

A Case of Adrenoleukodystrophy

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= Abstract = Adrenoleukodystrophy is a rare genetically determined disorder associated with progressive white matter degeneration of central nervous system.

Although it is known to occur in most parts of the world it is seldom reported in Korea. We report a case of adrenoleukodystrophy in a 6 year old boy that was diagnosed by adrenal biopsy and demonstration of characteristic cryptalloid inclusions seen in adrenal cortical cells. This patient also had a widespread white matter lesion and brain atrophy that could clearly be demonstrated with Magnetic Resonance Image.

Key words: *Adrenoleukodystrophy, Adrenal cortex, Leukodystrophy*

INTRODUCTION

Adrenoleukodystrophy (ALD) is genetically determined disorder associated with progressive central demyelination and adrenocortical insufficiency. All affected persons show increased levels of saturated unbranched very long chain fatty acids (ULCFA), particularly hexacosanoate(C 26:0). Clinically varying degrees of adrenal insufficiency are associated with a rapid progressive neurologic disorder of the white matter, resulting in blindness, quadriplegia, dementia and death.

We experienced a 6-year old boy with adrenoleukodystrophy, and so report him with review of literatures.

CASE REPORT

This 6 year old boy was admitted to the pediatric ward with the chief complaints of motor deficit and seizure. In October 1986, his mood seemed depressed and somewhat drowsy. But his parents neglected it. One month later, fever, headache and vomiting developed and was followed by seizure of generalized tonic-clonic type. So he had some medication for seizure. In January 1987, abnormal gait and dysarthria developed, which was progres-

sive inspite of medication.

On admission, he seemed dull and depressed, but orientation was intact. His motor response to verbal order was inappropriate. Optic discs were atrophied bilaterally. Skin pigmentation was observed, especially on axilla, umbilicus, both nipple areas and groin. Deep tendon reflex was enhanced moderately and cerebellar function was distorted.

24 hour urine concentration of 17-KS and 17-OHCS were 4.2 mg/d and 2.2 mg/d, respectively. The diurnal rhythm of cortisol secretion was absent (plasma level of cortisol; 9.8 ug/dl at 8:00 AM and 5.0 ug/dl at 8:00 PM). The response of cortisol secretion to ACTH stimulation was not elicited. The findings of MRI scan consisted of a mild degree of diffuse ventricular dilatation, prominence of cisternal space suggesting mild brain atrophy on T1-weighted image and symmetric high signal intensity were noted in both periventricular region of occipital horn of lateral ventricle and the peripheral margin of the high signal intensity was speculated and extending into the cortical gray matter.

PATHOLOGIC EXAMINATION

A 2×1×0.7cm sized adrenal tissue was submitted, surrounded by periadrenal fat. Cut sections showed a thin but bright yellow cortex measuring less than 1 mm in thickness. The medulla was gray

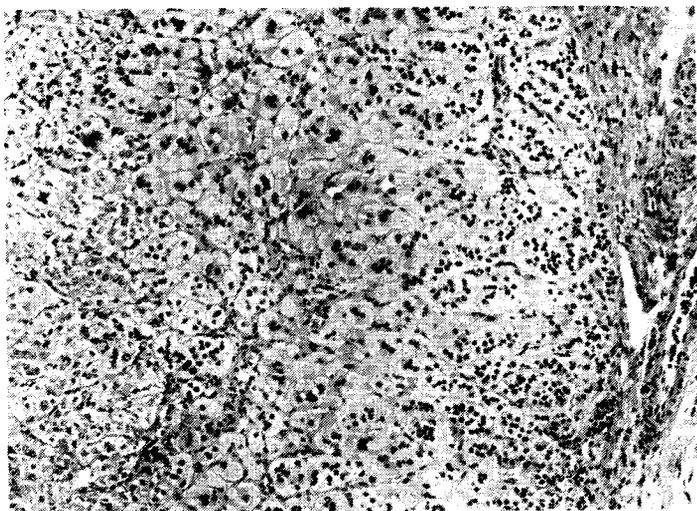


Fig. 1. Photomicrograph of adrenal biopsy specimen, showing cortical atrophy and distortion of zona fasciculata and zone reticularia. (H&E X100)

