Clinical Case Report

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A case report of motesanib-induced biliary sludge formation causing obstructive cholangitis with acute pancreatitis treated by endoscopic sphincterotomy

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Abstract

Background: Gallbladder toxicity was reported in most motesanib studies with varying frequency and at variable times after initiation of treatment.

Method and Results: A 44-year-old man was admitted due to severe epigastric pain. The patient was diagnosed with non–small cell lung cancer 9 months ago and received 6 cycles of chemotherapy with motesanib, paclitaxel, and carboplatin. Ultrasonography showed a large amount of sludge within gallbladder. Computed tomography scan demonstrated diffuse dilatation of biliary tree with distended gallbladder without evidence of stone and mild pancreatic swelling. Endoscopic retrograde cholangiopancreatography showed yellowish viscous mucoid plug impacting ampullary orifice and dilated bile duct with amorphous filling defect at distal half of common duct. Endoscopic sphincterotomy was performed to prevent biliary obstruction and recurrent pancreatitis after removal of mucoid material.

Conclusion: To the best of our knowledge, this is the first report of obstructive cholangitis and acute pancreatitis associated with sludge formation during motesanib therapy. Endoscopic sphincterotomy appears to be useful to treat and prevent biliary obstruction caused by motesanib-induced biliary sludge.

Abbreviations: CBD = common bile duct, CT = computed tomography.

Keywords: ERCP, motesanib chemotherapy, obstructive cholangitis

1. Background

Motesanib is an inhibitor of vascular endothelial growth factor receptors, platelet-derived growth factor receptor and kit receptors,[1,2] and is under clinical trials for chemotherapy of gastrointestinal stromal tumor, fallopian tube cancer, ovarian cancer, thyroid cancer, and non–small cell lung cancer.[3–5] Gallbladder toxicity has been reported in most motesanib studies. Here, we report on a first case of obstructive cholangitis and acute pancreatitis associated with sludge formation during motesanib therapy.

2. Method and Results

A 44-year-old man was admitted due to severe epigastric pain. The patient was diagnosed with non–small cell lung cancer 9 months ago and received 6 cycles of chemotherapy with motesanib, paclitaxel, and carboplatin.

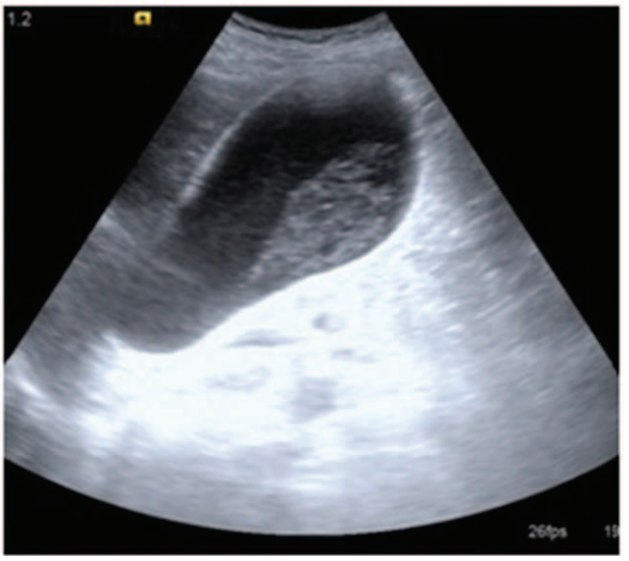

Figure 1. Ultrasonography at admission demonstrated dilated gallbladder filled with large amount of sludge.

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The authors have no conflicts of interest to disclose.

Patient's informed consent could not be obtained because the patient died due to progression of the disease before we wrote the case report.

