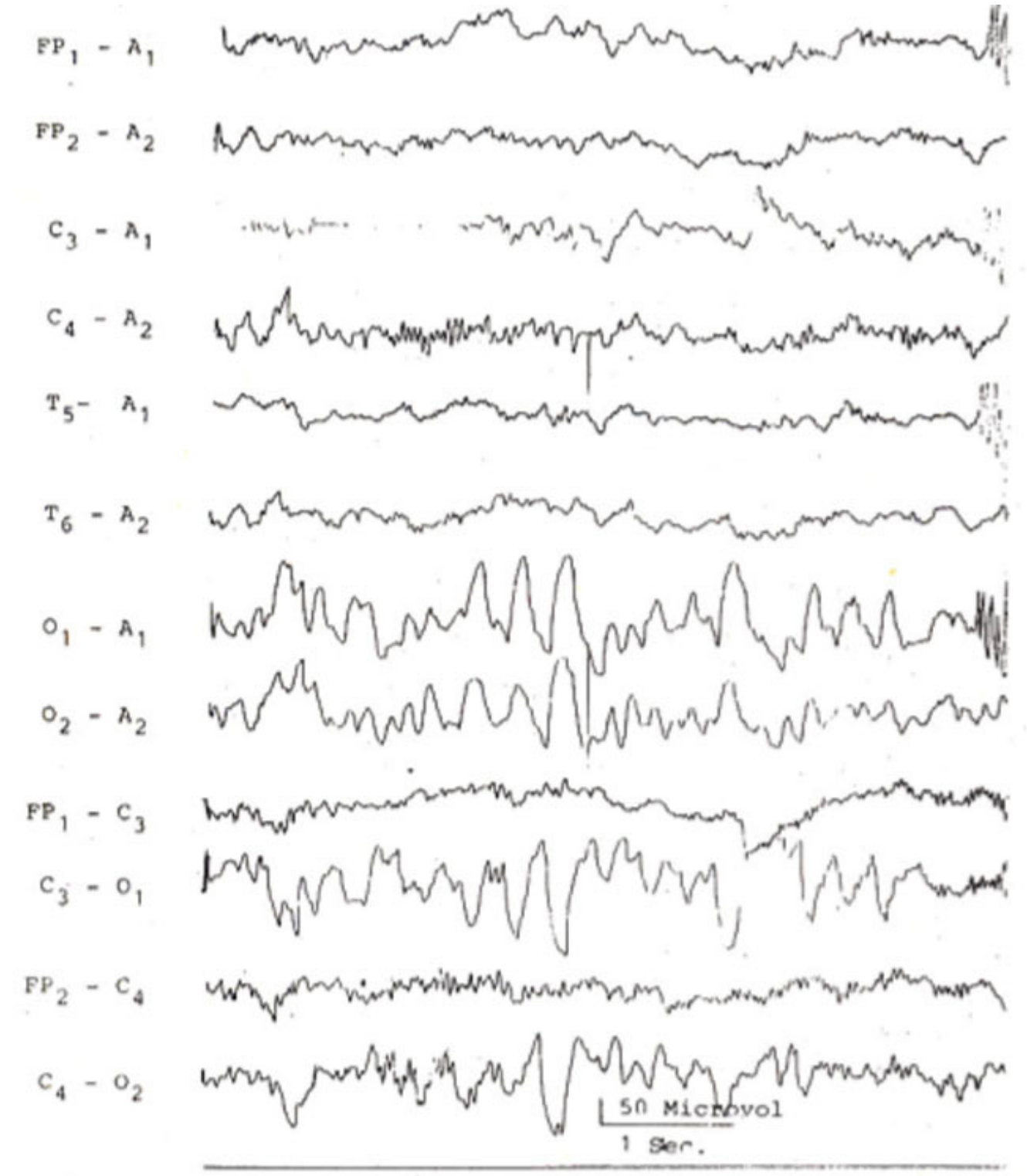

Figure 1. EEG showing high-amplitude slow waves in posterior leads and poorly organized background activity.

His EEG (Figure 1) was abnormal with high amplitude slow waves in posterior leads. CT scan of brain (Figure 2)