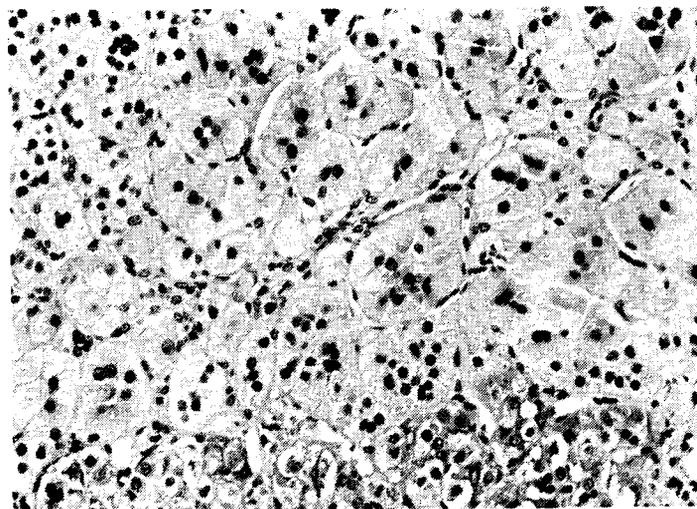


Fig. 2. Higher magnification of adrenal cortical cells, showing ballooning of cytoplasm and giant cell formation. (H&E X250)

white and prominent.

Microscopically the cortex was characterized by a diffuse atrophy and thinning, with distortion of zona fasciculata and reticularis (Fig. 1). There were scattered collections of ballooned cells and multinucleate giant cells with glassy homogeneous pinkish cytoplasm (Fig. 2). The cortex was fairly well distinguished from underlying medulla which was relatively prominent and showed scattered collections of lymphocytes.

Electron microscopically ballooned cells in the cortex showed numerous cryptaloid clefts (Fig. 3). Multilamellar structures and structures resembling twisted or flowing multilamellar forms were indeed (Fig. 4). Lamellae consisted of two parallel 25 nm thick electron dense leaflets separated by a variable electron-lucent space. Round bodies with vacuolar inclusions were also noted.

DISCUSSION

Since initial report of adrenoleukodystrophy by Siemerling and Creutzfeldt in 1923, similar isolated cases had been reported subsequently. In general, there are three different types of ALD; childhood type, adrenomyeloneuropathy (AMN) and the entirely separated neonatal or congenital form.

The possible contributing factor of adrenal insufficiency is that the abnormal fatty acid composition of the adrenal cholesterol ester may impair availability of the cholesterol for normal steroidogenesis. But the pathogenesis of ALD is not understood yet.

The rapid progression of the disease, the asymmetrical distribution of the lesion, and the striking accumulations of lymphocyte in active brain lesion suggest immunopathogenic mechanism. Childhood ALD is transmitted through sex-linked recessive trait.

The development of abnormal behavior and disturbance of vision or gait in a young boy should suggest a diagnosis of ALD. If there is any demonstrable evidence of diminished adrenocortical function, the diagnosis is invariably certain. The signs of CNS disturbance are consistently more prominent than the signs of adrenal insufficiency. Usually, behavioral change is the initial finding, ranging from withdrawn state to bizarre aggressive outburst. Disturbance of gait is also an early finding. Other findings which are usually observed are dysarthria, dysphagia, hearing loss, visual loss with optic atrophy, seizure, hemiparesis and eventually quadriplegia and death.

Symptoms and signs of adrenal insufficiency are insidious in onset and they are generalized weakness, intermittent vomiting, cutaneous pigmentation and hypotension. They develop pari passu with the neurologic disorders.

