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Radiological Findings of Congenital Lipoid Adrenal Hyperplasia: A Case Report[1]

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Congenital lipoid adrenal hyperplasia (CLAH) is a rare autosomal recessive disorder characterized by the marked accumulation of lipids and cholesterol in the adrenal cortex, and the failure of adrenal steroids to synthesise. We report the ultrasound (US), computed tomographic (CT), and magnetic resonance (MR) imaging findings in a four-day-old female neonate with CLAH.

Index words : Adrenal gland, hyperplasia
Adrenal gland, CT
Adrenal gland, insufficiency
Adrenal gland, MR

CLAH, the most severe genetic disorder of steroid hormone biosynthesis (1), is a rare autosomal recessive disorder characterized by the marked accumulation of lipids and cholesterol in the adrenal cortex and the failure of adrenal steroids to synthesise (2). The disorder is characterized clinically by profound salt loss, complete feminization of male external genitalia, and hyperpigmentation. Most patients have died in early infancy due to adrenal crisis (3). Early diagnosis and timely replacement treatment can, however, enable normal mental and physical development.

Prior to 1995 only one report describing a case of CLAH had been published in Korea (Lee et al.;4), though primarily a gene study of four Korean patients with CLAH, its findings based on clinical findings, has been published more recently (5). We describe the US, CT, and MR imaging findings of CLAH in a four-day-old female neonate.

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Case report

A four-day-old female neonate was referred to our hospital because of frequent vomiting, lethargy, and diffuse pigmentation. The baby, whose parents were healthy, was the 3.5-kg product of an uncomplicated 41-week pregnancy and delivery, and their second child. Their first, also a female, had died aged 3 days due to the same manifestation as this patient. Physical examination disclosed a moderately lethargic patient with diffuse hyperpigmentation, including the oral mucosa. The external genitalia were normal. The body temperature was 37.0, pulse rate 160, and respiratory rate 60. Laboratory studies indicated that blood urea nitrogen was 11 mg/dl, creatinine 0.4 (normal range, 0.7 - 1.5) mg/dl, sodium 123 (135 - 150) mEq/L, potassium 5.7 mEq/L, and chloride 111 (95 - 105) mEq/L. Serum aldosterone was 91.3 pg/ml, testosterone 0.04 (0.09 - 0.9) ng/ml, plasma adrenocorticotropic hormone 799.1 (12 - 76) pg/ml, and plasma renin activity 44 (0.2 - 2.5) ng/ml/h. The karyotype was normal.

Radiological studies

At 5 days of age, US examination revealed significant

enlargement of both adrenal glands, which were iso- to slightly hyperechoic compared to the liver (Fig. 1A). Follow-up US examinations at 18 and 32 days showed persistent adrenal enlargement with no change in echogeneity (not shown). CT scanning of the abdomen was performed at 9 days of age; the precontrast scan showed massively enlarged adrenal glands, with fat-tissue attenuation (H.U., -28) (Fig. 1B), enhanced scan demonstrated that blood supply to the lesion was much reduced (Fig. 1C). MR imaging using the spin-echo technique was performed at 10 days of age; compared with hepatic parenchyma, the enlarged adrenal glands were hyperintense on T2-weighted images (2000/60) (Fig. 1D) and iso- to slightly hyperintense on T1-weighted images (400/30) (Fig. 1E).

Clinical course

On the basis of the radiologic findings and laboratory data, CLAH was diagnosed and using the standard doses of glucocorticoid and sodium chloride, replacement therapy was initiated. This led to decreased pigmentation, and the subsequent clinical course was uneventful. At 20 days of age, the patient developed fever; antibiotic therapy was initiated under the impression of sepsis but the parents refused further management. The patient was discharged at 30 days of age and was lost to follow-up.

