Clinical Case Report

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Recurrent spontaneous subserosal hematoma of ileum causing intestinal obstruction in a patient with menkes disease

A case report

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Abstract

Background: Menkes disease (MD) is a disorder of copper metabolism due to *ATP7A* gene mutation that leads to severe copper deficiency. Deformed blood vessels can be found in many parts of the body, and intracranial hematoma is generally reported.

Methods: We report a Taiwanese boy with MD who had recurrent spontaneous subserosal hematoma of ileum presenting as intestinal obstruction, with the 2 episodes 23 months apart. The patient returned to the usual physical status after surgical removal of the hematoma.

Results: The defective copper metabolism causes dysfunction of a plenty of copper-dependent enzymes, giving rise to unique kinky hair appearance, progressive neurodegeneration, and connective tissue abnormalities. To our knowledge, this is the first report on recurrent subserosal hemorrhage of intestine in MD.

Conclusion: Owing to the fragile structure of blood vessels, subserosal hematoma should be considered when patients with MD having intestinal obstruction.

Abbreviations: ATPase = adenosine triphosphatase, MD = Menkes disease.

Keywords: intestinal obstruction, kinky hair disease, Menkes disease, subserosal hematoma

1. Introduction

Menkes disease (MD) is a rare neurodegenerative disorder caused by dysfunctional copper-transporting adenosine triphosphatase (ATPase), ATP7A.[1] Multisystemic manifestations result from severe copper deficiency as the reduced copper ion within the enteral cell failed to be pumped into the peripheral circulation.[2] Lacking of copper-depending lysyl oxidase leads to unstable structure of connective tissues,[3] and abnormal blood vessels at various sites including brain, neck, and limbs had been reported.[4–12]

Subserosal hematoma is a relatively rare cause of intestinal obstruction,[13] and most of the cases were related to coagulopathies or anticoagulants use.[14–19] This is the first case of MD with recurrent spontaneous subserosal hematoma of ileum, which induced intestinal obstruction.

The Institutional Review Board of MacKay Memorial Hospital approved this study (16MMHIS062), and a written informed consent was obtained from the participant.

2. Case report

A 3-year-1-month-old Taiwanese boy was born to a 37-year-old G2P2 mother at 36 3/7 weeks' gestation with the birth weight of 2620 g via Cesarean section. The Apgar score was 9 and 10 at 1 and 5 minutes, respectively. The prenatal examination and the result of newborn screening tests were normal. He has medical history of MD confirmed by molecular study which showed *ATP7A* gene point mutation [c.3502 C>T] when he was 7-month-old. The initial presentation which led to this diagnosis were focal seizure, hypotonia, and hypopigmented curly scalp hair when he was 5-month-old. Tortuosity of bilateral internal carotid arteries and right middle cerebral artery were demonstrated by magnetic resonance angiography. Copper-histidine injection was started since 8-month-old. Other documented history in the previous hospitalizations included global developmental delay, hyperbilirubinemia, bilateral inguinal hernias, pectus excavatum, microcytic anemia, left side grade III vesicoureteral reflux, diffuse multiple urinary bladder diverticula, gastroesophageal reflux, and osteopenia-related left distal femur fracture.

When he was 1-year-2-month-old, the first episode of intestinal obstruction was presented as postprandial vomiting for 3 days.

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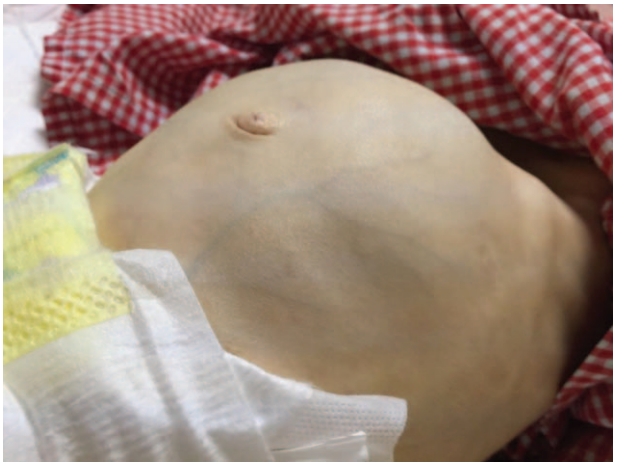

Figure 1. Distended abdomen with visible bowel loops on the abdominal wall.

Exploratory laparoscopy was performed, and a large subserosal hematoma was found at the ileum with proximal intestinal dilatation. The operation was converted to mini-laparotomy to open and evacuate the hematoma. Feeding was started with extensive hydrolysate formula since the eleventh post-operative day and he was discharged 18 days after the operation.