Neonatal or congenital ALD differs strikingly from childhood ALD. Apart from earlier onset and profound disabilities, severe seizure are observed frequently. The liver is usually enlarged with impaired function. Females are as severely involved as males. So the pattern of inheritance appears to be

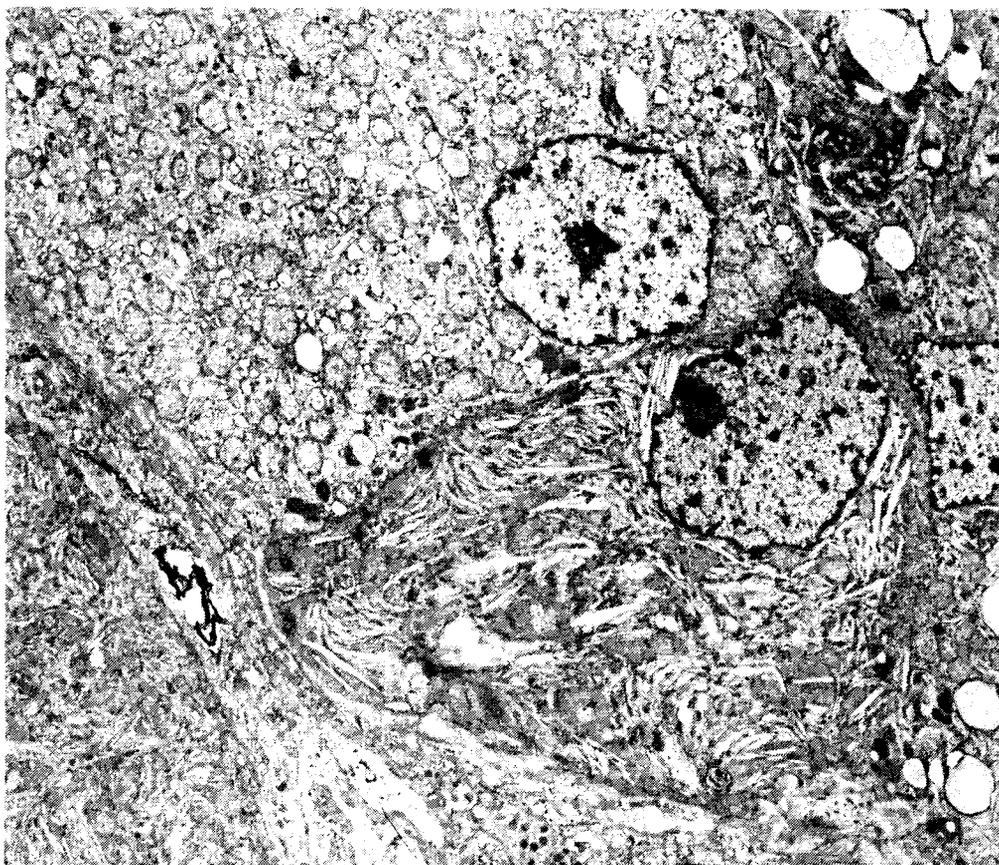


Fig. 3. Electron micrograph of adrenal cortical cells showing numerous intracytoplasmic crystalloid inclusions. (Lead citrate X7500)

