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Case Report

Common Bile Duct Stone Associated with Hemolytic Uremic Syndrome

Nakysa Hooman MD•*, Hassan Otoukesh MD*, Elham Talachian MD**, Farideh Hallaji MD***, Mitra Mehrazma MD†

Cholelithiasis is an unusual complication of hemolytic uremic syndrome. A 12-year-old boy with hemolytic uremic syndrome, established by renal biopsy, who developed cholestatic jaundice is presented here. Laboratory results for secondary causes of hemolytic uremic syndrome were normal. Abdominal ultrasonography and magnetic resonance cholangiopancreatography revealed extrahepatic obstruction. A common bile duct stone, discovered by retrograde cholangiopancreatography was extracted by sphincterotomy. In conclusion, cholelithiasis should be considered as a cause of abdominal pain and cholestasis in patients who are diagnosed as having hemolytic uremic syndrome.

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Keywords: Cholestasis • cholelithiasis • hemolytic uremic syndrome • thrombotic microangiopathy

Introduction

Hemolytic uremic syndrome (HUS) is defined by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. Gastrointestinal disease is a regular and self-limiting feature of HUS.[1] However, sometimes surgery is required for colonic necrosis,[2, 3] intussusception, pancreatic necrosis,[4,5] and infarction of celiac axis.[6] Cholelithiasis has been reported only in five cases as a late complication of HUS.[7 – 12] We present a patient with HUS and concurrent cholestatic jaundice that later proved to be due to biliary stone.

Case Report

A 12-year-old previously well boy was admitted to a local hospital with a history of fever, chills, nausea, and vomiting for four days. Gross hematuria, oliguria, periorbital edema, and petechia developed a day after the admission. The initial laboratory results were as follows: hemoglobin 8 g/dL, platelet count 84000 /mm^3, reticulocyte count 12.5%, and creatinine 1.6 mg/dL. Liver function tests were normal. Peripheral blood smear showed anisocytosis, poikilocytosis, schistocytes, helmet cells, and burr cells. Laboratory tests for antinuclear antibody, antineutrophil cytoplasmic antibody, cryoglobulin, viral hepatitis markers, and anticardiolipin antibody were negative. Serum complement levels were in the normal range. Results of hemoglobin electrophoresis, glucose-6-phosphate dehydrogenase assay, and osmotic fragility test were normal.

His first abdominal ultrasonography was reported normal except for hyperechoic parenchyma in both kidneys. One month later, the abdominal sonography was normal again except for thickening of the gallbladder wall with sludge in the lumen. During the hospital study, the patient developed overt renal failure that required hemodialysis despite high doses of systemic glucocorticoids and fresh frozen plasma (FFP) transfusions. Percutaneous renal biopsy was consistent with thrombotic microangiopathy (Figure 1). On the 21st day of admission, he was

Authors' affiliations: *Department of Pediatric Nephrology, **Department of Gastroenterology, ***Department of Radiology, †Department of Pathology, Ali-Asgar Children's Hospital, Iran University of Medical Sciences, Tehran, Iran.
•**Corresponding author and reprints:** Nakysa Hooman MD, Department of Pediatric Nephrology, Ali-Asgar Children Hospital, Vahid Dasgerdi St., Moddarress Blvd., Tehran, Iran.
Tel: +98-212-222-041-3, Fax: +98-218-800-2904,
E-mail: hakiwa@iums.ac.ir; nakisa45@yahoo.com.
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transferred to our tertiary care center for further management. With the primary diagnosis of secondary HUS, he received ceftriaxone, a single pulse of cyclophosphamide, and additional pulses of methylprednisolone as well as transfusion of packed red blood cells and FFP. Plasmapheresis was commenced on a daily basis.

On the 50th day of admission, several bouts of tonic-clonic convulsions that were controlled by phenytoin and phenobarbital were noted. The next day he experienced severe colicky abdominal pain followed by jaundice. Liver function tests were consistent with cholestatic jaundice with a total bilirubin of 11 mg/dL and direct bilirubin of 7.8 mg/dL. Abdominal ultrasonography revealed dilation of the common bile duct with a 16 mm diameter and the gallbladder was full of sludge, and small stones. The liver span was 120 mm but spleen and pancreas were normal. Magnetic resonance cholangiopancreatography (MRCP) showed severe dilation in both intra- and extrahepatic biliary ducts, highly suggestive of obstructive biliary stone (Figure 2). Endoscopic retrograde cholangiopancreatography was performed followed by endoscopic sphincterotomy that promptly led to resolution of jaundice. There was no complication after the procedure. Regarding the recalcitrant hemolysis, abnormal liver function tests, and biliary stone, Wilson's disease was also suspected. Serum ceruloplasmin was 21.2 mg/dL (normal range: 18.8 – 32.2) and 24-hour urine copper level was 128.7 µg/24 hr (normal range: 15 – 60). The ophthalmologic examination by slit lamp was negative for Kayser-Fleischer ring. The following day, D-penicillamine challenge test was performed and 24-hour urine collection for copper was 65.5 µg/24 hr.

