Iliac Artery Aneurysms in Menkes Disease: A Case Report

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Background: Menkes disease is a disorder of copper transportation that results in multi-systems involvement including neurological deterioration, seizure, dysmorphic facies and kinky hair. The authors report a case of Menkes disease that was complicated with bilateral iliac artery aneurysms.

Case Report: A 6-month-old Thai male infant presented with seizure, global delayed development, hypotonia and sparse, short, lightly pigmented and kinky hair. Light microscopic hair analysis showed pili torti. His serum copper and ceruloplasmin levels were low and were compatible with Menkes disease. Radiological finding from magnetic resonance angiography (MRA) revealed irregular tortuosity of abdominal aorta, a large right internal iliac artery aneurysm and a small left common iliac artery aneurysm. Genetic counseling and supportive treatment were provided for this patient.

Conclusion: Iliac aneurysms are a serious complication of patients with Menkes disease. Careful investigation with computed tomographic angiography (CTA) or MRA is helpful in those patients.

Keywords: Menkes disease, Iliac aneurysm, ATP7A, Pili torti

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Menkes disease is a rare X-linked recessive inherited metabolic disorder with incidence of 1:250,000 live births(1). It is caused by ATP7A mutation that results in copper transportation protein defect. The clinical presentation includes hypotonia, failure to thrive, progressive neurological deterioration, seizure, dysmorphic facies and abnormal pigmentation of skin and hair. Abnormal characteristic feature of hair is pili torti (hair shaft twisting 180°)(2). Laboratory findings of an affected individual reveal low level of serum copper and ceruloplasmin. Without early treatment, patients with Menkes disease usually die by the age of three years(2). Arterial tortuosity is a mainly vascular complication, but on the other hand large arterial aneurysm is extremely rare in the disease. The authors describe a case report of Menkes disease with unusual complication of iliac artery aneurysms. This case report was approved by the Ethics Committee in Human Research, Khon Kaen University, with the approval number of HE561229.
Wormian bones were found on skull radiography (Fig. 3). Urinary bladder diverticulum was not found on ultrasonography of the KUB system but there was evidence of arterial aneurysm at right lower abdomen. Magnetic resonance angiography (MRA) of abdominal aorta was further investigated and revealed a large right internal iliac artery aneurysm and a small left common iliac artery aneurysm (Fig. 4A). Magnetic resonance imaging (MRI) of brain showed tortuous and dilated vessels within circle of Willis and diffused brain atrophy (Fig. 4B). Regarding poor clinical outcome due to late diagnosis in this patient, management was supportive treatment and follow-up without any surgery. The patient suffered from several episodes of aspiration pneumonia and died when he was 1.5 years old.

**Discussion**

Menkes disease is an inherited metabolic
disorder that has a defect of copper metabolism. It is caused by mutation in ATP7A gene that regulate copper exportation from intestinal cells and results in copper deficiency. Copper is required for cuproenzymes such as cytchrome-c-oxidase, superoxide dismutase, ceramidigalactosyl transferase, dopamine beta-hydroxylase, tyrosinase, phenylalanine hydroxylase and lysyloxidase that plays an important role in many cellular functions in several organ systems especially brain. Thus, reducing of cuproenzymes activities and lysyloxidase that plays an important role in many hydroxylase, tyrosinase, phenylalanine hydroxylase such as cytochrome-c-oxidase, superoxide dismutase, deficiency. Copper is required for cuproenzymes exportation from intestinal cells and results in copper complication and a significant leading cause of death.