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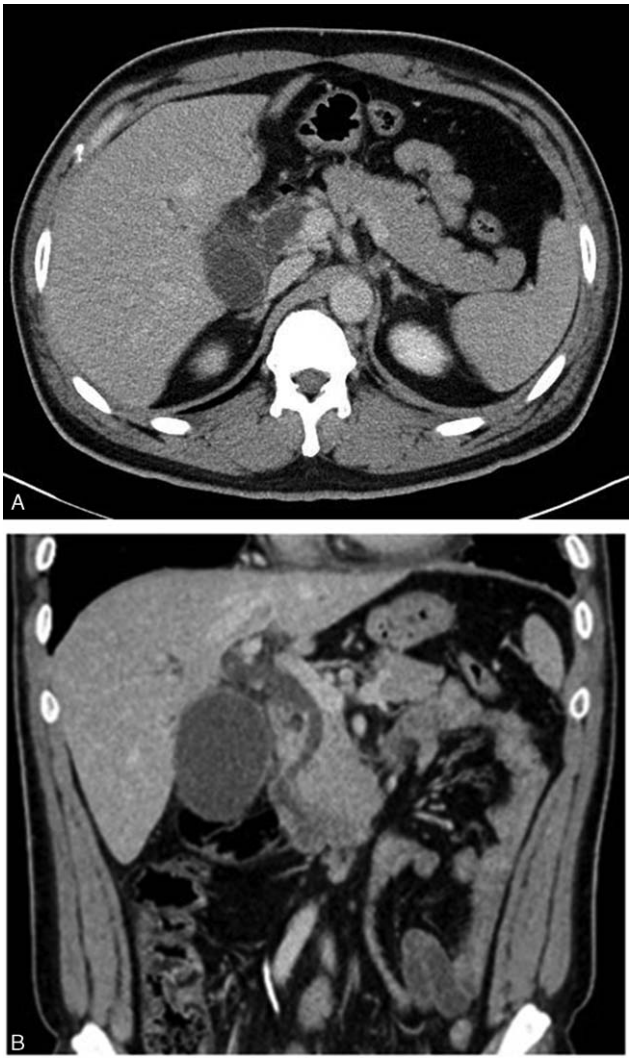

Figure 2. Contrast-enhanced computed tomography scan demonstrated mild pancreatic edema (A) and diffuse biliary tree dilatation and distension of gallbladder without evidence of stone (B).

Physical examination was notable for abdominal tenderness in right upper quadrant.

Laboratory findings were as follows: white blood cell count 3100/mm^3, total bilirubin 5.8 mg/dL, AST 240 IU/L and ALT 316 IU/L, alkaline phosphatase 1643 IU/L, GGT 968 IU/L, and serum lipase 1228 U/L (normal range: 10–67 IU/L). An abdominal ultrasound showed a large amount of sludge within gallbladder (Fig. 1). An abdominal computed tomography (CT) revealed diffuse dilatation of the biliary tree, a distended gallbladder, and mild pancreatic edema (Fig. 2A and B). There was no evidence of gallstones on CT.

Endoscopic retrograde cholangiopancreatography noted a yellowish viscous mucoid plug impacting the ampullary orifice (Fig. 3A and B). After cannulation of the common bile duct (CBD), there was significant CBD dilation with an amorphous filling defect in distal half of common duct (Fig. 4). The mucoid material was removed with a stone retrieval basket, and an endoscopic nasobiliary drainage tube was placed without performing sphincterotomy because there was increased risk of postsphincterotomy bleeding due to thrombocytopenia and septic cholangitis. Four days later, the patient had an endoscopic

