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Case Report

Menkes Syndrome: A Case Report

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Abstract
Menkes disease is a rare x-linked recessive disorder of copper metabolism characterized by neuro-degeneration and brittle kinky hair. We are presenting a case of a 7 month old male infant who was admitted to the hospital with history of convulsions since 4 months of age along with history of on and off cold since 5 months of age. Infant had delayed milestones for his age and truncal hypotonia. The infant had fair complexion with cherubic appearance along with light colored fuzzy, brittle and sparse hair. Based on clinical presentation, menkes disease was suspected and hence serum copper and ceruloplasmin levels were also checked along with the routine blood profile. Routine blood profile analysis were normal but serum copper and ceruloplasmin levels were found to be low. Serum copper was 80.77ug/dl and serum ceruloplasmin was <8mg/dl. Light microscopic examination of brittle kinky hair showed pili torti (flattened and twisted hair). MRI showed prominent extraaxial spaces with gliosis. Based on clinical appearance, hair microscopy findings, low serum copper and ceruloplasmin levels, infant was diagnosed as a case of Menkes disease and was managed symptomatically. Genetic study could not be done due to lack of facilities.
Keywords: *Menkes disease, Copper, Ceruloplasmin, Pili Torti.*

Introduction

Menkes disease is also referred to as Menkes Kinky Hair syndrome, Kinky Hair Disease and Steely hair disease. It is described as a rare X-linked recessive disorder of copper metabolism[1]. Characteristic clinical features of menkes disease are progressive neurological deterioration, delayed milestones, intractable seizures and typical cherubic facial appearance with brittle kinky hair showing hair abnormalities[2]. The onset of its clinical features typically occurs during infancy. The infant usually dies within 3–4 years of age. It occurs due to mutation of pATPase7 gene .It is an x-linked recessive copper metabolism disorder with low copper levels in different tissues of body. Estimated prevalence of disease is 1 in 1,00,000 to 1 in 2,50,000[3]. In 1962, Menkes first described the syndrome and Drank et.al noted the association with copper metabolism[4].

Case Report

A 7 months old male patient was brought to the hospital with complaints of recurrent episodes of convulsions since 4 months of age, delayed milestones along with hypotonia since 5 months of age and intermittent episodes of cold and cough since 5 months of age. He was born at full term following a normal pregnancy and was third child of his parents. His parents had a consanguineous marriage. Elder two siblings of the child were

normal without any history of seizures or neuro developmental delay. The seizures were recurrent and myoclonic type, involving only the limbs. Child was managed symptomatically for the seizures with Sodium valproate and Phenobarbital, obtaining partial control of his seizures. Child had delayed milestones along with sluggish reflexes and poor head control since 5 months of age. His early development was appropriate for the age till the age of 3 months and then started regressing. There was hypotonia predominantly of the trunk along with laxity of skin. Child also had intermittent episodes of cold and cough since 5 months of age which was managed accordingly. PEM was ruled out as the anthropometric measurements of the child were appropriate for his age and were as follows – Head circumference = 44cms, chest circumference = 40 cms, length = 68cms and weight = 8 kgs.

On clinical examination, child had cherubic appearance with fair complexion (Figure 1). His scalp hair were light coloured, sparse, kinky, fuzzy and easily breakable (Figure 2). Brittle hair were viewed under light microscope and showed flattening and twisting of hair shaft. This hair shaft abnormality is called as pili torti (Figure 3). Based on clinical examination findings, menkes disease was suspected. Hence along with routine blood profile, serum copper and ceruloplasmin levels were also checked and were found to be below normal levels. Serum copper level was 80.77 ug/dl (ref. range is 90-190 ug/dl). Serum ceruloplasmin was <8mg/dl (ref. range is 20-60 mg/dl). There was no abnormality in other standard blood analysis. X-ray of the long bones showed osteopenia and metaphyseal widening. MRI brain showed prominent extra axial spaces with gliosis. Typical history of the child along with the findings of clinical examination and the investigations lead us to the diagnosis of Menkes disease. However genetic work up could not be done in this case due to lack of availability.

