MENKES SYNDROME

Patchrin PEKANAN, Sirintara PONGPECH, Siriporn THANAMEE

ABSTRACT

Menkes syndrome was reported in a 4-month-old boy. The patient had a seizure problem and recurrent urinary tract infection. His serum copper and cereluplasmin was very low. Imaging study showed bladder diverticuli by voiding cystography, brain atrophy by CT and MRI, bizarre elongation and kinking of the intracranial arteries by MRI and MRA.

INTRODUCTION

Menkes syndrome is a rare x-linked recessive disorder, first described by Menkes et al in 1962 (1,2). The gene defect is located near Xcen. Its synonyms are Kinky hair syndrome, trichopoliodystrophy, steely hair disease and copper transport disease. Clinical manifestations (1) are 1) sparse, stubby, twisted, and fractured hairs; variation in diameter of the hair shaft 2) developmental regression, mental retardation, seizure, ataxia, irritability, hypothermia, intracranial hemorrhage, death in early infancy 3) laboratory findings: low level of copper in plasma, urine, and hair; low level of plasma ceruloplasmin; an increased number of free sulfhydryl groups and decreased number of disulfide bonds in hairs; cultured fibroblasts containing four to six times higher concentrations of copper than control cells; postmortem diagnosis by copper measurement in the muscle tissue (high); copper measurement in the chorionic villi of the affected fetus in the first trimester (high) 4) malabsorption and maldistribution of copper in body organs; 5) other reported abnormalities; cryptorchidism, cataracts, atypical form (hypotonicity, fine myoclonic movements, ataxia, delayed psychomotor development, pili torti, etc.), etc.

Radiologic manifestations (1) include 1) bilateral symmetrical metaphyseal spurring of long bones in infancy 2) flaring of ribs 3) osteoporosis, fracture (s) 4) diaphyseal periosteal reaction of long bones 5) thickening of scapulae and clavicles 6) microcephaly, excessive wormion bones in the posterior fontanelle region 7) computed tomography (CT): progressive development of diffuse cortical brain atrophy, subdural accumulation of fluid, multifocal areas of ischemic infarction 8) widespread arterial changes: narrowing of the lumen, dilatation, tortuosity, elongation 9) cerebral angiogram, CT: loop-the-loop appearance, supernumerary serpentine branches, marked tortuosity 10) other reported abnormalities: hydronephrosis, hydroureter, bladder diverticula, polypoid lesion in the stomach, emphysema, round lumbar and thoracic vertebral bodies, ureteropelvic junction obstruction, vesicoureteral reflux and urinary tract infection.

A case of Menkes syndrome was presented, abnormalities were noted at the urinary tract and brain.

CASE REPORT

A 4-month-old boy admitted to the hospital due to seizure problem. The patient was pre-term-delivered by a Caesarian section with a birth weight of 2600 gram and moderate meconium stain. The Apcar score was 8,8,8 and with respiratory distress. He was noticed to have blond hair at birth though his parents' hair was black. However, he was discharged at that time in a good condition. The HIV Ag was negative and the urine Fecl 3 was also negative. At

Department of Radiology, Ramathibodi Hospital, Rama 6 Steet, Bangkok 10400, Thailand.

this admission, he was found to have kinky hair with coarse and blond color, microphthalmos, high arch palate, stiffy nose, and pectus excavatum. The development was delayed. The serum level of copper and cereluplasmin was very low and measured 2.27 ug/dl (normal 80-150 ug/dl) for the copper and 0.35 mg/dl (normal 20-46 mg/dl) for the cereluplasmin.

Phenobarbital was given to control seizure and copper-sulphate was supplemented. His hair became black and white (Fig. 1).

He was sent to study the urinary tract due to recurrent urinary tract infection. Multiple bladder diverticuli were noted (Fig. 2) without reflux. Skeletal survey showed no abnormality.

Contrast enhancement CT scan of the brain showed cerebral and cerebellar atrophy with lateral and third ventricular dilatation (Fig. 3) MRI of the brain revealed tortuousity of the intracranial vessels, especially at the circle of Willis and both middle cerebral arteries (Fig. 4). MRA of the brain also showed kinking and tortuousity of the intracranial blood vessels (Fig. 5).