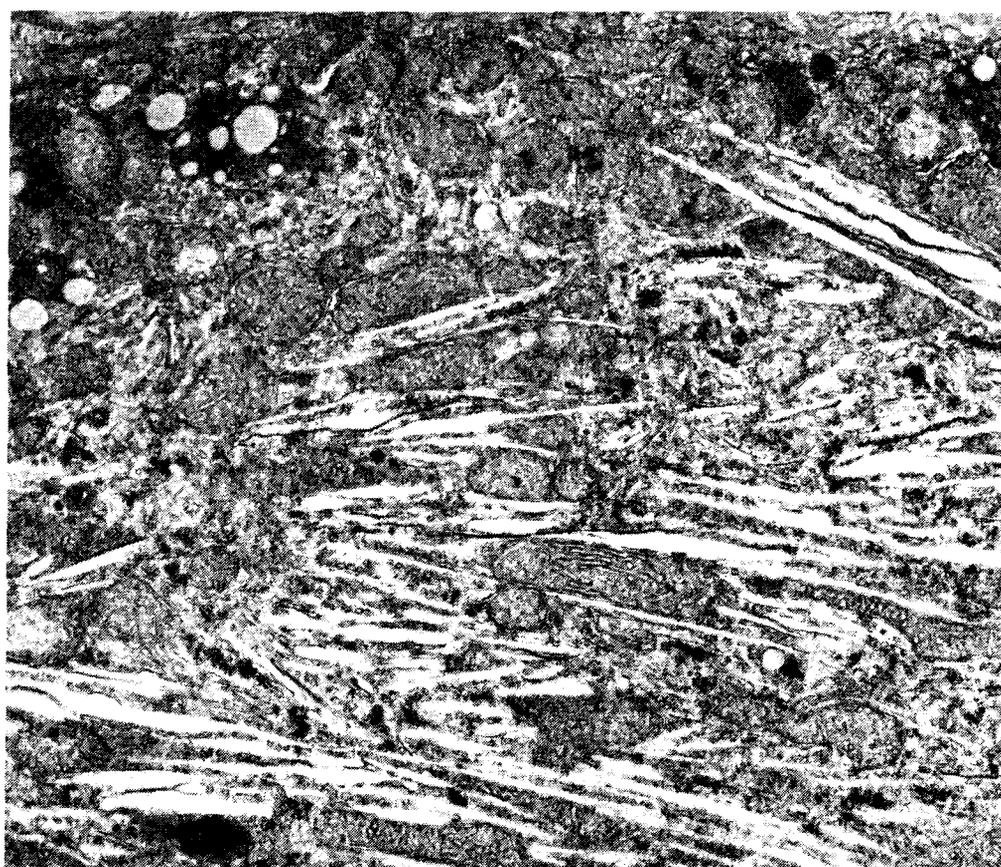


Fig. 4. Electron micrograph of cytoplasmic inclusions, showing parallel structure. (Lead citrate X20000)

