Worsening Cholestasis after Endoscopic Retrograde Cholangiopancreatography

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Abstract

Prolonged cholestasis is a rare complication of endoscopic retrograde cholangiopancreatography (ERCP) with few cases reported in literature. A case of a 39-year-old Jordanian woman who presented with abdominal pain and jaundice was reported. Clinical investigations revealed cholestasis with dilatation of the intrahepatic biliary system. A cholecystectomy had been performed 15 years earlier. ERCP findings were consistent with a mild biliary obstruction. The symptoms were thought to be due to a biliary stone that had passed spontaneously. Her abdominal pain subsided and she was discharged. A few days later the patient's jaundice worsened and she developed severe pruritus. A viral and autoimmune screen were negative and a repeat abdominal ultrasound was normal. She was treated with ursodeoxycholic acid for 10 days, but with no improvement. The patient declined to undergo a liver biopsy. A dramatic improvement was achieved following a short course of oral corticosteroids.

Keywords: Cholestasis; prednisolone; endoscopic retrograde cholangiopancreatography; ursodeoxycholic acid.

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Introduction

An endoscopic retrograde cholangiopancreatography (ERCP) is a procedure that aims at visualizing the biliary and pancreatic ducts after opacification with a contrast medium. It is valuable for the diagnosis and treatment of various biliary and pancreatic disorders. The most common complications of ERCP are pancreatitis, bleeding, infections, and perforation.[1, 2] Rare complications have been reported as case reports such as common bile duct thrombus and pethidine-induced hepatitis. [3,4] Prolonged cholestasis is a very rare complication of ERCP. [5- 8] A case of worsening cholestasis associated with severe pruritus following ERCP for removal of a presumed common bile duct obstruction by a stone was reported.

Case Report

A 39-year-old Jordanian woman presented with a 3-day history of right upper quadrant pain. She gave a history of open cholecystectomy 15 years earlier. She was on oral contraceptive pills (OCP) for 1 year, in the form of Microgynon (ethinylestradiol 30 μg and levonorgestrel 150 μg). She had no risk factors for viral hepatitis and denied alcohol consumption. Physical examination was remarkable for apparent jaundice and right hypochondrial tenderness. Liver function tests (LFT) showed a cholestatic picture with a total bilirubin of 79 μmol/L (normal up to 23 μmol/L), direct bilirubin 55 μmol/L, alanine aminotransferase (ALT) 68 U/L (normal up to 31 U/L), aspartate aminotransferase (AST) 22 (normal up to31), alkaline phosphatase

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(ALP) 424 U/L (normal up to 240 U/L), and gamma-glutamyl transpeptidase (γ-GT) 225 U/L (normal up to 42 U/L). An abdominal ultrasound showed dilatation of the intrahepatic biliary system but the common bile duct (CBD) was not visualized. On the second day of admission, an ERCP was performed for the assumption of distal biliary obstruction. An injection of a sufficient amount of non-ionized contrast material that visualized the biliary tree totally showed a normal biliary tree with no definite filling defect. A 12-mm biliary sphincterotomy and a CBD sweep with a balloon were performed. It was thought that her abdominal pain was probably due to a biliary stone that had passed spontaneously. Abdominal pain subsided and she was discharged home. A few days later her serum bilirubin was rising, and she developed severe pruritus. She had no fever and her leukocyte count was normal. Ursodeoxycholic acid (UDCA), 15 mg/kg/day, was prescribed, and it was advised to stop OCP. She continued to have severe pruritus and rising bilirubin and ALP levels (Figure 1). Serological tests for viral hepatitis were negative. Anti-nuclear, anti-mitochondrial, and anti-smooth muscle antibodies were all negative. Repeat abdominal ultrasound showed normal intra- and extra-hepatic biliary system. The patient refused to undergo a liver biopsy. Ursodeoxycholic acid was stopped and she was started on oral prednisolone (50 mg/day). The response was dramatic with the disappearance of pruritus and normalization of her LFT within 10 days. Prednisolone was stopped after 10 days. A month later her LFTs were normal. She restarted taking OCP 3 months after this incident with no adverse effects and repeat LFTs were normal 3 months and 1 year after resuming OCP.

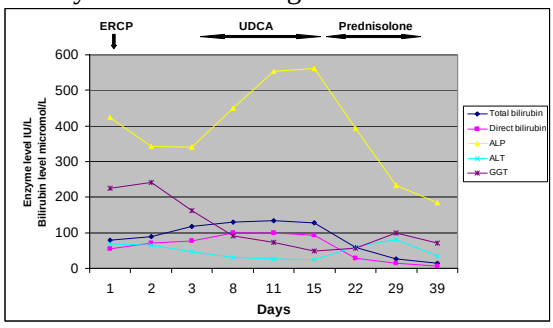

Figure (1): Liver biochemistry and response to

Discussion

This patient's symptoms at the time of presentation were thought to be due to a stone in the CBD. Both the cholestatic picture and intrahepatic biliary dilatation were suggestive of that, although the CBD was not visualized by ultrasound. ERCP did not reveal any significant abnormality in the biliary tree, and a stone that had passed spontaneously was thought to be the cause of her symptoms, as her abdominal pain subsided shortly after the ERCP. However, worsening of her cholestatic picture associated with severe pruritus was unexpected. Investigations to rule out other medical causes of cholestasis such as viral and autoimmune hepatitis, or other cholangiopathies were negative. A liver biopsy would have been helpful to make a diagnosis in case of intrahepatic cholestasis, but the patient refused to undertake the procedure.

