INTRODUCTION

A few examples have been reported in the literature of the uncommon but significant complication of acute pancreatitis following liver resection. Acute pancreatitis is one of the complications associated with liver resection; however, this is not generally included in textbooks. So there will be little coverage of this. After liver resection, it is acceptable to take acute pancreatitis into account if there is any morbidity or mortality in the patient. Some hypotheses have been put out, but more research is needed to support them before we can determine the specific reason.

A moderately frequent condition, pancreatitis affects 17 out of every 100,000 people each year and has a death rate close to 10%. Gallstones in the common bile duct and alcohol use together account for 75% of acute pancreatitis. The additional etiologies, characterized by the mnemonic “I get smashed,” include significant trauma, steroids, the mumps, autoimmune diseases, scorpion stings, hypercalcemia, hypertriglyceridemia, and ERCP. Additionally, we are aware that 20% of cases are caused by idiopathic causes.

Miyagawa et al. also reported pancreatitis following liver resection for primary and secondary hepatic malignancy. One case out of 175 liver resections was their experience. However, in patients who unanticipatedly worsen postoperatively, pancreatitis is a challenging diagnosis to make. It needs to be regarded as a crucial differential diagnosis. Early diagnosis and treatment of pancreatitis may have improved the result for the current patients.

We have a strong hypothesis that in our situation, a white test to check for bile leakage following liver resection is linked to acute pancreatitis in the postoperative phase. One of the major side effects of liver resection that affects between 3.8 and 10% of patients is bile leakage. Following liver resection, bile leakage raises the risk of death, length of hospital stay, and occurrence of intraabdominal infection and liver failure. The bile leak test is conducted selectively; in addition to the standard white test, other options included the methylene blue test, indocyanine green test, and saline test. Every test has benefits and drawbacks, but some experts claim that the white test is the best since it is simple, rapid, affordable, and patient-safe.

CASE DESCRIPTION

Male, a 41-year-old, suffered from abdominal pain, especially at right upper quadrant, constantly for six months before visiting our hospital. The pain had...
worsened, chronically and progressively, till manifested vomiting and low intake. At initial admission, the patient had stable hemodynamics and was alert. The abdominal examination didn’t reveal any abnormalities, no palpable mass, and no sign of acute abdomen. The patient has a history of hepatitis B on tenofovir treatment.

We performed abdominal CT with contrast; the result was a liver tumor characteristically associated with hepatocellular carcinoma, accompanied by free fluid collection, maybe ascites or hemorrhagic material from the tumor. Its feeding comes from the right hepatic artery. The CT finding measured the size of the tumor at 7.8 x 7.4 x 6.7 cm in segment VI, right liver lobe (Figure 1). There was no sign of liver cirrhosis on the CT.

The working diagnosis for this patient was hepatocellular carcinoma, and our team with the internal medicine department performed TACE (Transarterial Chemoembolization) using doxorubicin complexed with lipiodol as an embolization agent. After the TACE procedure, evaluate the tumor with abdominal CT, with the tumor downsizing from 7.8 x 7.4 x 6.7 cm to 6.7 x 6.3 x 6.9 cm (Figure 2).

The next step for this patient was preparation for surgery due to its resectability. Patient under general anesthesia, starting with a J-shaped incision. We found a mass in segment VI in the right liver lobe with a diameter of about 8 cm, solid with an unclear margin. We performed anatomical resection in segments V, VI, and VII, pringle maneuver intermittently, each cycle comprising 15 minutes of clamping followed by 5 minutes of reperfusion, collaborated with anesthesia to set low CVP under 4 cmH2O, transection of the liver with a harmonic scalpel, bile leak test with fat emulsion via the cystic duct, and hemostasis agent with surgical. The duration of this surgery was about 3 hours, and the bleeding was about 450 cc. We also performed a cholecystectomy and put the drain in the perihepatic area. Figure 3 depicts the operational findings. During this operation, the patient was in stable condition without episodes of hypotension or desaturation. Post-operatively, this patient was transferred from the operating room to the ICU for further monitoring. In the ICU, the patient had stable hemodynamics, underwent a transfusion of packed red cells, and showed no obvious sign of ongoing bleeding from the hepatic surgical bed.

