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Case Report

Menke's Kinky Hair Syndrome- a rare medical condition

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Abstract

The case of a 16-month-old boy is described who had typical clinical and radiological features and was proven biochemically to be a case of Menke's disease. Clinical manifestations began in the first few months with hypothermia, hypotonia, seizures and death occurring at the age of 18 months.

Introduction

Menkes' kinky-hair syndrome (MKHS) is an X-linked recessive lethal disorder of copper transport. This disorder is also known as kinky-hair syndrome, steely-hair syndrome, and Menkes' disease. It is a multisystem disease that manifests with hair abnormalities, hypo pigmentation, connective tissue changes, and neuro-degenerative symptoms. Unfortunately, the prognosis for MKHS is still grim, with most patients dying by the age of 3-4 years.

Case Report

A 16-month boy was admitted with history of sudden attacks of generalized tonic-clonic contractions, each episode lasting for about 2 minutes with loss of consciousness. The boy also had repeated attacks of bronchial asthma which responded well to bronchodilators. Two months back the patient was hospitalized due to massive broncho -pneumonia with acute respiratory failure which required assisted ventilation. Family history revealed that one of his elder brother died within 3 days of delivery, rest of the siblings i.e. one brother aged 8 years and a sister aged 6 years were all healthy and normal.

Detailed physical examination showed that the child had pudgy cheeks, depressed nasal bridge, and highly arched palate. There were eczematous lesions on his cheeks and neck folds, skin was pale, doughy and lax with prominent folds notably on the upper arms, thighs and posterior neck (Figure 1). The scalp hair was sparse, short, brittle, fragile and kinky steel wool-like. There were patches of hypo-pigmented hair on the scalp, light microscopy demonstrated hair twisted longitudinally with narrowing at intervals (Figure 2). In addition erosions on the shaft of the hair could be seen. The hair on the eyebrows and eyelashes were also scanty. Central nervous system examination revealed that anterior fontanale was flat, there was hypotonia with diminished deep tendon reflexes. Developmental milestones such as rolling from side to side, sitting, crawling or holding objects in hand and head control were delayed. The

Figure 1. The child with sparse, short, kinky steel wool-like scalp hairs. Lax skin with prominent folds notable on the upper arms.

Figure 2. The scalp hair twisted longitudinally with narrowing at intervals, as seen under light microscope. child had feeding difficulties and the speech was incomprehensive.

Blood counts and blood chemistry was normal except serum copper was low 12mg/ dL (normal 80mg/dL-

associated low serum copper and ceruloplasmin levels resulting in a deficiency in copper-dependent enzyme activity. The resulting defects are reflected in the clinical phenotype which is marked by fine silvery wiry hair, doughy skin, connective tissue disturbances, and progressive neurologic deterioration. KHD has been estimated at 1 in 114,000 to 1 in 250,000 live births.² No racial predilection exists. The phenotype of this syndrome is manifested in male patients while female carriers may have pili torti and uneven skin pigmentation, which appears unilaterally or along the lines of Blaschko.

The initial diagnosis of MKHS is suggested by clinical features. The cutaneous manifestations in our patient included eczematous lesions on his cheeks, neck folds and prominent skin folds over his forearms, similar description of prominent skin folds in the forearms and groins have been reported in the past.³ The child had pudgy cheeks, depressed nasal bridge, and highly arched palate. Grover et al observed that children with this disorder had cherubic facial appearance with a depressed nasal bridge and reduced movements.⁴ Congenital malformations such as micrognathia, premature closure of the lambdoidal sutures, pectus excavatum, and clubfeet have also been reported in the past.⁵