DISCUSSION

Menkes' disease is characterized by deficiencies of copper in the liver and serum and more significantly, of a number of specific copper-proteins including cytochrome C oxidase, ceruloplasmin and lysyl oxidase (3). Copper is essential to human life, apparently only as a prosthetic element irreversibly bound to one of about a dozen copper-proteins. Normally there must be available, in vivo, sufficient copper to complete the synthesis of these copper-proteins by incorporation into specific apoproteins. Virtually all disturbances in copper metabolism involve either a deficiency of one or more of these essential copper-proteins, or the presence in tissues and organs of more copper than these apoproteins can bond. Genetic mechanism regulates both the synthesis of specific copper-proteins and the balance of copper.

An abnormality in copper binding or copper utilization which results in enzyme dysfunction is responsible for the neurodegenerative changes and fragmentation of elastic fibers noted in various types of arteries in patients with this condition. No known therapy, including the oral or parenteral administration of copper, can prevent death in the first decade of life.

The cause of the bladder diverticula in children with Menkes disease is not known. The walls of the diverticula of the bladder in a case reported by Harcke (4) were composed almost exclusively of elastic tissue and was considered acquired. Bladder diverticula may be a consequence of an increasing disturbance in innervation of the bladder (4). The diverticula constitute sites of urinary stasis which may lead to infection in our patient.

Widespread arterial tortuosity and variation in lumen size were demonstrated angiographically, in the brain, intraabdominal and peripheral arteries (6). Histologically, fragmentation of the internal elastic lamina and intima thickening were the findings of the most severely affected vessels. This bizarre appearance of the intracranial vessels were previously shown by MRI (6-8) and by MRA (9).

Cerebral atrophy are fairly nonspecific findings that can be seen in numerous conditions. It has been postulated that the cerebral atrophy and myelin deficiency may be the result of the arteriopathy (10).

ACKNOWLEGMENT

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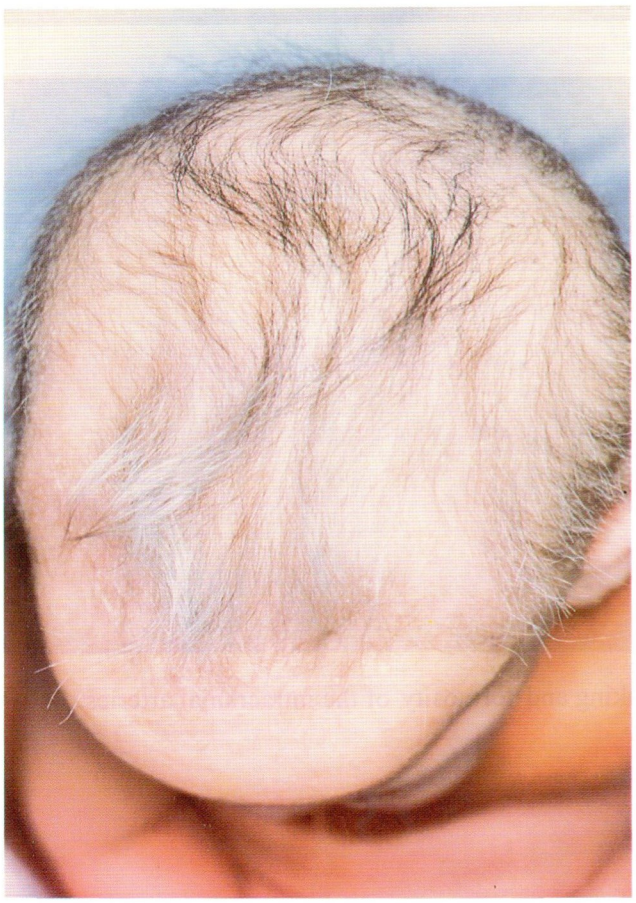

Fig. 1 The coarse hair with black and white colour of the patient was noted.