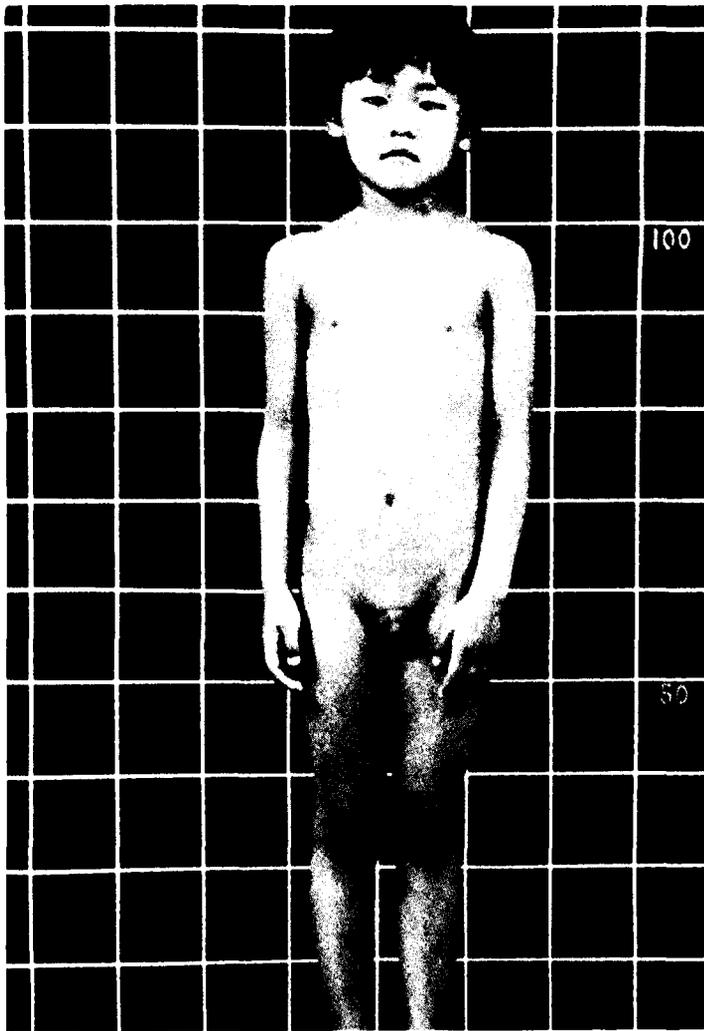


Fig. 5. General body appearance of the patient: He seems dull and increased pigmentation of the skin was noted at both nipple areas, umbilicus, axilla, groin.

autosomal recessive.

Diagnosis is suggested by clinical and laboratory findings of primary adrenal failure and by neurological signs referable to the degeneration of the white matter. Confirmative diagnosis can be drawn by adrenal biopsy and biochemical assay for VLCFA. The single most reliable test for diagnosis has been found to be an open adrenal biopsy. Measurement of VLCFA, especially hexacosanoate is the most sensitive test for the diagnosis of ALD.

Most heterozygous women for ALD can be detected by the assay of VLCFA. The fetus with ALD can be detected prenatally by the measurement of VLCFA in amniotic fluid.

There is not any satisfactory treatment for ALD and once the first symptoms referable to the CNS appear, the course is always that of relentlessly

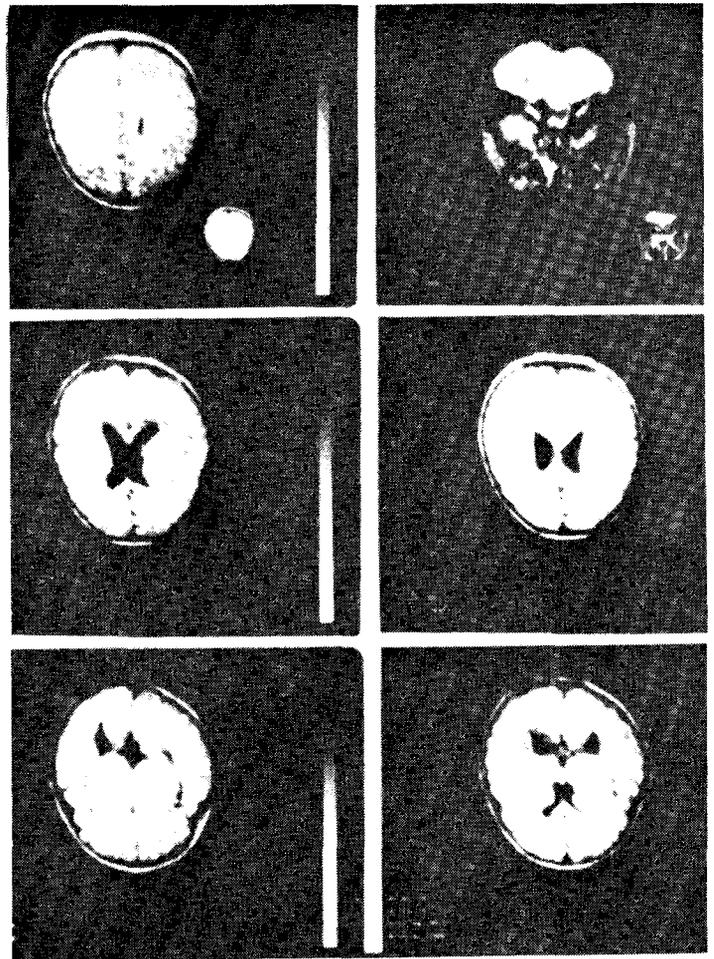


Fig. 6. MRI brain scan; T1-weighted image. Mild degree of diffuse ventricular dilatation and prominence of cisternal space suggesting mild brain atrophy.

progressive neurologic deterioration. In 1975, Herbert reported that the duration of illness was ranging from 9 months to 9 years.

