

Menkes disease: A rare disorder

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Abstract

Menkes disease (MD) (OMIM: 309400) is also known as kinky hair disease, trichopoliodystrophy, and steely hair. A 7-months-old, male infant presented to our outpatient department in June 2016 with history of developmental delay and seizures. Seizures started at 3 months of age and worsened progressively to clusters of extensor spasms.

Physical examination showed sparse and kinky hair. Neurological examination revealed a central hypotonia with marked decrease in muscle power with normal deep tendon reflexes.

The serum ceruloplasmin level and serum copper level were decreased. Ultrasound KUB showed Hutch diverticulum along left ureteric orifice. Magnetic resonance imaging (MRI) carried out at five months of age showed frontal cortical atrophy. His EEG was consistent with hypsarrhythmia pattern.

Patients with classic MD usually exhibit a severe neurodegenerative course, with poor long term outcome and death before the third year of life.

Keywords: Menkes disease, Infantile spasms, Hypsarrhythmia.

Introduction

Menkes disease (MD)(OMIM: 309400) is also known as kinky hair disease, trichopoliodystrophy, and steely hair.¹ It is a rare disorder with frequency being estimated to be 1 in 114,000-250,000 live births.² Menkes disease is diagnosed on the basis of history, physical findings and lab investigations including copper and ceruloplasmin level as well as hair shaft microscopy.³ Mutation analysis leads to the definitive diagnosis. Epilepsy is one of the main clinical features of this disease⁴ but it has been described in detail by only a few authors. Most patients develop seizures from 2 to 3 months of age, accompanied by neurodevelopmental regression and followed by poor long term outcome and death before the third year of life and the cause of death is usually respiratory failure

secondary to pneumonia.⁵ The history of epilepsy is usually characterized by 3 stages: a first stage is marked by focal clonic seizures and status epilepticus occurring at mean 3 months of age. It is followed by, an intermediate stage with infantile spasms, and a late stage with multifocal, myoclonic, and tonic seizures.⁶ The management involves copper histidine supplementation.⁷ Hence it is extremely important to identify and report as many cases of this disease as possible.

We report a case of classic MD diagnosed in Aga Khan University Hospital, a university tertiary hospital Karachi who presented in June 2016.

Case Report

A 7-months-old, male infant presented to our outpatient department in June 2016 with history of developmental delay and seizures. Seizures started at 3 months of age, comprising of uprolling of eyes and upper limb extension lasting for 3 minutes. Second episode occurred at 4 months of age with similar presentation along with blinking movements. Subsequently, the episodes increased such that the infant had 3-4 episodes daily now consisting of clusters of extensor spasms. He was born at term via Caesarian section. The mother had no known comorbidities. There were normal foetal movements but at the time of delivery, there was foetal distress and meconium stained liquor. He developed respiratory



Figure-1: Seven months old infant with generalized hypotonia.

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Figure-2: Scanty and hypopigmented scalp hair.



Figure-3: Gross microscopic image of the hair shaft showing occasional kink.

distress and required oxygen. He remained hospitalized for 8 days. The milestones were also delayed such as he had not achieved neck holding as yet. He was kept on direct breast feeding for 3 months but later had issues of aspiration therefore requiring nasogastric feeds. The parents were non-consanguineously related and the elder two siblings were healthy.

Physical examination showed a haemodynamically stable infant with fair complexion with lax and loose skin folds and sagging pudgy cheeks. He also had a generalized increase in subcutaneous fat with loose and thin skin. He had sparse and kinky hair. Neurological examination revealed a floppy baby, without social smile. He was also hypotonic, with diminished muscle tone in the axial muscles, unable to lift head against gravity. There was marked decrease in muscle power with normal deep tendon reflexes (Figure-1 and 2).

The lab workup showed that red and white blood cell count, platelet count, sodium, potassium, creatinine, alanine aminotransferases, creatine kinase, lactate, thyroid hormones, urine for organic acids and plasma for amino acids were all within normal ranges. The serum ceruloplasmin level (20 mg/L; normal value >200 mg/L) and serum copper level (30 µg/dL; normal value: 90 to 190 µg/dL) were decreased. Ultrasound of kidneys and urinary bladder showed Hutch diverticulum along left ureteric orifice.

Magnetic resonance imaging (MRI) carried out at five months of age showed frontal cortical atrophy.

On the first electroencephalogram (EEG) done at 6 months of age, there was bilateral independent with dominant posterior quadrant at time seen to be generalized spike, poly spikes, sharp and slow wave discharges. His next EEG was carried out at 9 months of age showed an abnormally disorganized background activity with frequent multifocal, bilateral posterior dominant as well as generalized spikes, polyspikes, sharp and slow wave discharges followed by diffuse voltage suppression, which was consistent with hypsarrhythmia pattern.

Light microscopic examination of the hair showed pili torti (twisted hair shafts) (Figure-3). Mutation analysis could not be performed due to lack of resources.

The patient was initially managed with phenobarbital and levetiracetam. Later on, Vigabatrin and ACTH were added to the regimen as his seizures could not be adequately controlled. At present, he is profoundly delayed and has not achieved any of the motor milestones but his seizure frequency has reduced.

The Ethical Review Board of the hospital approved the publication of this case and written consent was obtained from the father of the child.

Discussion

Menkes disease (MD) belongs to a group of diseases that mainly affect the gray matter of the brain.² It is one of the three known disorders of copper homeostasis. There have been various case reports on the clinical features of Menkes. Infants with classic Menkes Disease typically remain healthy until 2 to 3 months of age and then recognition of seizures and hypotonia and failure to thrive begin and they usually die by the age of 3 years.⁸ They have a peculiar hair type i.e. scanty, short and hypopigmented. Children have lax skin and joints, bladder diverticula, inguinal hernia, vascular tortuosity, and normal or slightly below average intelligence.⁹ There is also significant truncal hypotonia with hyperactive

deep tendon reflexes. There have been case reports on infantile spasms and epilepsia partialis continua¹⁰ as the only presenting manifestation of this disease.

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Conflict of Interest: None to declare.

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