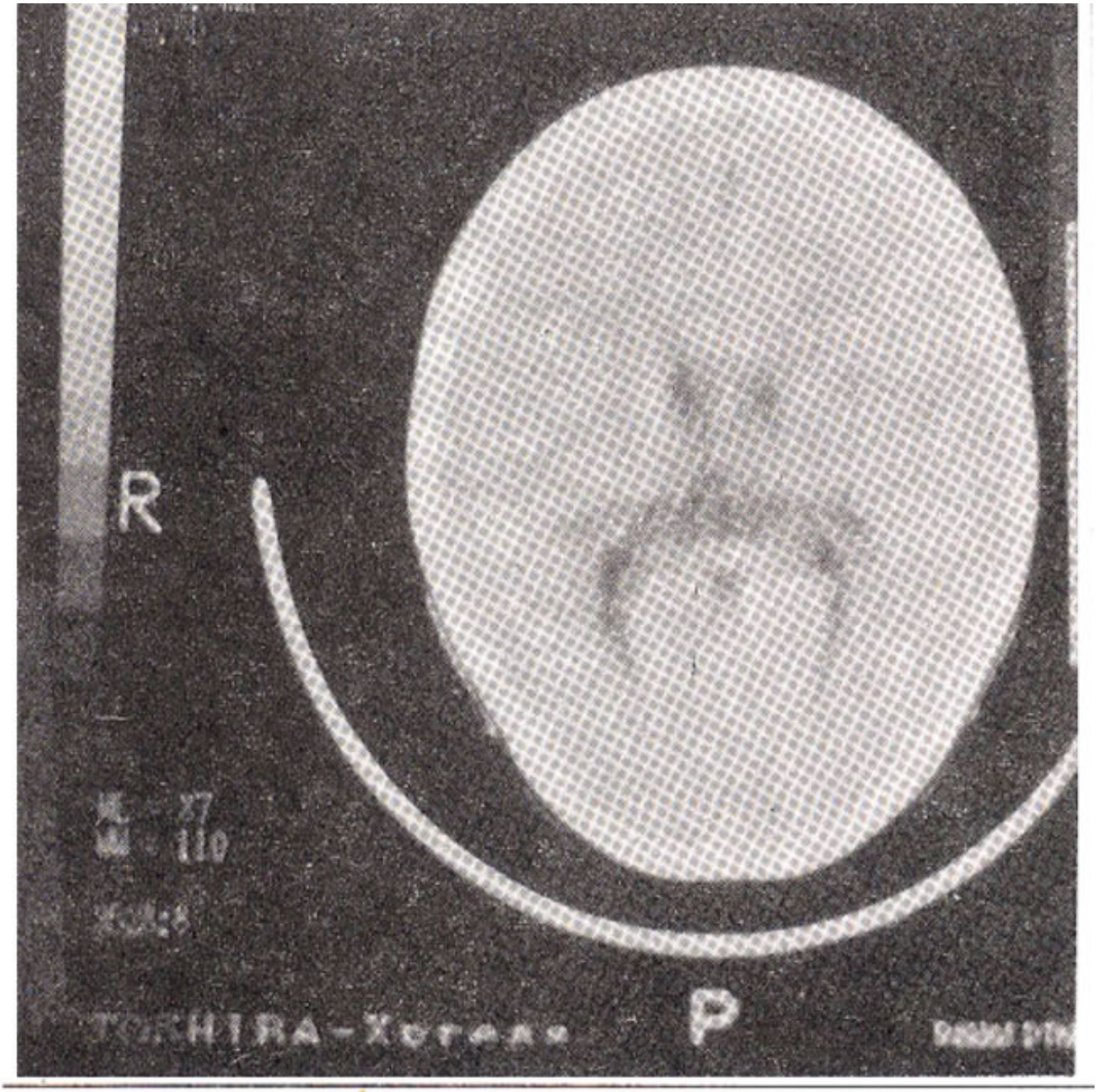

Figure 2. CT scan brain showing symmetrical hypodense lesions in the white matter around the posterior hours of lateral ventricals.

revealed symmetrical hypodensities in parieto-occipital lobes along the posterior horns bilaterally. Brain stem auditoiy evoked responses and plasma VLCFA were not done. Patient was given a trial of prednisolone for several weeks but without any benefits.

Discussion

Incidence of neurodegenerative diseases of infancy and childhood inPakistanis not known. However, as a group, they constitute a significant neurological problem inpaediatric age group[13]. The present case manifested characteristic features of degenerative brain disease. Spasticity, exaggerated tendon reflexes and bilateral Babinski sign indicated upper motor neuron disease. Determination of plasma VLCFA is

diagnostic, however, because of lack of facility, this was not done. The CT scan of brain demonstrated characteristic pattern of symmetrical hypodensities in parieto-occipital white matter. Abnormal findings of adrenoleukodystrophy on CT scan distinguish it from other white matterdisease& . EEG showed bursts of irregular high voltage slow waves in posterior leads. It has been suggested that ALD can be diagnosed on the basis of abnormal EEG findings even before the appearance of clinical manifestations and MRI abnormalities[5]. The patient did not manifest clinical evidence of adrenal dysfunction and levels of serum cortisol were normal. In a large series of adrenoleukodystrophy, only 22% patients had clinically evident Addison's disease[6]. There is no relationship between ALD and meningitis, though our patient was treated for bacterial meningitis before the appearance of clinical manifestations and preceding viral meningitis has been reported previously[5]. It is suggested that a male child presenting with features indicating degenerative brain disease, should have BEG and CT scan, if possible. We may, see more cases of ALD.

References

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