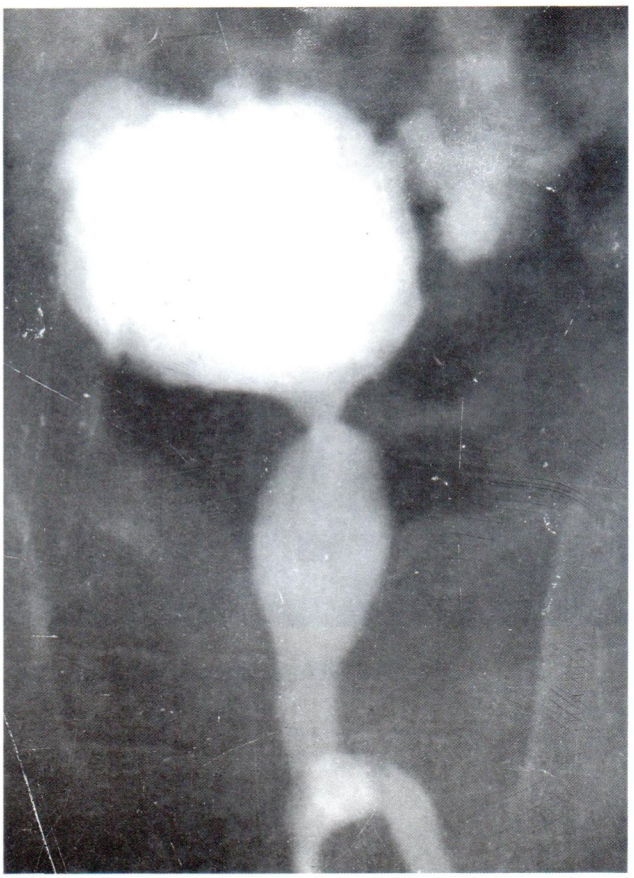

Fig. 2 Urinary bladder diverticuli were shown by voiding cystourethrogram without uretero-vesical reflux.