Figure 1 Showing phenotypic appearance of the child - fair complexion with chubby cheeks and sparse hair

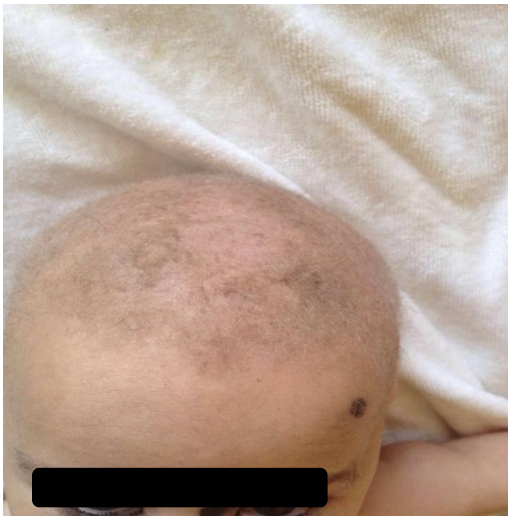

Figure 2- Showing sparse, light coloured, kinky and fuzzy scalp hair.

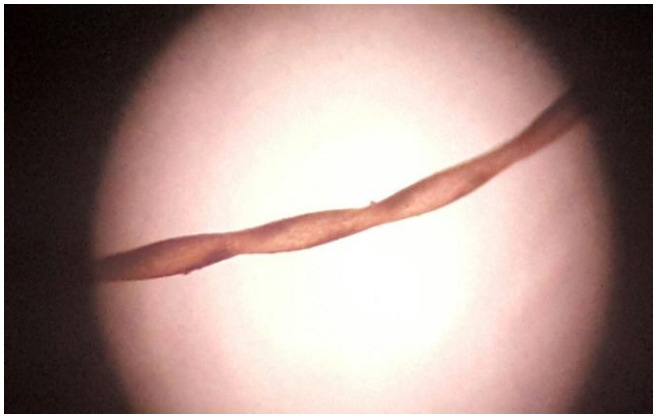

Figure 3- Light microscopic examination of the hair showing characteristic Pili torti- flattened and twisted hair

Discussion

First case of menkes disease was described by Menkes in 1962 [5]. Underlying biochemical defect in copper metabolism was discovered ten years later in 1993 [6]. Genetic mutation in menkes disease results in defective production of intracellular protein involved in copper transport[7]. Absence of copper can secondarily impair the action of other enzymes such as cytochrome C oxidase, superoxide-dismutase, tyrosinase and lisine oxidase, which then leads to a multisystemic compromise, especially the central nervous system[8].

Menkes disease is a systemic copper deficiency syndrome and the infants start manifesting the clinical features at the age of 2 to 3 months. Racial predilection is not seen as such[9]. Males are more affected than females. Our patient was also a male infant who started manifesting the symptoms at the age of 4 months. Main clinical features include developmental delay, neurological degeneration, seizures and hair abnormalities[10].

Children with classic Menkes disease typically appear healthy upto 3 months of age and then after 3 months, they start to demonstrate central nervous system manifestations such as intractable seizures, developmental delay and hypotonia[1,11]. Children often have cherubic appearance of face with sparse, fuzzy, twisted and light colored hair on scalp[12]. There are various hair shaft abnormalities in menkes disease like pili torti (twisted and flattened hair), monilethrix (varying diameter of hair shafts) and trichorrhexis nodosa ; out of which pili torti is the commonest hair shaft abnormality[13].

