Letter to the Editor

Evolocumab induced short-term biliary stent blockage and acute cholangitis in a jaundice patient with pancreatic carcinoma: a rare complication of PCSK9 inhibitor

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Evolocumab, an inhibitory monoclonal antibody of proprotein convertase subtilisin-kexin type 9 (PCSK9), presents as an effective method to decrease low-density lipoprotein cholesterol (LDL-C) and reduce the risk of major adverse cardiovascular events, which has attracted widespread attention. Compared to statins, it is reported to be more efficient and less restricted to liver function. However, up to now, there has been no relevant reports about the safety of evolocumab in patients with biliary dysfunctions (1). Here, we presented a rare case with an unprecedented complication of evolocumab in a jaundice patient with pancreatic carcinoma, who suffered from short-term recurrent jaundice and acute obstructive suppurative cholangitis (AOSC) due to biliary stent blockage after successful stent implantation.

A 73-year-old woman was hospitalized following a 1-month painless jaundice, with medical history of old myocardial infarction and hyperlipidemia. Laboratory examinations showed total/direct bilirubin of 545.1/453.3 μmol/L, CA199 of 816.0 U/mL, and LDL-C of 22.52 mmol/L. Enhanced CT scan revealed head of pancreas mass leading to biliary obstruction (*Figure 1A*). Endoscopic retrograde cholangiopancreatography (ERCP) was taken and showed segmental stenosis of distal bile duct (*Figure 1B*), which was solved by plastic biliary stent (8.5 Fr × 7 cm) and a conservative plastic pancreatic stent. Biliary brushing cytology confirmed pancreatic adenocarcinoma. Jaundice improved rapidly after operation, and evolocumab, 140 mg, was given by subcutaneous injection to control hyperlipidemia (*Figure 1C*).

However, the patient was admitted to resuscitation room in our hospital 3 days after discharge due to recurrent biliary obstruction, AOSC and secondary septic shock, with total/direct bilirubin elevated from 204.6/171.9 to 376.9/327.4 μmol/L (*Figure 1C*) and biliary dilatation in emergency abdominal CT scan. In consideration of the poor general condition and previous cardiovascular disease, percutaneous transhepatic cholangiodrainage (PTCD) rather than ERCP was taken immediately with experienced broad-spectrum antibiotics and vasoactive drugs at the same time, which showed blockage of biliary stent without displacement (*Figure 1D*). Re-examination of tumor presented no signs of rapid progression, with decreased CA199 and stable image findings.