He was admitted again due to nonbilious vomiting for 3 times and decreased activity for 1 day this time. He was bedridden and head trauma history was denied by the mother. There was no fever, cough, bowel habit change, or contact history to persons with fever or gastroenteritis. Physical examination showed soft but distended abdomen with visible bowel loops over the abdominal wall (Fig. 1), decreased bowel sounds, regular heart beats with grade I systolic murmur, severely depressed sternum, and normal skin turgor. Vital signs at admission were: body temperature 37.9 °C, pulse rate 120/min, respiratory rate 26/min, and blood pressure 86/52 mm Hg. Initial laboratory data showed normocytic anemia (hemoglobin 10.7 g/dL, mean corpuscular volume 85.6 fl), leukopenia (3.0×10^9/L), hypokelemia (3.3 mEq/L), and slightly elevated C-reactive protein (1.3 mg/dL; normal range <0.8 mg/dL). Segmental dilatation of jejunal loops was seen on the plain abdominal film (Fig. 2). Under the tentative diagnosis of intestinal obstruction, intravenous fluid and electrolytes support was conducted, and nasogastric tube was placed for decompression while the boy was kept nil per os. Abdominal sonography showed diffused intestinal ileus with bowel wall thickening, but no intussusception or intra-abdominal mass was demonstrated. Serial plain abdominal film revealed total obstruction of the intestine; thus, ampicillin (200 mg/kg/day) and cefotaxime (150 mg/kg/day) were administered and exploratory laparotomy was done 1 day after admission. A large subserosal hematoma with proximal dilated bowel loop was found at the ileum approximate the site of the first hematoma (Fig. 3A). The hematoma was evacuated and the intestine looked healthy after releasing the mass (Fig. 3B). There was no laboratory evidence of bleeding tendency (platelet count 140×10^9/L, Prothrombin time 11.5 seconds, INR 1.10, activated partial thromboplastin time 29.5 seconds, bleeding time

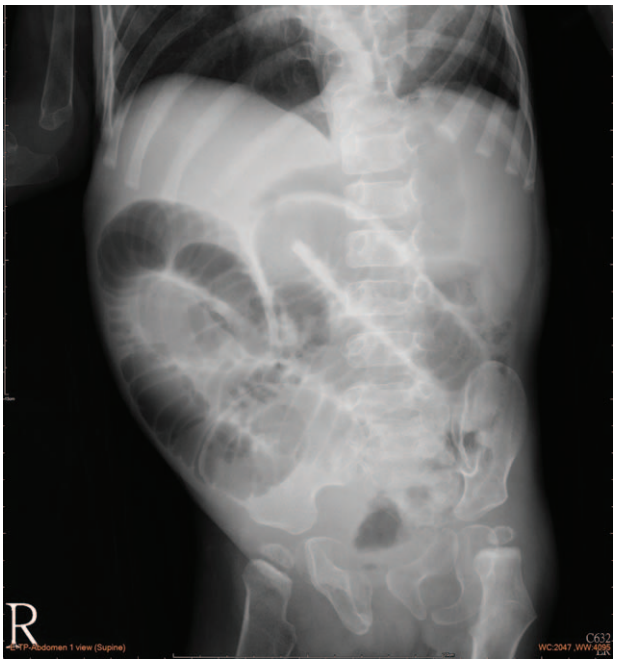

Figure 2. Plain abdominal film at admission showed segmental dilatation of jejunal loops.

