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Case Report

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E. coli Causing De Novo Bile Duct Stone Association Revisited

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Abstract

The finding of a common bile duct (CBD) stone after living donor liver transplant (LDLT) is a rare occurrence. We report a case of a post-transplant patient who was admitted for gastroenteritis caused by Escherichia coli (E.coli). Three weeks later, following the acute episode, he developed a CBD stone.We hypothesize that ascending infection by E.coli in immunocompromised patients plays a role in the pathogenesis of CBD stone formation.

Keywords: Living Donor Liver Transplant, Common Bile Duct Stone, E.coli

Introduction

Biliary complications, the 'Achilles heel' of LDLT remains a common source of morbidity and mortality in patients [1,2]. Hepatic artery thrombosis, ischaemia-reperfusion injury and biliary infections are common causes of biliary complications and subsequent biliary stone formation [3].

Bile duct stones are known to be associated with bacterial infection, with E.coli as the predominant bacteria [4]. Maki et al. demonstrated that the enzymatic activity of E.coli plays a key role in pathogenesis of pigmented gallstones [5]. We present a case of a patient who is on immunosuppressant following LDLT, who had recent gastroenteritis with E.coli, developing primary bile duct stones [6].

Case Report

A 53-year-old Chinese man who is on immunosuppressant, following LDLT performed five months ago, presented to the hospital with a one day history of gastroenteritis caused by E.coli. At the time of his admission, he was hypotensive (65/52 mmHg), tachycardic (139 bpm) and pyrexic (37.5 degrees Celsius). Blood cultures revealed E.coli as the causative organism. He was treated with Azithromycin for his E.coli, and there was a subsequent resolution of his gastroenteritis.

Following the resolution of his gastroenteritis, his liver function test (LFT) showed normalization and improvement. Total bilirubin (73 to 15 umol/L), ALT (249 to 106 U/L), AST (210 to 50 U/L), GGT (900 to 221 U/L) and ALP (163 to 84 U/L) decreased towards near normal levels (Figure 1).

However one month later, there was an acute exacerbation of his LFTs, which showed a marked increase in ALT (106 to 527 U/L), AST (50 to 248 U/L), GGT (221 to 1049 U/L) and ALP (84 to 260 U/L). A magnetic resonance cholangiopancreatography (MRCP) was conducted, revealing biliary dilatation and CBD stone. An endoscopic retrograde cholangiopancreatography (ERCP)was later performed to remove the CBD stone.

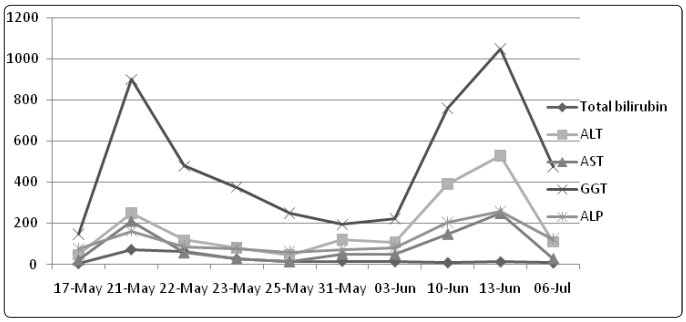

Figure 1: Series of LFTs taken for our patient

Discussion

Bacteria infections have been known to play a structural and functional role of the formation of pigment and cholesterol gallstones. Scanning electron microscopic (SEM) studies reaffirmed the findings of bacteria in pigment gallstones and the pigment portion of "composite" stones [7, 8]. Speer et al. also reported the presence of bacteria in cholesterol stones and suggested an association of the role of bacteria in both cholesterol and pigment stone formation [9].

In our case report, our patient had undergone LDLT and was commenced on long term immunosuppressant five months prior to his presentation to hospital with a bout of gastroenteritis caused

by E.coli, along with findings three weeks later of a CBD stone by MRCP.

Pathogenesis of E.coli and Gallstone Formation after LDLT

Following LDLT, immunosuppressive agents are used. A major side effect is bone marrow suppression leading to increased risk of fulminant infections. E.coli is the predominant pathogen for ascending infection in the bile duct [10].

As mentioned previously, infection contributes to the creation of brown pigment stones. Clemente et al. had isolated 133 microorganisms from the bile of 73 patients with intrahepatic stone and E.coli is the predominant microorganism.

Some of the possible infective ways include ascending infection via the sphincter of oddi (SOD), haematogenous dissemination via portal system and also spread via the lymphatic system. Ascending infection can cause damage to the bile duct mucosa.Consequently, this will promote bile duct stone recurrence.

There are several ways in which E.coli can promote the formation of bile duct stones [11-14]:

E.coli infecting the biliary duct via ascending infection is capable of converting conjugated bilirubin to unconjugated bilirubin.The bacteria contain an enzyme, β-glucuronidase, which hydrolyses bilirubin glucuronide into free bilirubin and glucuronic acid.Calcium levels will also rise in the biliary tract in inflammatory conditions. Calcium then binds to the free bilirubin at its free carboxyl radical to yield water-insoluble calcium bilirubinate.

E.coli produces phospholipase A1 which turns phosphatidylcholine to free fatty acids and lysophosphatidylcholine. This stimulates the deposition of fatty acid calcium and secretion of mucin from bile duct epithelium, enhancing stone formation.

Endotoxins produced by E.coli stimulate liver cells, bile duct epithelium cells and white blood cells in bile to release β-glucuronidase, increasing stone formation.

E.coli contains lipopolysaccharide which increases production of mucin 5AC (MUC5AC) through the tumour necrosis factor-converting enzyme (TACE)/transforming growth factor-α (TNF-α)/ growth factor receptor (EGFR) pathway in biliary epithelial cells. This results in increased mucosity and bile flow reduction. Meanwhile, bacterial infection exacerbates cholestasis and cholangitic stenosis, thus promoting the formation of stones.

Summary

In summary patients with E.coli septicaemia may be more prone to bile duct stone formation especially in immunocompromised patients. A high index of suspicion should prompt early radiological investigations of the biliary system.

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