Hair is the most striking sign in this syndrome. This 16-month-old patient showed scanty, lusterless, kinky hair which when under light microscope showed hair twisted longitudinally with narrowing at intervals along-with many erosions on the hair shaft, this twisting of the hair fiber creates the illusion of wide and narrow areas along the hair shaft. The hair was fragile and fractured easily, resulting in apparent generalized alopecia. Examination for hair shaft abnormalities can usually be accomplished with light microscopy using phase contrast optics. In addition, scanning electron microscope can be used to identify abnormalities not detected by light microscopy.⁶ Several hair shaft abnormalities have been documented, with pili torti being the most common, also trichorrhexis nodosa, trichoclasia, and trichoptilosis have been reported.^{1,7,8} The scalp hair may appear normal at birth, but by approximately three months of age the hair on the scalp and eyebrows becomes kinky, coarse, and lightens in colour. The cutaneous hypopigmentation may be generalized or localized to the skin folds especially in the region of the-posterior neck, leg folds, and eyebrows. The pigmentary abnormalities are due to a functional deficiency of the copper-dependent enzyme tyrosinase. Hair shafts in MKHS have been found to contain nine times the normal amount of free sulfhydryls.⁷

Non-skin manifestations in our patient included delayed developmental milestones such as head control, sitting, crawling or holding objects, also the child had hypotonia, with diminished deep tendon reflexes. Baerlocher and

Figure 3. Radiograph of the long bones showing laminated periosteal elevation with spurs at the proximal metaphysis and widening of the distal metaphysis of the right femur.

150mg/dL), serum ceruloplasmin 6mg /dL (normal 20mg/dL-70mg/dL). Toxoplasmosis, Rubella, Cytomegalovirus, Herpes (TORCH) profile was negative. Radiographs of the long bones revealed laminated periosteal elevation with spurs at the proximal metaphysis and widening of the distal metaphysis (Figure 3). Abdominal scan showed an enlarged liver, there was no other organomegaly. C.T brain at the age of 2½ months showed mild frontal atrophy and early leucomalacia which appeared as accentuation of gray and white matter differentiation due to diffuse hypo density of the white matter. CT scan repeated at the age of 8 months showed diffuse brain atrophy with prominent and widened sylvian fissure and lateral ventricles. EEG was normal. The course was inexorably downhill with rapid neurological deterioration and the patient died at the age of 18 months.

Discussion

Menke's kinky hair syndrome is an X-linked recessive multisystemic lethal disorder of copper metabolism. In 1962, Menkes¹ first described the syndrome and 10 years later Danks noted the association with copper metabolism and described a defect in intestinal copper transport with

hypotonia, with diminished deep tendon reflexes. Baerlocher and Nadal provided a comprehensive review on similar findings.⁹ The progressive neuro-degeneration in this disease usually begins at the age of about two months as a result of gliosis and demyelination of the cerebrum and cerebellum resulting in symptoms such as seizures, developmental regression, and muscle hypotonia and feeding difficulties.^{1,5} Skeletal abnormalities are manifested as infantile cortical hyper-osteosis, metaphyseal widening and spurring of the long bones and a diaphyseal periosteal reaction.¹⁰ Our patient had a low serum copper and ceruoplasmin levels which correlated with the clinical findings, these levels are usually low but interpretation may be difficult in the first few months of life.⁵ Copper levels are also low in liver and brain, but are elevated in several other tissues, notably intestinal mucosa, muscle, spleen, and kidney. The copper content of cultured fibroblasts, myotubes and lymphocytes derived from patients with KHD is several times greater than as compared to the control cells.¹¹

Medical care is symptomatic and mainly supportive. Early treatment with intravenous or oral copper supplements may be of some benefit, but will not stop the progression of the disease. The prognosis is therefore poor and patients usually die within the first decade of life.

These patients usually get repeated chest infections which is also the most common cause of death. These chest infections are sometimes the precipitating factor for bronchial asthma.

With the isolation of the MNK gene, it is now possi-

ble to do DNA-based prenatal diagnosis however, mutation detection is difficult in MKHS due to the fact that the MNK gene is widely expressed, therefore gene therapy is unlikely in the near future.

In short Menke's hair disease proved a designation useful in detection of new cases, since the hair change is an easily remembered feature by which physicians can be alerted for the early diagnosis and management of this condition.

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