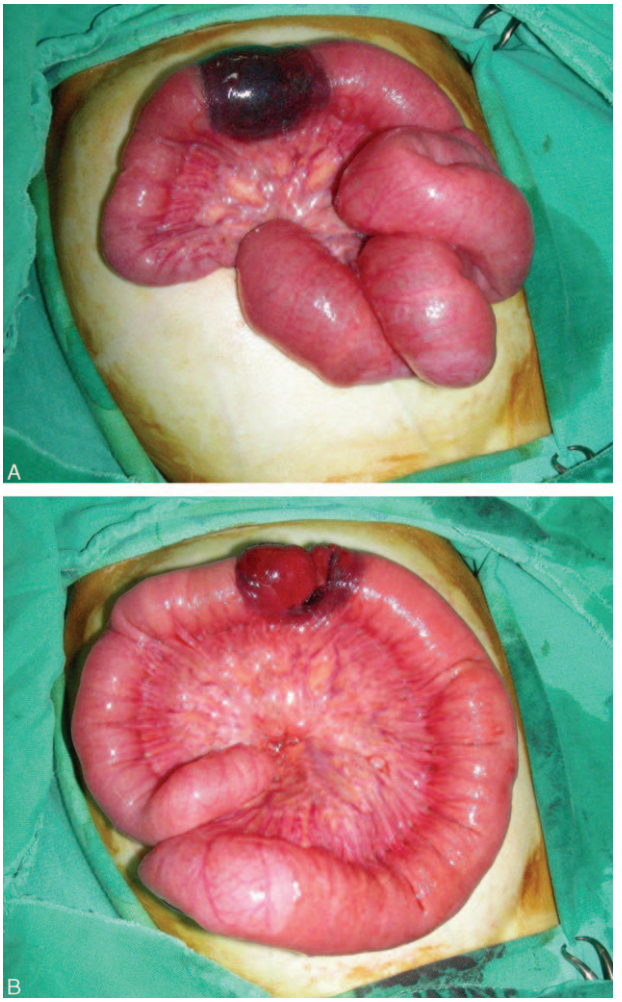

Figure 3. Exploratory laparotomy revealed. (A) A large subserosal hematoma with proximal dilated bowel loop at the ileum. (B) The intestine looked healthy after the hematoma was evacuated.

**33′0″). Parenteral nutrition was started 2 days post-operation, and enteral feeding was started since the 12th post-operation day. Full feeding was achieved 16 days after the operation and he was discharged 17 days after the operation.

3. Discussion

MD, also known as kinky hair disease, is a rare X-linked recessive disorder of copper metabolism caused by *ATP7A* gene mutation, result in deficiency or dysfunction of the copper-transporting ATPase, ATP7A.[1,20] Progressive neurodegeneration is the main symptom, which included hypotonia, generalized myoclonic seizures, mental retardation, and prominent feeding difficulties. Death occurs by 3-year-old if left untreated.[21]

ATP7A functions as an intracellular pump to transport copper into the trans-Golgi network for incorporation into copper requiring enzymes, and also mediates copper exodus from cells.[20] Owing to the wide distribution of copper-requiring proteins, the impact of ATP7A dysfunction is multisystemic. For the intestinal tract, the uptake of the reduced copper ion (Cu^{1+}) from the bowel lumen to the enteral cell via the high-affinity Cu^{1+} transporter is not changed, but failure to pump Cu^{1+} across the basolateral membrane into the peripheral circulation leads to the intestinal copper hyperaccumulation with severe copper deficiency in peripheral tissues.[2]

The formation, maturation, and stabilization of connective tissue are also affected by copper deficiency. Copper plays a role in lysyl oxidase, which catalyzes the cross-linking of elastin and collagen fiber.[3] Aortas from copper-deficient animals and humans exhibit fissures and rupture due to altered architecture of elastic fiber,[22] and tortuosity of the cerebral vessels is frequently noted in MD. Vascular events had been reported in various sites in MD, including different pictures of intracranial hemorrhage,[7–9] internal jugular phlebectasia presenting as unilateral neck masses,[10] and brachial and iliac artery aneurysms.[11,12] To our knowledge, this is the first report on recurrent subserosal hemorrhage of intestine in MD.

Subserosal hematoma is a relatively rare cause of small bowel obstruction.[13] Compared to the traumatic etiology, spontaneous intramural small bowel hematoma is rare, and most of the reported cases were related to coagulopathies or anticoagulants use.[14–19] Vascular malformation of the gastrointestinal tract behaves differently from each other. Dieulafoy's lesion, presenting as an ulcerated or polypoid lesion containing the caliber-persistent left gastric artery, can produce severe and even fatal hemorrhages.[23] In 1 study describing the characteristics of small intestinal diseases on single-balloon enteroscopy,[24] a total of 186 patients underwent 196 procedures. Thirteen patients were found to have vascular malformation, with the mean age of 57.6 years old and the most common location of the lesions was in the jejunum. In 1956, White and Wollenman reported a 6-year-old boy with congenital hemangiomatous malformation with spontaneous subserosal hemorrhage of the jejunum, resulted in chronic intestinal obstruction.[25] Another 11-month-old boy presenting with subserosal hematoma leading to marked narrowing of the lumen and to intestinal obstruction was reported in 1960 by Martins.[26] Our case is another one of the rarely reported case of spontaneous subserosal hematoma induced by the anomalous blood vessel.

4. Conclusion

In MD, although feeding difficulty is frequently encountered, any symptoms and signs of intestinal obstruction should be carefully observed and managed promptly and correctly. Subserosal hematoma should be taken as one of the differential diagnosis of intestinal obstruction in these patients because of the fragile structure of blood vessels derived from copper deficiency.

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