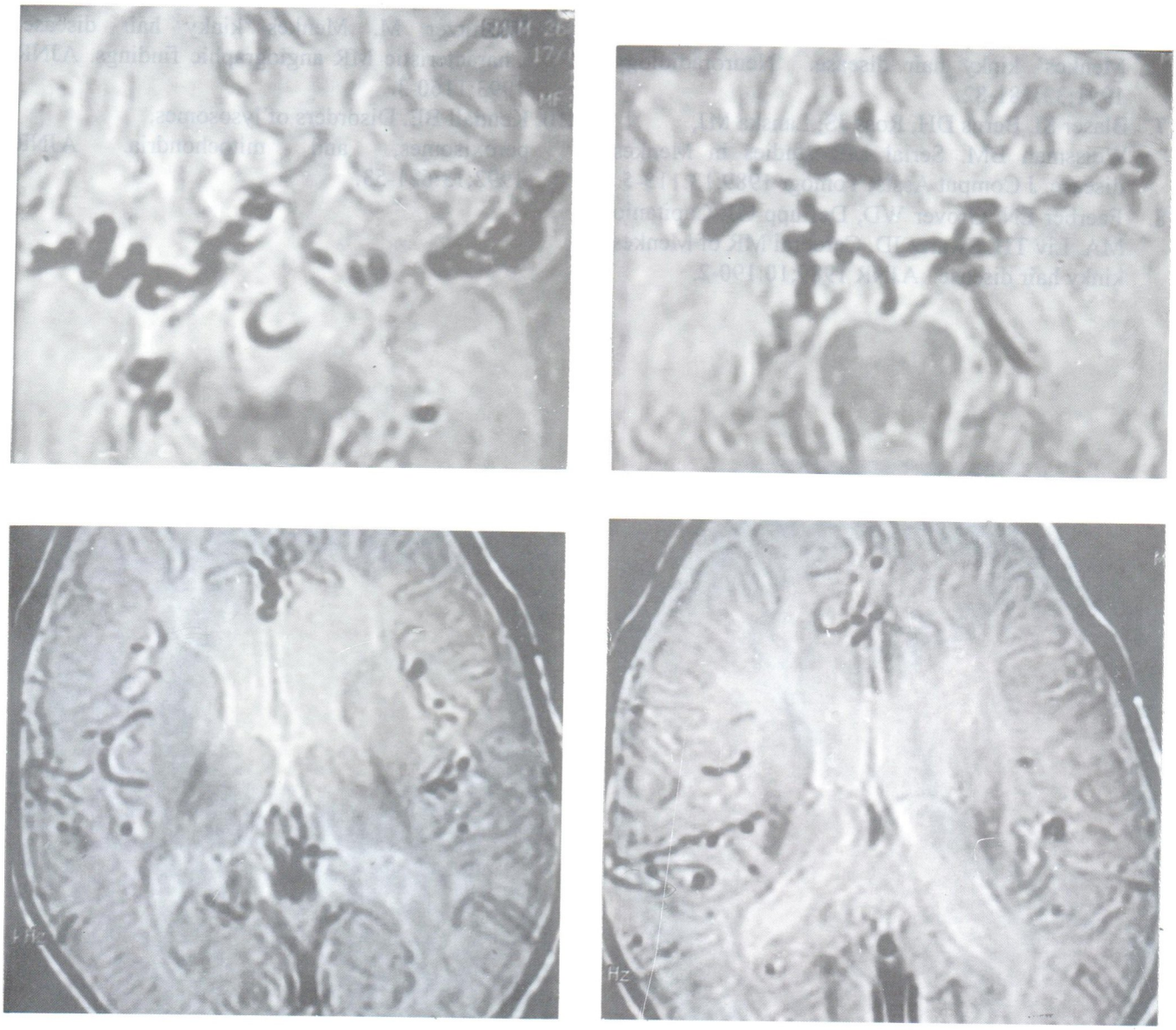

Fig. 3 PD axial MRI images of the brain shows kinking and tortuosity of the intracranial arteries.

