ENDOCRINOLOGY RESEARCH AND PRACTICE

SOCIETY OF ENDOCRINOLOGY AND METABOLISM OF TURKEY

Primary Bile-Duct Stone in a Patient on Liraglutide

LETTER TO THE EDITOR
Endocrinol Res Pract. 2023;27(3):183-184

Dear Editor,

Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist that has recently been used for the medical treatment of obesity. Liraglutide stimulates insulin secretion in a glucose-dependent manner, while decreasing plasma glucagon concentrations, delaying gastric emptying, and suppressing appetite through neuronal pathways.[1] Glucagon-like peptide-1 analogs reduce gastrointestinal motility; therefore, most of their adverse effects are associated with the gastrointestinal tract. Moreover, they increase the frequency of gallbladder-related events, including cholelithiasis and cholecystitis.[2] Most bile duct stones are secondary. Primary bile duct stones are formed de novo within the liver or choledoch and are more common in the Asian population. These stones are often believed to develop secondary to biliary stasis and sphincter of Oddi dysfunction.[3] Here, we present a case of primary choledochal stone on liraglutide. Written informed consent was obtained from the patient who agreed to take part in the study.

A 49-year-old woman presented with epigastric pain, yellow eyes, and dark urine. She had no history of any chronic disease. She had undergone cholecystectomy 5 years ago and has been using liraglutide for weight loss for the past 10 weeks and has lost about 10 kg. Her examination revealed full-body jaundice, especially scleral icterus, with significant epigastric tenderness. The following blood tests were significant: alanine aminotransferase, 510 IU/mL; aspartate aminotransferase, 227 IU/mL; gamma-glutamyl transferase, 314 IU/mL; alkaline phosphatase, 164 IU/mL; total bilirubin, 7.17 mg/dL; and direct bilirubin, 4.83 mg/dL. Magnetic resonance cholangiopancreatography showed dilated intrahepatic bile ducts and choledoch, with a millimetric choledochal stone at the distal end. A stone of 5-6 mm diameter was removed by Endoscopic retrograde cholangiopancreatography (ERCP).

To our knowledge, this is the first case of primary choledochal stone on liraglutide in the literature.

Glucagon-like peptide-1 decreases gallbladder contractility because it suppresses the meal-induced intestinal cholecystokinin (CCK) secretion and decreases the CCK response of gallbladder myocytes.[2,4] Furthermore, experimental studies have shown that cholangiocytes are susceptible to GLP-1 and respond with increased proliferation and functional activity, which may increase the risk of stasis.[5] Thus, chronic use of GLP-1 analogs may increase the risk of sludge and gallstone formation.[2]

We do not know whether the choledochal stone in our case was de novo secondary to liraglutide or was retained in the cystic duct and migrated into the choledoch years later. However, this stone is more likely to be primary because of the long interval between cholecystectomy and stone and the potential of GLP-1 receptor agonists to slow down bile flow with CCK and form stones.

In conclusion, patients with multiple risk factors for gallstones (e.g., female gender, obesity, dyslipidemia, and diabetes) may be susceptible to re-develop gallstones even if they had undergone cholecystectomy. Therefore, caution should be exerted when initiating these patients on liraglutide. Ursodeoxycholic acid with the potential to prevent stone formation can also be considered if necessary. Further studies are needed on this subject.

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Declaration of Interests: The author has no conflicts of interest to declare.

Enver Avcı

Gastroenterology Department, Private Medova Hospital, Konya, Türkiye

Corresponding author:
Enver Avcı
✉ enver.a.dr@gmail.com

Received: February 21, 2023
Revision Requested: February 27, 2023
Last Revision Received: February 28, 2023
Accepted: March 7, 2023
Publication Date: July 4, 2023

Cite this article as: Avcı E. Primary bile-duct stone in a patient on liraglutide. *Endocrinol Res Pract.* 2023;27(3):183-184.

DOI: 10.5152/erp.2023.23228

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