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Cerebral MR of Menkes Kinky-Hair Disease

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Menkes kinky-hair disease (trichopoliodystrophy, steely-hair disease) is an X-linked neurodegenerative disorder that occurs predominantly in males. It was first described by Menkes in 1962 [1]. The characteristic clinical features are steely hair, profound retardation, spastic quadriparesis, seizures, and hypothermia. The disease is caused by an underlying defect of copper metabolism; and the serum and hepatic copper levels are below normal [2, 3]. The radiologic features of this disorder include bone changes, tortuous cerebral vessels, cerebral atrophy, extracerebral fluid collections, and bladder diverticula [4–7]. Cerebral atrophy, extraaxial accumulation of fluid, and low-density cortical areas have been described in the limited number of children with this disorder who have had cerebral CT [8, 9].

We report on the cerebral MR imaging appearances in three patients with Menkes disease. MR was correlated with CT in each case.

Subjects and Methods

Three male children with Menkes disease ranging in age from 6 months to 13 years were studied by MR using a 0.3-T Fonar Beta 3000M permanent magnet. T1- and T2-weighted spin-echo (SE) sequences, 28,56/500,1999 (TRs/TEs), were used in all three patients. Inversion recovery (IR) sequences, 333/1545 (TI/TR), were also used in one patient (case 2). Images (512^2 matrix) were obtained in the axial plane initially, followed by coronal and/or sagittal planes. Patients fasted for 4 hr before the study, and they were sedated with oral chloral hydrate (80–100 mg/kg) 30 min before the study.

Case Reports

Case 1

J.D. is a 13-year-old boy in whom Menkes disease was diagnosed at 3 days of age. Physical examination at 8 hr of age revealed knots of friable kinky hair covering the scalp, a cephalhematoma, small mandible, talipes equinovarus, icterus, and thrombocytopenia. Skull radiographs demonstrated multiple wormian bones. The serum cop-

per level was 16 μg/dl, (normal, 90–110 μg/dl), serum ceruloplasmin 4 mg/dl (normal, 20–40 mg/dl), and hepatic copper concentration of 14 μg/gm dry weight (normal, 226 ± 57). Low serum levels of dopamine-β-hydroxylase activity were documented by enzyme assay. Elevated levels of dopamine and decreased levels of norepinephrine were found both in blood and CSF. A scalp biopsy performed in the second week of life showed miniature hair follicles, pili torti, and monilethrix.

Although no seizures have been documented in this patient, a slowly progressive loss of motor, cognitive, and language abilities has been noted over a 12-year period.

Cerebral angiography performed in infancy revealed no abnormalities. A second angiogram at 5 years of age demonstrated typical arterial tortuosity. Cerebral CT, performed at the age of 9 years, demonstrated tortuosity of the middle cerebral arteries, dilated ventricles, and cortical atrophy.

At 12 years of age multiplanar cerebral MR scans were obtained. Vascular tortuosity (Fig. 1), increased ventricular size, and cortical atrophy were well demonstrated.

Case 2

D. McF. was admitted to our hospital at the age of 6 months for the evaluation of steely hair, seizures, and developmental delay. The serum copper level was 19 μg/dl. Serum catecholamine values were consistent with defective activity of dopamine-β-hydroxylase. CT scans revealed evidence of cerebral atrophy and a large left extracerebral fluid collection.

An MR scan at the age of 15 months demonstrated the large extracerebral fluid collection and underlying cortical atrophy (Fig. 2). The subdural hygroma was subsequently drained by a ventriculoperitoneal shunt. Tortuosity of cerebral vessels was demonstrated.

