CASE REPORT

Neuroimaging findings in Menkes disease: a rare neurodegenerative disorder

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SUMMARY

Menkes disease is a rare neurodegenerative metabolic disease with a reported incidence of 1 per 300 000 live births. It occurs due to mutations in ATP7A gene located on X-chromosome leading to deficiency of several copper-containing enzymes. The patient presents with history of neuroregression with characteristic kinky hair. MRI is the imaging modality of choice. Characteristic imaging findings are: bilateral subdural hygromas, cerebral and cerebellar atrophy, white matter changes and tortuous intracranial vessels on angiography. The rarity of this condition prompted us to report this case of Menkes disease along with the characteristic neuroimaging findings and brief review of literature.

BACKGROUND

Menkes disease (MD) is a rare neurodegenerative metabolic disease, which occurs due to mutations in ATP7A gene located on X-chromosome.^{1,2} It is due to deficiency of several copper-containing enzymes, which lead to defective absorption of copper at intestinal level and subsequently to defective metabolism of copper at cellular level.³ Clinically, patients present with neuroregression and kinky hair. MRI shows bilateral subdural hygromas, cerebral and cerebellar atrophy, tortuous intracranial vessels and white matter changes.¹ Biochemical investigations reveal low serum copper and ceruloplasmin levels.⁴ Close differential includes shaken baby syndrome. However, characteristic neuroimaging findings and biochemical parameters help us to differentiate between them. As MD is a rare disease, every radiologist should know the neuroimaging findings so as to diagnose the disease early and aid in further prompt management of the patient.

Figure 1 (A, B) Sparse hypopigmented hair (kinky hair appearance) with fair complexion.

Figure 2 T2W axial (A) and FLAIR (B) images show bilateral subdural hygromas.

CASE PRESENTATION

An male child aged 11 months born out of a consanguineous marriage with history of normal delivery and no history of perinatal asphyxia presented to our department for investigation. Patient had an unremarkable neonatal period until 5 months of age. After that he started suffering from fever, intermittent episodes of myoclonic seizures and regression of milestones.

Family history

Patient was the first and only child of the parents. Similar history and presentation was not present in any of the first-degree relatives.

On clinical examination, patient had sparse, kinky and hypopigmented hair with easy pluckability ([figure 1](#)). This patient had fair complexion, was hypotonic and irritable. Head circumference of the patient was 42.8 cm, which was below third percentile for that age.

INVESTIGATIONS

Patient was referred for neuroimaging. MRI findings revealed bilateral subdural hygromas on both T2 weighted sequence (T2W) and Fluid attenuated inversion recovery (FLAIR) images ([figure 2A, B](#)) with associated cerebral atrophy. T2W axial and coronal images ([figure 3A, B](#)) showed bilateral cerebral and cerebellar atrophy. Axial diffusion-weighted imaging (DWI) and ADC ([figure 4A, B](#)) showed white matter lesion with restricted diffusion on both sides. MR angiography (time-of-flight) images showed tortuous extracranial and intracranial vessels ([figure 5A, B](#)).

After MRI, patient was advised biochemical investigations. Findings revealed low serum copper 40 mg/dL (normal range 70–140 mg/dL) and low ceruloplasmin level 5 mg/dL (normal 15–60 mg/dL).

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Figure 3 T2W axial (A) and coronal (B) images show bilateral symmetric cerebral and cerebellar atrophy.

DIFFERENTIAL DIAGNOSIS

- ▶ Shaken baby syndrome
- ▶ Biotinidase deficiency
- ▶ Organic acidurias
- ▶ Aminoacidurias
- ▶ Mitochondrial myopathies

TREATMENT

Patient was started on intravenous copper and histidine.

OUTCOME AND FOLLOW-UP

Patient was started on copper and histidine therapy; however, patient expired after 2 months of initiation of therapy at the age of 13 months due to severe respiratory infections.

DISCUSSION

MD is a rare multisystem neurodegenerative disorder of copper metabolism.^{1,2} It has incidence of 1 per 300 000 with male predominance. It is caused due to mutations in ATP7A gene and has X linked recessive Mendelian inheritance with genetic locus on Xq13.3.³ This is also called Menkes kinky hair disease or trichopoliodystrophy.

In MD, there is defective activity of several copper-containing enzymes causing impaired absorption of copper at intestinal level. This in turn leads to impaired metabolism at cellular level.

Clinically, patients present at the age of 5–6 months with history of neuroregression including loss of already developed

Figure 4 Axial diffusion-weighted imaging (A) and ADC (B) images show drop-shaped lesions in bilateral centrum semiovale with restricted diffusion.

Figure 5 MR angiography time-of-flight images show tortuous extracranial and intracranial vessels.

milestones, intermittent episodes of seizures, myoclonic jerks, poor weight gain, failure to thrive, sparse hypopigmented and easy pluckable hair (kinky hair appearance) and progressive hypotonia.³

On conventional skeletal radiography, the following findings are noted: diffuse osteoporosis, periosteal reaction, metaphyseal spurs especially at the knees, excessive epiphysal spurring leading to fragmentation and fractures and scalloping of posterior border of vertebral bodies.^{5,6}

MRI is the imaging modality of choice. Common findings include: diffuse symmetrical cerebral and cerebellar atrophy, bilateral diffuse white matter changes, hyperintense drop-shaped lesions in both centrum semiovale which show restricted diffusion on DWI, bilateral subdural hygromas representing subdural hematomas of varying stages and tortuous intracranial vessels.¹

Biochemical parameters reveal low serum copper and ceruloplasmin levels, which are characteristic of MD.⁴

Treatment includes intravenous copper and histidine therapy. Death usually occurs due to respiratory compromise by the age of 3 years; however, early diagnosis and treatment is essential.

Learning points

- ▶ Although Menkes disease is rare, characteristic imaging findings of tortuous intracranial vessels along with bilateral subdural hygromas, low serum copper and ceruloplasmin levels and kinky hair appearance help both radiologist and referring doctor to diagnose the disease early and differentiate it from shaken baby syndrome, which is a close differential.
- ▶ This goes a long way in initiating early treatment of the patient.

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REFERENCES

- 1 Manara R, D'Agata L, Rocco MC, *et al.* Neuroimaging changes in menkes disease, part 1. *AJNR Am J Neuroradiol* 2017;38.
- 2 Manara R, Rocco MC, D'agata L, *et al.* Neuroimaging changes in menkes disease, part 2. *AJNR Am J Neuroradiol* 2017;38:1858–65.
- 3 Gandhi R, Kakkar R, Rajan S, *et al.* Menkes kinky hair syndrome: a rare neurodegenerative disease. *Case Rep Radiol* 2012;2012:1–4.
- 4 Kodama H, Fujisawa C, Bhadhprasit W. Inherited copper transport disorders: biochemical mechanisms, diagnosis, and treatment. *Curr Drug Metab* 2012;13:237–50.
- 5 Kabra M, Gangakhedkar AK, Pasi GR, *et al.* Menkes' kinky hair disease: new considerations. *Indian Pediatr* 1996;33:956–9.
- 6 Adams PC, Strand RD, Bresnan MJ, *et al.* Kinky hair syndrome: serial study of radiological findings with emphasis on the similarity to the battered child syndrome. *Radiology* 1974;112:401–7.

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