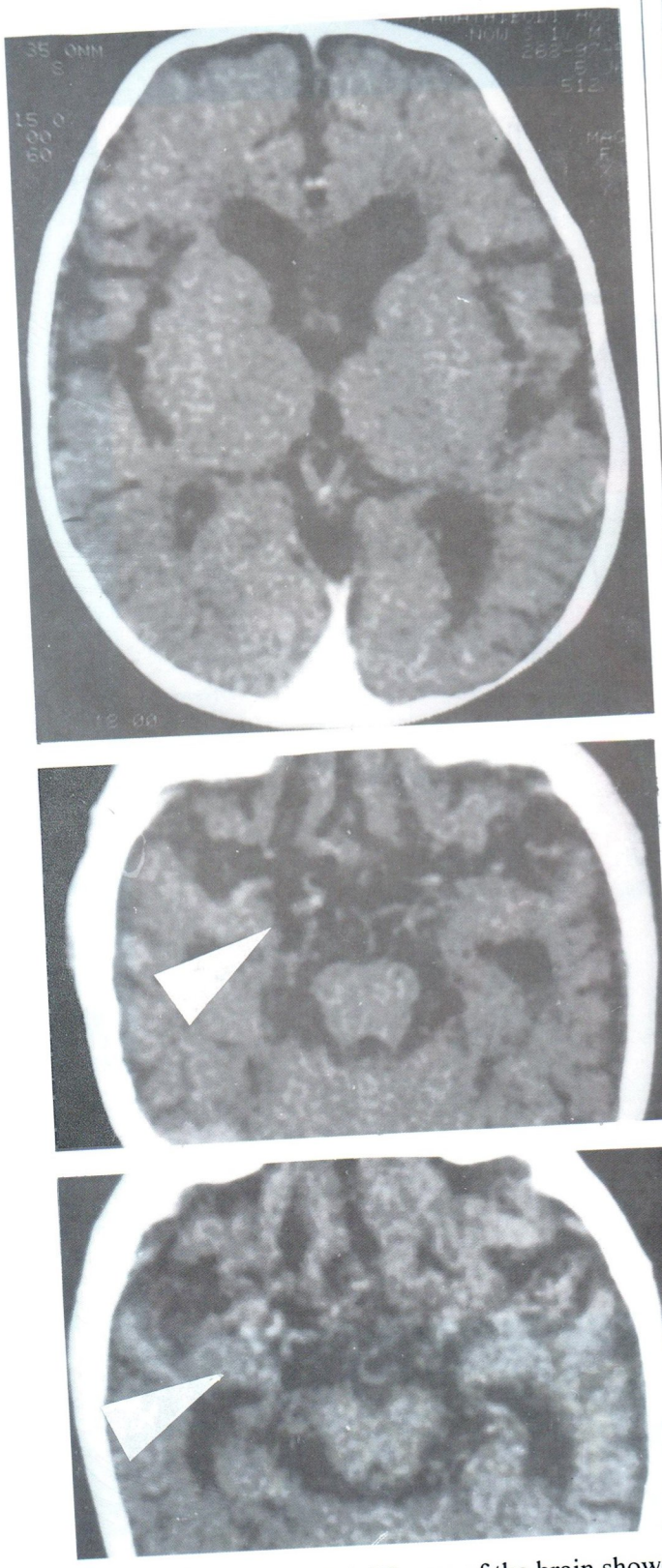

Fig. 4 Enhanced axial CT scan of the brain showed cerebral and cerebellar atrophy with tortuosity of the arteries in the region of the circle of Willis

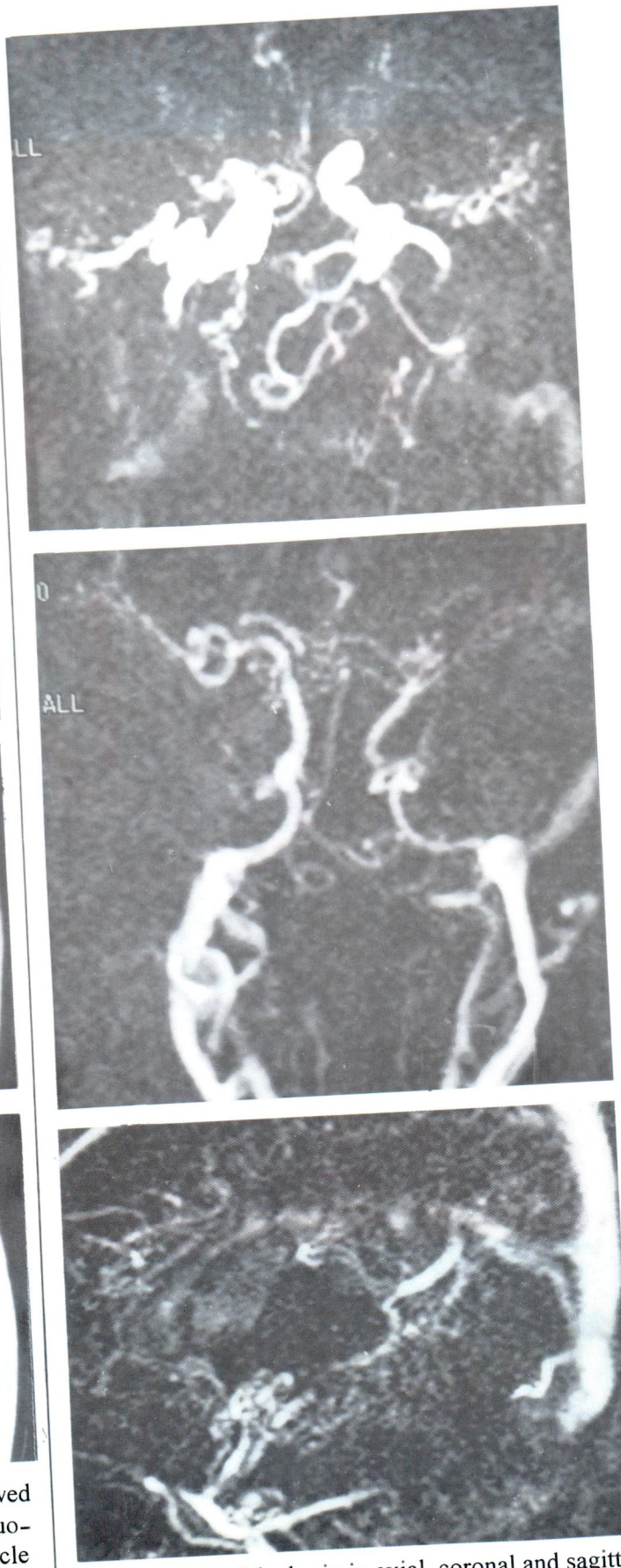

Fig. 5 MRA of the brain in axial, coronal and sagittal views shows loop- the-loop appearance of the intracranial arteries.