Case 3

F.S., a 21-month-old boy, was admitted to our hospital at the age of 9 months for evaluation of Menkes disease. The initial physical examination revealed steely scalp hair, infantile spasms, mild spastic quadriplegia, and a functioning level of 3 months. The serum copper level was 17 μg/dl, and serum ceruloplasmin was 9 mg/dl, confirming the diagnosis.
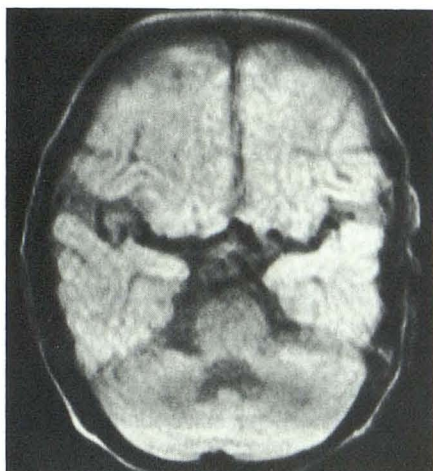
Fig. 1.—Spin-echo axial MR image (TE = 56/ TR = 1999) of 12-year-old boy shows tortuosity of both middle cerebral arteries.

Fig. 2.—Inversion-recovery MR image (TI = 333/TR = 1545) of 15-month-old boy shows compression of left frontal horn and contralateral ventricular shift by the subdural collection.

Fig. 3.—Spin-echo coronal MR image (TE = 28/TR = 500) of 15-month-old boy shows cortical atrophy and increased ventricular size.

A CT scan at 6 months of age revealed evidence of cortical atrophy. An MR scan at 15 months of age, which employed similar pulse sequences to those used for the previous two patients, revealed evidence of cortical atrophy and increased ventricular size (Fig. 3). Tortuosity of cerebral vessels was not noted.

Discussion

Menkes disease is associated with an underlying abnormality of copper metabolism. Biochemical features of the disease include low serum, hepatic, and brain-copper levels. Defective intracellular binding and membrane transport of copper have been related to an abnormal metallotheonein (a copper-binding protein). Decreased absorption of copper from the gastrointestinal tract and the variations in copper concentrations from normal levels are noted in all organs [10]. There is decreased activity of copper-dependent enzymes, cytochrome oxidase A1 and A3 in liver, brain [11], and white cells [12]. Deficiency of dopamine-β-hydroxylase, with abnormal catecholamine levels in the blood and CSF, has been described [13]. The disease is typically recognized between 2 and 3 months of age, although it has been detected as early as 3 days (case 1) [14, 15]. The scalp hair is sparse, coarse, stubby, and devoid of pigment [1]. The microscopic examination of the hair demonstrates twisting of the hair shaft (pili torti), periodic narrowing (monilethrix), and fragmentation (trichorrhexis nodosa). Microcephaly and growth failure are common. Other congenital abnormalities frequently associated with this disorder include pectus excavatum, high arched palate, undescended testes, hiatal or inguinal hernias, and club feet [14].

The intracranial abnormalities encountered in this disorder have been attributed to numerous pathogeneses. The large subdural fluid collections (Fig. 2) are considered to be a consequence of the marked cerebral atrophy and the abnormal vascular structures. As the atrophied brain recedes from the dura, the bridging cortical veins tear, resulting in subdural

effusions [8]. The extracerebral fluid collections, originally demonstrated by ventriculography [7], are now easily demonstrated by both CT and MR. Early in infancy, these children may have infractions of the metaphyses of the long bones. The infractions and subdural effusions may suggest an erroneous diagnosis of the battered child syndrome. The diagnosis of Menkes disease should be considered in infants with large bilateral subdural collections who fail to respond to both medical and surgical treatment [2, 8].

Pathologic examination of the brain reveals multifocal areas of infarction and edema [8]. Neuronal loss and gliosis have been demonstrated in the cortex, basal ganglia, and thalami. The neuronal loss especially affects cells in the neocortex and cerebellum, and may be accompanied by calcification and iron deposition [16, 17]. Secondary axonal degeneration and gliosis are most intense during the first postnatal year [17–19]. Two etiologies for CNS pathology include an abnormality of copper metabolism [19, 20] and ischemic encephalomalacia secondary to vascular abnormalities [19].

Excessive tortuosity of the cerebral arteries has been demonstrated on angiography [7]. Tortuosity of the abdominal arterial system has also been described [9]. The tortuosity of the intracerebral vasculature may be well demonstrated by both CT and MR, and the relative ease with which this feature is demonstrated on MR will obviate the need for cerebral angiography.

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