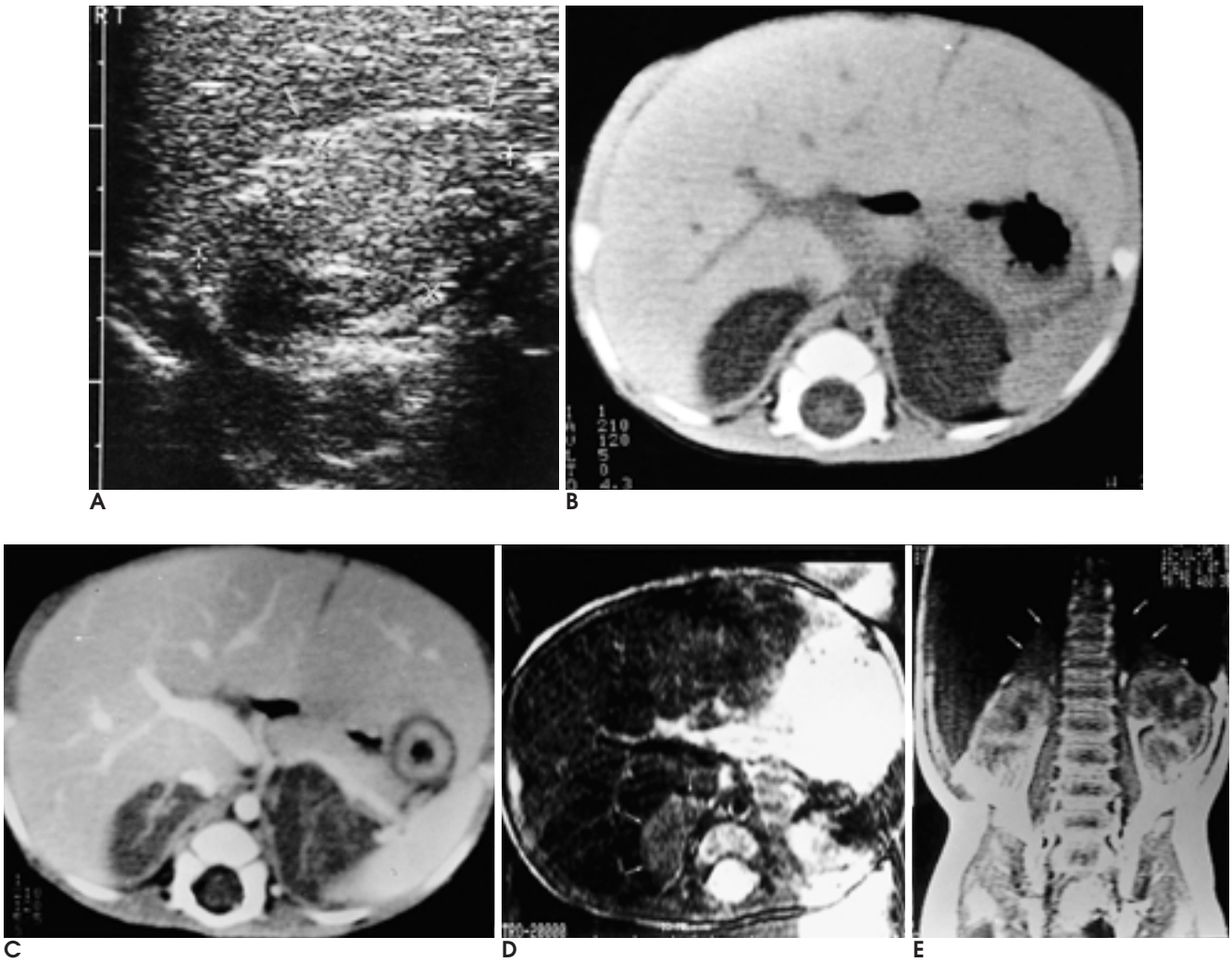

Fig. 1. Imaging features of CLAH in a 4-day-old female neonate.
A. A transverse scan of the upper abdomen with 7 MHz linear transducer demonstrates iso- to hyperechoic lesion in the right adrenal gland (arrows) with globular enlargement.
B. Precontrast CT scan shows massively enlarged both adrenal glands of fat-tissue attenuation (H.U., -28).
C. Enhanced CT scan demonstrates poor enhancement of the lesions (H.U., -20).
D. Axial T2-weighted image of the abdomen reveals diffusely enlarged right adrenal gland with slightly hyperintensity comparing to the hepatic parenchyma (arrows).
E. Coronal T1-weighted image shows slightly hyperintensity of the both adrenal glands compared to the liver (arrows).

Discussion

Congenital lipoid adrenal hyperplasia (CLAH) is the most severe form of congenital adrenal hyperplasia and is the most severe genetic disorder of steroid hormone biosynthesis (1). This failure to convert cholesterol to pregnenolon is due to a defect in 20, 22 desmolase. There is a marked accumulation of lipids and cholesterol in the adrenal cortex, and adrenal steroids including all glucocorticoid, mineralocorticoid and the sex hormones fail to synthesise (2). The same enzyme defect is present in the testis, preventing the synthesis of testicular hormones. As a consequence, males are phenotypically female while females exhibit no genital abnormality (3).