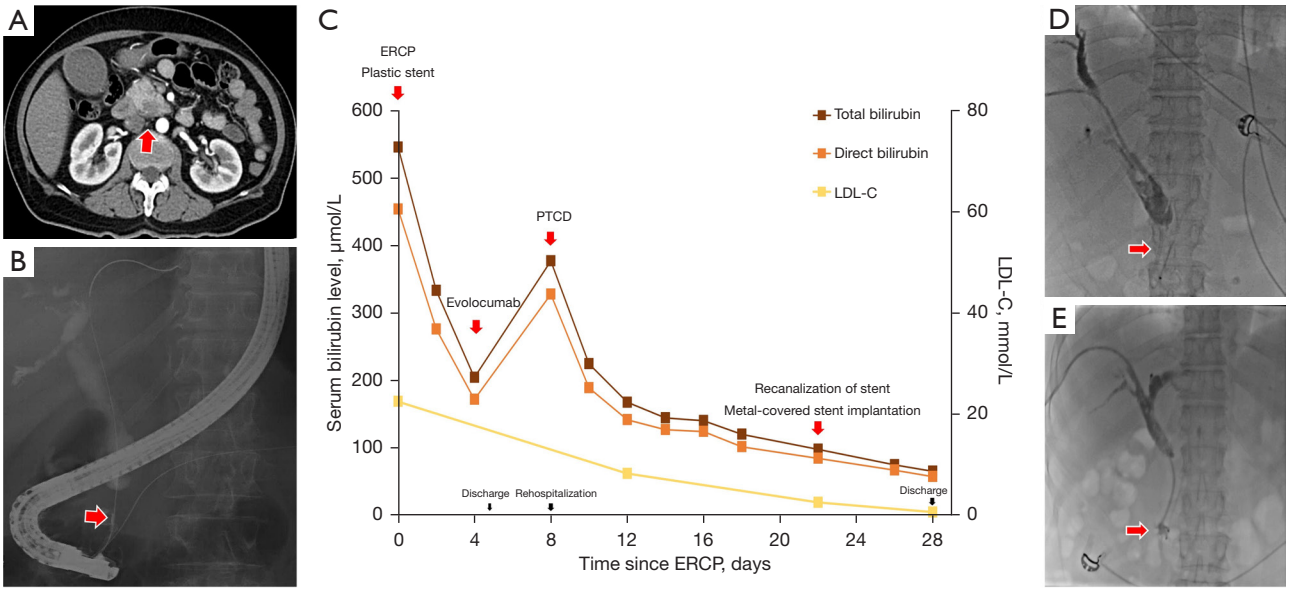

Figure 1 Changes in serum bilirubin level and LDL-C after jaundice-reducing and lipid-lowering therapy. (A) Abdominal and pelvic enhanced CT scan in arterial phase showed low-enhanced mass in head of pancreas (red arrow). (B) ERCP with double guide-wire technique showed segmental stenosis of distal bile duct with a length of 1.5 cm (red arrow). (C) Changes in serum bilirubin level after ERCP and intervention therapy. The graph showed total/direct serum bilirubin level improved well a few days after ERCP and plastic biliary stent implantation, which rebound rapidly following evolocumab injection. Biliary stent blockage without displacement was confirmed and drainage was successfully performed through PTCD, leading to continuous improvement of jaundice. Recanalization of stent was found by repeated PTC about 14 days after PTCD. Meta-covered stent was implanted through PTCD for better patency and quality of life. (D) PTCD showed filling defect in distal bile duct with stent in place (red arrow), suggesting blockage of biliary stent. (E) Repeated PTC showed recanalization of biliary stent with contrast agent appearing in the descending duodenum (red arrow). ERCP, endoscopic retrograde cholangiopancreatography; PTCD, percutaneous transhepatic cholangiodrainage; PTC, percutaneous transhepatic cholangiography; LDL-C, low-density lipoprotein cholesterol; CT, computed tomography.

Afterwards, the patient recovered well with decreased jaundice, and the drainage volume decreasing from 300–400 to 100–200 mL per day about 14 days after PTCD. Repeated cholangiography was then taken and proved recanalization of biliary stent (*Figure 1E*). Meanwhile, metal-covered stent was implanted through PTCD tube for better patency, since the malignant biliary obstruction was confirmed and the patient denied further surgical treatment and ERCP concerning the advanced age, poor status, cardiovascular diseases and operational risks. The serum bilirubin level continued to improve following metal-covered stent implantation and the PTCD tube was removed subsequently. The female soon discharged for tumor associated pharmacotherapy. In addition, statins were taken orally to control hyperlipidemia instead of evolocumab by the time the liver function recovered, which was suspected to the prime culprit of short-term biliary stent blockage. No jaundice recurred during 3-month follow-up after discharge.

Endoscopic biliary stent implantation has become the preferred palliative treatment for distal malignant biliary obstruction (2). Plastic stent blockage has shorter patency time of 3 to 4 months at average than self-expandable metal stents, due to tumor overgrowth, biliary sludge, granulation tissue hyperplasia, biliary tract hemorrhage and so on (3). However, in this case, it is uncommon for short-term recurrent stent blockage with successful stent implantation and well-improved jaundice at the beginning without stent displacement and tumor rapid progression, not to mention the spontaneous stent recanalization about two weeks later, indicating potential reasons behind it.

Evolocumab, a PCSK9 inhibitor, is recommended for secondary prevention for patients at very high-risk but not well-controlled by statins and ezetimibe, intolerant to statins-based regimen, or with familial hypercholesterolemia, based on American and European guidelines. It has received

approval by the Food and Drug Administration (FDA) in 2015, presenting good effectiveness and safety (4,5).

Evolocumab works by binding to and degrading PCSK9 in plasma, reducing PCSK9-mediated degradation of low-density lipoprotein receptors (LDL-R) and enhancing the clearance of LDL-C, primarily through mediating the endogenous pathway to metabolize LDL-C into bile acids and excrete into the intestines via bile ducts (6). Evolocumab is taken through a single subcutaneous dose of 140 or 420 mg, with an estimated absolute bioavailability of 72%, an effective half-life of 11 to 17 days, and a median peak serum concentration in 3 to 4 days (7).

Therefore, based on the time correlation of stent blockage (about 4 days after evolocumab) and recanalization of biliary stent (about 14 days after evolocumab) to pharmacokinetic, recurrent extrahepatic biliary obstruction secondary to evolocumab was highly suspected. And the potential mechanism is speculated to be that evolocumab mediates the rapid clearance of LDL-C to bile acids and excretion into bile duct in a large quantity and short time, which may lead to cholestasis, especially in patients of biliary dysfunction such as the situation in this case with tumor invasion and stent implantation.

Up to now, the reported adverse reactions of evolocumab in digestive systems includes gastrointestinal discomfort such as diarrhea and gastroenteritis. This is the first case reporting a PCSK9 inhibitor as evolocumab induced short-term recurrent biliary obstruction due to stent blockage in the patient with pancreatic carcinoma, indicating cautious application of evolocumab in similar situation for potential risk and calling for more attention on the safety of evolocumab in patients with biliary dysfunction (1).

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-24-601/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this article and accompanying images.

References

1. AMGEN incorporation. REPATHA (evolocumab) [package insert]. U.S. Food and Drug Administration. Available online: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125522s033lbl.pdf. Revised Februray 2021. Accessed August 27, 2015.
2. Dumonceau JM, Tringali A, Papanikolaou IS, et al. Endoscopic biliary stenting: indications, choice of stents, and results: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline - Updated October 2017. Endoscopy 2018;50:910-30.
3. Isayama H, Hamada T, Yasuda I, et al. TOKYO criteria 2014 for transpapillary biliary stenting. Dig Endosc 2015;27:259-64.
4. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol

2019;74:e177-232.
5. Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J 2020;41:111-88.
6. Stellaard F. From Dietary Cholesterol to Blood Cholesterol, Physiological Lipid Fluxes, and Cholesterol Homeostasis. Nutrients 2022;14:1643.
7. Raschi E, Casula M, Cicero AFG, et al. Beyond statins: New pharmacological targets to decrease LDL-cholesterol and cardiovascular events. Pharmacol Ther 2023;250:108507.

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