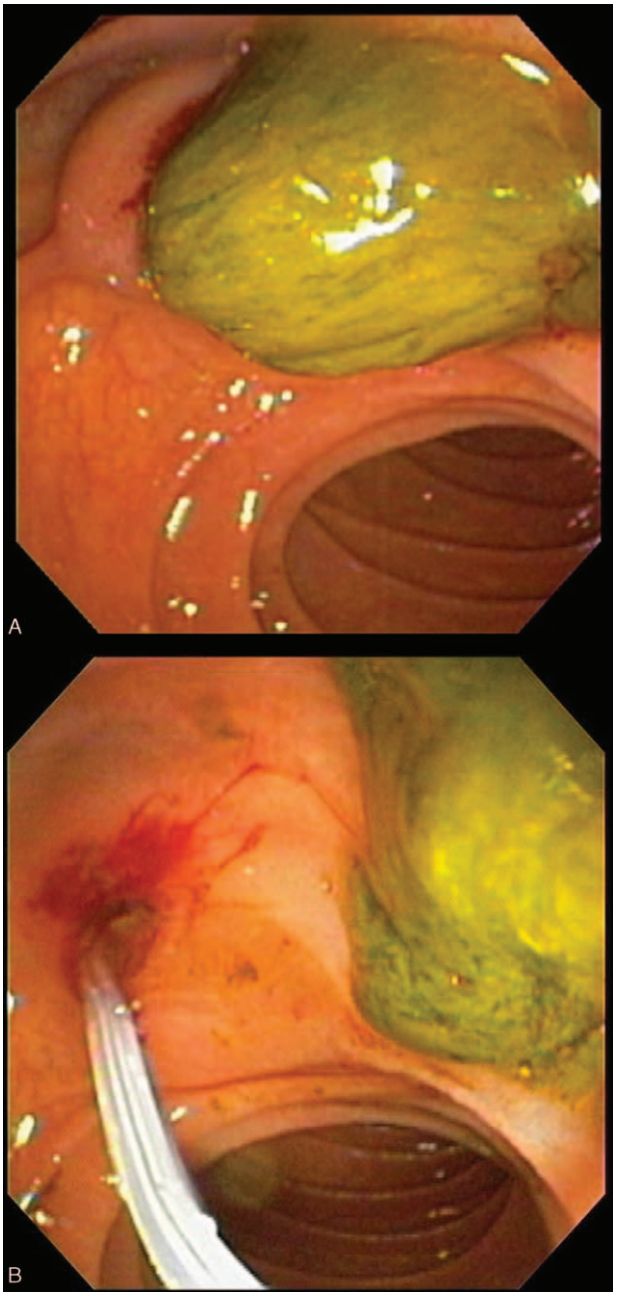

Figure 3. Duodenoscopy showed yellowish viscous mucoid plug impacting ampullary orifice (A) and eroded ampullary orifice after removal of mucoid plug with basket (B).

sphincterotomy to prevent biliary obstruction and recurrent biliary pancreatitis.

The patient received further chemotherapy with different regimens due to progression of lung cancer and had no further biliary complications. After 3 months of chemotherapy, the patient died due to progression of lung cancer.

3. Conclusion

Gallbladder toxicity was reported in most motesanib studies with varying frequency and at variable times after initiation of treatment.[4] A recent phase 1b study revealed that motesanib treatment was associated with increased gallbladder volume, decreased ejection fraction, biliary sludge, gallstone formation,

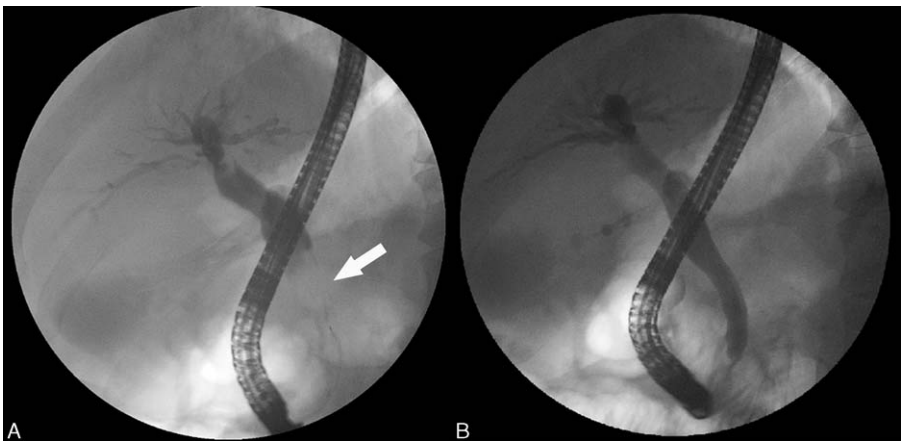

Figure 4. Endoscopic retrograde cholangiopancreatography findings showed diffusely dilated extrahepatic bile duct with amorphous filling defect at distal half (arrow) and no filling defects or stricture in the biliary tree after the removal of the sludge.

and infrequent cholecystitis.[1] Accumulation of motesanib in gallbladder lumen with subsequent excretion of its metabolites in the bile may result in sludge formation via gallbladder irritation and possibly ischemia. In the present case, motesanib treatment attributed to extensive sludge formation in the gallbladder with migration of the sludge into the bile duct results in acute biliary obstruction and biliary pancreatitis. This was successfully treated with endoscopic sphincterotomy, and CBD sludge was cleared with a stone retrieval basket.

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