Prior to 1985, CLAH had been reported in 33 patients, 56% of whom were Japanese (3), recent studies have suggested that CLAH is more common in both Koreans and Japanese than in other ethnic populations (4 - 7). The mutation Q258X, which is the leading defect in the key protein, has been found in 80% of affected alleles from Japanese and Korean patients (7), and a recent study reported four Korean patients with CLAH and an estimated incidence of the Q258X mutation of approximately 1 in 250,000 among the Korean population (5). This figure seems relatively high and CLAH is thus not a particularly rare disease in Korea.

The clinical findings of CLAH are remarkably constant : neonatal hyponatremia, hyperkalemia, hyperpigmentation, and complete female external genitalia irrespective of the gonadal sex (3 - 7). Hyperpigmentation, a sign of corticotropin hypersecretion, occurs in two thirds of newborns with CLAH (7), and because adrenal steroid levels are not elevated, affected infants are apt to be confused with those with other forms of adrenal hyperplasia. Furthermore, the disease does not show ambiguity of the external genitalia, and early diagnosis and correct treatment tend to be delayed, resulting in early death from adrenal crisis in the majority of patients. If appropriate mineralocorticoid and glucocorticoid replacement therapy is initiated, however, patients can survive to adulthood (3, 7).

To our knowledge, only two reports have described the role played by imaging in the diagnosis of CLAH (8, 9). Ogata et al. first described the CT findings of CLAH in a eight-day-old female infant in whom massively enlarged adrenal glands, with fat-tissue attenuation, were seen, as in our case (8). US also can provide a useful method of evaluating the size and appearance of adrenal glands in neonates and young infants, and US has unequivocally demonstrated enlarged adrenal glands (4, 5, 9). Both CT and US findings have correlated closely with known pathologic changes in adrenal glands characterized by the accumulation of lipid and cholesterol ester (2). In the case we describe, CLAH was diagnosed on the basis of the CT findings, and through a clinical approach the differential diagnosis of diseases causing adrenal crisis in neonates and young infants was narrowed. According to Ogata et al., a CT scan obtained after 9 months of replacement therapy demonstrated intra-adrenal calcification and reduced adrenal size (8). Takaya et al. described the serial changes in the adrenal glands depicted by US: after 24 days of replacement therapy the glands became smaller and their cortical echogenic pattern changed from hyperechoic to isoechoic (9). In our case, the size and echogenicity of imaging showed that adrenal glands did not change within one month of replacement therapy. MR imaging, both adrenal glands were diffusely enlarged and isointense on T1-weighted images and iso- to slightly hyperintense on T2-weighted images. Viable fat may be isointense to subcutaneous fat on T1-weighted images and exhibit low signal intensity with fat suppression on T2-weighted images (10). Due to the failure of sedation we were unable to apply the fat saturation technique. The iso- to slight hyperintensity seen on T1-weighted images in our case may be due to field inhomogeneity or a technical problem. Takaya et al. (9) stated that whereas the adrenal cortex was hypointense, the adrenal medulla was markedly hyperintense, but did not attempt to explain why this was so.

The differential diagnosis includes adrenal hypoplasia, bilateral adrenal hemorrhage, congenital neuroblastoma and Wolman disease, all of which cause adrenal crisis in newborn infants. In an appropriate clinical setting, however a diagnosis of CLAH would be suggested by findings of unequivocally delineated enlarged adrenal glands due to fat accumulation, as revealed by CT or MR imaging.

In summary, we have presented the US, CT and MR imaging findings of CLAH. A familarity with these facilitates the diagnosis of CLAH, and appropriate management of this disorder is thus possible.

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김미정 · 신주용 · 이희정 · 이진희 · 손철호 · 이성문 · 김 홍 · 우성구 · 서수지

선천성 유지질 부신증식증은 체염색체 열성유전으로 부신의 모든 스테로이드 생합성의 장애로 인해 부신 피질에 유지질이 축적되는 매우 드문 질환이다. 저자들은 생후 4일 된 여자 신생아에 발생한 선천성 유지질 부신증식증 1예를 경험하여 초음파 (US), 전산화단층촬영 (CT), 및 자기공명영상 (MR) 소견을 보고하고자 한다.