Our patient showed cherubic facial appearance, sparse, kinky and light colored scalp hair with pili torti on hair microscopy. These features were similar to those reported in other studies [1,11,14] . Presence of non skin manifestations in our patient such as intractable seizures , truncal hypotonia and delayed developmental milestones were similar to other reported cases [1,11,14]. Thus the typical history and clinical features of our patient were suggestive of classical menkes disease. Low levels of both serum copper and ceruloplasmin are needed to confirm the diagnosis[15]. Our patient also had low levels of both serum copper and serum ceruloplasmin. Findings of skeletal survey and MRI are supportive to the diagnosis. Due to lack of facility, genetic work up could not be done in our case. Treatment mainly with parenteral copper histidine might be beneficial when given early in the course of the disease[15]. However our patient was managed symptomatically only for his seizures . As parenteral copper histidine was not available at our setup, patient was referred to higher centre for parenteral copper histidine therapy.

Prevention

By genetic analysis and/ or by measurement of the copper concentration in culture of amniotic liquid cells and chorionic villi cells, prenatal diagnosis of menkes disease can be done[16]. Menkes disease shows an x-linked inheritance pattern but 33% cases can occur due to mutation[9]. Early diagnosis of this condition can help in genetic counseling.

Conclusion

Since Menkes disease is a rare entity, one needs to be familiar with its clinical presentation so as to diagnose it at the earliest. Maintaining a high index of suspicion for menkes disease is also necessary so as to provide early treatment to the child as well as for prenatal genetic counseling.

References

1. Menkes JH. Kinky hair disease, Pediatrics 1972;50(2):181-3.
2. M Barzegar, Fayyazie A et al. Menkes Disease: Report of Two Cases. Iran J Pediatr 2007;17(4):388-392.
3. Kirodian BG, Gogtay NJ, Udani VP, Kashirsagar NA. Treatment of Menkes disease with parental copper histidine. Indian Pediatrics 2002; 39**:**183-185.
4. Drank DM, Cartwright E, Stevens BJ, Townley RR. Menke's kinkey hair disease: Further definition of the defect in copper

transport. Science 1973; 79(78**):**1140-2. [Medline].

5. Menkes JH, Alter M, Steigleder GK et al. A sex-linked recessive disorder with retardation of growth, peculiar hair, and focal cerebral and cerebellar degeneration. Pediatrics 1962; 29:764-779.
6. Danks DM, Campbell PE, Stevens BJ et al. Menkes kinky hair syndrome: An inherited defect in copper absorption with widespread effects. Pediatr 1972;50(2): 188-201.
7. Chelly J, Tumer Z, Tonnesen T et al. Isolation of a candidate gene for Menkes disease that encodes a potential heavy metal binding protein. Nat Genet 1993;3:14-19.
8. Voskoboinik I, Camakaris J. Menkes copper-translocating P-type ATPase (ATP7A): biochemical and cell biology properties and role in Menkes disease. J Bioenerg Biomembr 2002;34:363-371.
9. Datta AK, Ghosh T, Nayak K, Ghos Mrinalkanti. Menkes kinky hair disease: A case report. Cases Journal 2008; 1:158.
10. Aicardi J. Menkes disease (kinky hair disease, steely hair disease, trichopoliodystrophy). In: Aicardi J (ed). Diseases of the nervous system in childhood. 2nd ed . London: Mac Keith Press; 1998. p.306-308.
11. Menkes JH. Kinky hair disease: twenty five years later. Brain Dev 1998;10(2):77-9.
12. Proud VK, Mussell HG, Kaler SG et al. Distinctive Menkes disease variant with occipital horns: delineation of natural history and clinical phenotype. Am J Med Genet 1996; 65(1):44-51.
13. Whiting DA. Structural abnormalities of the hair shaft. J Am Acad Dermatol 1987;16(1.1):1-25.
14. Menkes JH, Wilcox WR. Inherited metabolic disease of the nervous system. In: Menkes JH, Sarnat HB, Maria BL, (eds). Child Neurology. 7th ed. Philadelphia: Lippimcott Williams & Wilkins; 2006. p.115-7.
15. Kodama H, Murata Y, Kobayashi M. Clinical manifestations and treatment of Menkes disease and its variants. Pediatr Int 1999;41:423-429.
16. Gu YU, Kodama H, Sato E et al. Prenatal diagnosis of Menkes disease by genetic analysis and copper measurement. Brain Dev 2002; 24(7):715-8.