This is a consequence from insufficiency of lysyl oxidase due to defects in collagen and elastin cross-linking. It is a reduction of tensile strength of blood vessels wall extremely rare. Pathogenesis of vascular abnormalities, vascular tortuosity is the vast majority complications, while arterial and venous aneurysms are included. Radiographic findings of bones including generalized osteoporosis, flaring metaphyses of the long bones, short clavicles, rib fractures and wormian bones in the cranial sutures are observed. The specific characteristic of hair including short, coarse, sparse, silver, pili torti (hair shaft twisting 180°), monilethrix (varying diameters of the hair shaft), trichorrhexis nodosa (nodes along the hair shaft), trichoclasia (transverse fractures of the hair shaft) and trichoptilosis (longitudinal splitting of the hair shaft) on microscopic hair analysis is very helpful to determine the diagnosis. Serum copper and ceruloplasmin levels are useful biochemical markers that support the diagnosis of Menkes disease. Detection of mutation in ATP7A gene is used to confirm the diagnosis and also helpful for prenatal diagnosis and genetic counseling.

An individual with Menkes disease can be complicated with bladder diverticulum, umbilical hernia and vascular abnormalities. Among vascular abnormalities, vascular tortuosity is the vast majority complication, while arterial and venous aneurysms are extremely rare. Pathogenesis of vascular abnormalities is a reduction of tensile strength of blood vessels wall due to defects in collagen and elastin cross-linking. This is a consequence from insufficiency of lysyl oxidase activity. Arterial aneurysms are a serious complication and a significant leading cause of death. They have been reported in various vessels including brachial, hepatic, iliac, lumbar and splenic arteries. Venous aneurysm or phlebectasia is another rare vascular complication that is also found in Menkes disease. This evidence supports that either computed tomographic angiography (CTA) or MRA is necessary for early detection of this disease.

Conclusion

Menkes disease should be considered in an infant with neurological deterioration and abnormal hair. The authors report bilateral iliaca artery aneurysms as rare complications of this disease. Investigation with CTA or MRA is necessary for early detection of this complication.

What is already known on this topic?

Menkes disease is a rare X-linked recessive inherited metabolic disorder of Copper transportation. The clinical presentation includes hypotonia, failure to thrive, progressive neurological deterioration, seizure, dysmorphic facies and kinky hair. Individual with Menkes disease has low levels of serum copper and ceruloplasmin. Some patients have arterial tortuosity, a vascular complication, due to decreased lysyl oxidase activity.
What this study adds?
The authors report an atypical case of Menkes disease with unusual complication of bilateral iliac artery aneurysms.

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Potential conflicts of interest
None.

References
หลอดเลือดแดงอัลตราไปโฟ่งในโรค Menkes: รายงานหน้าใหม่

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�ูมหลัง: โรค Menkes disease เป็นโรคที่มีความติดปิดของสารส่งต่อกันไปยังหลอดเลือดในระบบโลหิต ซึ่งต้นกำเนิดในศูนย์ปัจจัยและส่งผลกระทบต่อชีวิตหลอดเลือดแดงโรค Menkes disease ที่มีภาวะกลางของหลอดเลือดแดงอัลตราไปโฟ่งที่สิ้นชีวิต รายงานหน้าใหม่: เคยพบการหายจะ 6 เดือน ผ่านการ缎ทบ้าน แต่ละเดือนมีวัน ช่วงนี้ ติดสิ่งและยิ่งกิจการวิเคราะห์ส่วน คือการดูหลอดเลือดเล็ก ๆ pil i tori ผู้ป่วยมีระดับของแลดและระดับปิดของรูผลหญิงในชนิดและได้รับการวินิจฉัยเป็นโรค Menkes disease สามารถกระทำหลอดเลือดแดงผู้ป่วยได้เมื่อวันที่ 1 หลอดเลือดแดงอัลตราไปโฟ่งจะคลายภาวะ โรคหลอดเลือดแดงกลุ่มอัลตราไปโฟ่งหลอดเลือดแดงผู้ป่วยได้ผ่านการรักษา พันธุสืบสวนและรักษาแบบประหยัดของ

สรุป: หลอดเลือดแดงอัลตราไปโฟ่งเป็นภาวะที่หน่วยเหลือผู้ป่วยโรค Menkes disease การตรวจเพิ่มเติมของระบบหลอดเลือดแดง หรือวางแผนต่อไปหลอดเลือดพิษชีวิตในผู้ป่วยกลุ่มนี้