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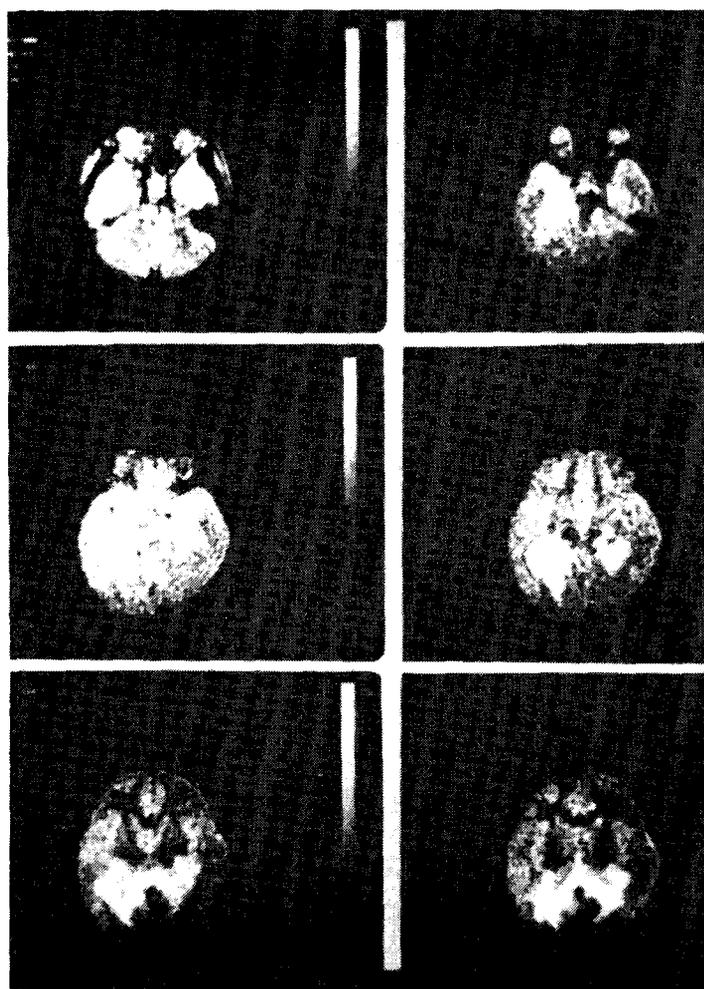


Fig. 7. MRI brain scan; T2-weighted image. Symmetric high signal intensity are noted in both periventricular region of occipital horn of lateral ventricle and the peripheral margin of the high signal intensity are speculated and extending into cortical gray matter.

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= 국문초록 =

부신 뇌백질 이양증(1증례 보고)

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부신 뇌백질이양증은 성염색체 열성으로 유전되며 4~8세에 호발하는 질환으로 신경학적 증상과 부신기능 저하증상을 나타낸다. 신경학적 증상이 더 잘 나타나 행동변화 및 치매가 최초의 증상이며 그 이외에 걸음걸이의 장애, 심건반사 항진, 구음 장애, 연하 장애, 시력감퇴, 청각장애, 마비, 경련 등이 나타나며 부신피질기능저하로 표피 색소 침착, 피로감, 간헐적인 구토, 저혈압 증 등이 나타난다.

이 질환에서는 모든 환아에서 hexacosanoate의 농도가 증가되어 있기때문에 여성 heterozygote감지 및 prenatal 진단에 이용되고 있으며 이 질환의 의심이 있으면 뇌생검보다는 부신피질검이 더 효과적인 진단 방법으로 이용될 수 있는 것으로 생각된다.

저자들은 표피색소 침착 및 걸음걸이 장애 및 시력감퇴를 나타낸 6세 남아에서 부신피질검을 시행하여 부신 뇌 백질이양증과 일치하는 소견을 발견하여 문헌고찰과 함께 보고하는 바이다.