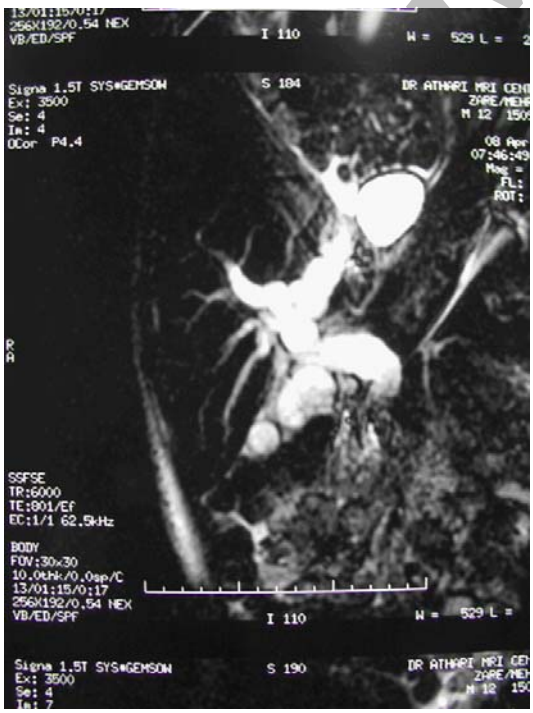

Figure 2. MRCP shows dilation of intra- and extrahepatic bile ducts.

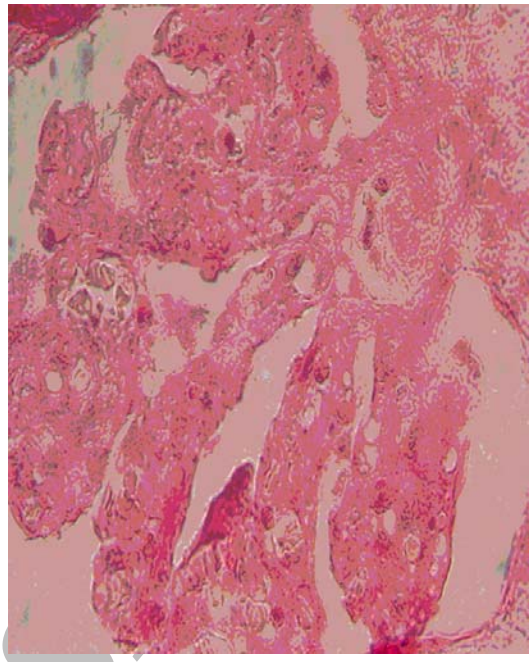

Figure 1. The glomerulus demonstrates hyaline thrombi in arteriole, lobular accentuation and capillary wall thickening (Hematoxylin and Eosin [H&E] ×40).

The patient's recovery was uneventful. He was discharged two months after his second hospital admission. On follow-up 24 months later, he still had moderate renal failure (creatinine 2.5 mg/dL), proteinuria, and hypertension. The liver function tests were normal and repeated abdominal ultrasonography showed normal gallbladder with no calculi.

Discussion

The patient's presentation was unusual because of recalcitrant hemolytic anemia, cholestasis, cholelithiasis, and high amounts of copper in 24-hour urine collection; the features that mimic Wilson's disease.

Wilson's disease rarely presents as HUS.[13] Although our patient had high initial urinary copper with a normal ceruloplasmin level, the urinary copper decreased with D- penicillamine challenge test after removing bile duct stone by

sphincterotomy. Urinary copper excretion may be elevated in Wilson's disease, autoimmune hepatitis, primary sclerosing cholangitis, acute liver failure, and other cholestatic diseases.[14] Urine copper levels greater than 1,600 microgram in 24 hours with D-penicillamine administration is strongly in favor of Wilson's disease.[14] Obstructive hepatitis was thought to be the cause of increasing urinary copper level in this patient as it was normalized after relieving biliary obstruction.

Gallstones in older children are usually secondary to obvious hemolytic processes such as sickle cell disease or spherocytosis. Searching MEDLINE from 1960 through 2006 showed that cholelithiasis has only been reported as a late complication of HUS in five patients.[7, 9 – 12] Pigment stones due to biliary stasis induced by parenteral nutrition, biliary obstruction, bacterial infection, chronic hemolysis, or increased catabolism are noted. Ceftriaxone is well known as an etiology of pseudolithiasis and biliary sludge.[15,16] Our patient had been treated with ceftriaxone for two weeks. It is possible that ceftriaxone administration during acute hemolytic episode predisposed him to early bile stone formation.

Cholelithiasis should be considered as a cause of abdominal pain and cholestasis in patients who are diagnosed as having HUS.

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