Preparations containing estrogen are well known to cause several cholestatic syndromes. [9] This effect is mediated by glucuronidated metabolites of estrogen, which inhibit canalicular bile salt and glutathione excretion, resulting in the inhibition of bile salt transport.[10] In one study, about two thirds of patients who developed cholestasis following estrogen use gave a history of intrahepatic cholestasis during pregnancy. [11] The withdrawal of the estrogenic effect by delivery or drug withdrawal leads to an improvement in liver functions. This usually takes weeks or even months. The use of UDCA seems to be more effective than corticosteroids in relieving pruritus and reducing bilirubin level in cases of intrahepatic cholestasis of pregnancy. [12] This effect is mediated by a reduction in the glucuronidation of estrogens, thereby decreasing the production of cholestatic metabolites.[13]

In another report, two patients developed prolonged cholestasis following ERCP, both were taking estrogens. The first patient responded to a 8-week course of steroids. The second patient responded slowly over 40 weeks to UDCA. Estrogens were discontinued for both patients. [7]

ursodeoxycholic acid (UDCA) and prednisolone.

It was postulated that a biliary obstruction with an associated inflammatory response sensitized the biliary canaliculi to the cholestatic effects of estrogens, thus leading to prolonged cholestasis. However, two similar patients that were not taking estrogens (both were males) were reported to have developed prolonged cholestasis following ERCP. Both responded to a 12-day course of corticosteroids. It was felt that the radiocontrast material may have a toxic effect on the liver with a disruption of the canalicular plasma membranes.[5] An allergic reaction to the radiocontrast material or prophylactic antibiotic has been suggested to cause prolonged cholestasis. [6] Other very rare causes of prolonged or worsening jaundice following ERCP has also been reported, such as common bile duct thrombus [3] and pethidine induced hepatitis. [4]

Saritas and colleagues reported a case of cholestasis and intense pruritus following ERCP in a 73-year old man who failed to respond to UDCA and cholestyramine but had a partial response to prednisolone in the form of a reduction in the bilirubin level, but the intense pruritus promptly responded to plasmapheresis. [14] Our case had no previous history of an intrahepatic cholestasis of pregnancy or a history of sensitivity to cephalosporins so she received fentanyl and midazolam with a second generation cephalosporin as premedication. The worsening of her bilirubin started immediately after the ERCP and she developed severe pruritus soon afterwards, and did not respond to UDCA. The dramatic response to corticosteroids within a short period of time made an allergic reaction to the radiocontrast material a more likely explanation for her condition, although an allergy to pre-ERCP medications given routinely for an endoscopy cannot be totally excluded. The fact that she resumed taking OCP for one year without any adverse events excluded estrogens as a contributing factor.

We believe that unexplained cholestasis should be added to the list of infrequent complications of ERCP and that a short course of corticosteroids appears to be of value in such cases.

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الركود الصفراوي المزمن بعد عمليات تنظير القنوات المرارية

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الملخص

يعتبر الركود الصفراوي المزمن من المضاعفات النادرة لعملية تنظير القنوات المرارية وهناك توثيق لحالات قليلة جداً في المجلات الطبية. في مقالتنا هذه توثيق لحالة مريضة أردنية عمرها 39 عاماً حضرت إلى المستشفى تشكو من ألم في البطن مع يرقان. اثبتت التحاليل السريرية وجود ركود صفراوي مع توسع في القنوات المرارية داخل الكبد. تم استئصال المرارة عند هذه المريضة قبل 15 عاماً. نتيجة تنظير القنوات المرارية تتماشى مع وجود انسداد بسيط في قنوات المرارة يعتقد أنه نتيجة حصوة مرارية خرجت تلقائياً من قنوات المرارة. اختفت آلام البطن عند المريضة وأخرجت من المستشفى. ثم رجعت المريضة بعد أيام قليلة تشكو من ازدياد اليرقان مع حكة شديدة في الجلد. لم تثبت التحاليل المخبرية وجود أي التهاب فيروسي أو مناعي في الكبد ونتيجة فحص الكبد والقنوات المرارية بالموجات فوق الصوتية كانت طبيعية. أعطيت المريضة علاج يورسي دي أوكسي كوليك أسيد لمدة عشرة أيام دون جدوى، وبعد أن رفضت المريضة أخذ خزعة من الكبد أعطيت حبوب بريدنيزولون لمدة قصيرة نتج عنها اختفاء اليرقان والحكة بصورة سريعة.

الكلمات الدالة: ركود صفراوي، تنظير القنوات المرارية، بريدنيزولون، يورسي دي أوكسي كوليك أسيد.