One week after liver resection, the patient suffered from epigastric pain that radiates to the back. We consider its complaint to be associated with increased gastric acid due to major surgery or an analgetic component. Evaluation of the pain is blurred in the postoperative state; patients feel pain progressively without any improvement, which makes us do abdominal CT with contrast, which helps us solve this problem. On abdominal CT in the postoperative period, we found surprisingly diffuse enlargement of the pancreas, heterogeneous enhancement of the gland, an irregular contour of the pancreatic margin, and blurring of peripancreatic fat. This finding is associated with acute pancreatitis. We continue to complete the pancreatitis panel, checking the pancreatic enzymes (amylase and lipase) to confirm the diagnosis. Laboratory results show leukocytosis, hypoalbuminemia, and an increase of amylase and lipase by 3x from baseline.

After acute pancreatitis has been established, we give symptomatic and...
supportive treatment. The patient's condition gradually improves, and patients are discharged from the hospital with Clavien-Dindo Grade 2 after 34 days of hospitalization.

**DISCUSSION**

Pancreatitis is a relatively common disease, affecting 17 per 100,000 patients annually, with a mortality rate approaching 10%. Mostly due to gallstones in the common bile duct or alcohol consumption. About 30% of the etiology of acute pancreatitis is idiopathic; the cause of acute pancreatitis is unidentifiable despite a comprehensive history, physical examination, laboratory investigation, and radiologic evaluation. These patients are conventionally classified as having idiopathic acute pancreatitis.

Acute pancreatitis, which is a discrete episode of cellular injury and inflammation in the pancreas, is triggered by the release of activated digestive enzymes into the pancreas and peripancreatic tissues. The pathophysiology of acute pancreatitis divides into three categories: duct obstruction, acinar cell injury, and defective intracellular transport.

Alcohol usage and gallstones in the common bile duct contribute to 75% of acute pancreatitis. For the other, less frequent etiologies, such as severe trauma, steroids, mumps, autoimmune diseases, scorpion stings, hypercalcemia, hypertriglyceridemia, ERCP, or medication, the well-known mnemonic “I get smashed” might be utilized. Furthermore, we are aware that idiopathic reasons account for 20% of instances.

Pancreatitis following liver resection has been described by Miyagawa et al. Their experience was one case in 175 patients undergoing liver resection. There are no published studies that specifically examine the association between pancreatitis and liver resection. So the exact mechanism of pancreatitis following liver resection is still under investigation. We will investigate some factors that are associated with pancreatitis in this patient, such as comorbidities, drugs, and interventions. A review of the notes for this patient did not reveal any evidence of biliary stones or a significant alcohol intake history.

Many viral infections may lead to acute pancreatitis, with the mumps virus being the most common viral cause of acute pancreatitis. Some authors also reported that acute pancreatitis is associated with the hepatitis B virus. The mechanism behind these associations has been hypothesized to include an immune response or direct cytotoxicity against the infected acinar cell. Another author proposed the edema of the ampulla of Vater with the obstruction of pancreatic juice flow as a possible mechanism of viral damage to the pancreas.

Rarely does hepatocellular carcinoma spread to the biliary tree. In a similar process to gallstone pancreatitis, clots or tumor emboli traveling through the bile...
duct can result in pancreatitis. We describe a patient who experienced recurrent acute pancreatitis that was previously thought to have a biliary etiology. He continued to experience acute pancreatitis despite having a cholecystectomy. The third incident resulted in the diagnosis of hepatocellular cancer. According to ERCP results, there may be a fistula between the tumor and the biliary tree. Hepatocellular carcinoma was removed from the patient during surgery. Its pathological examination supported the tumor and the biliary duct's connections.15

Pancreatitis has been linked to several medications.9 The majority of these connections are not supported by evidence but rather result from singular, isolated incidents. In a clinical context where numerous medications are administered concurrently, it is challenging to pinpoint one specific medication as the root cause of pancreatitis. The identification of a single medicine that is causally related requires proof in experimental research or actual circumstances. Therefore, it is challenging to track every medication we give this patient.

Treatment with antivirals for hepatitis B, like Tenofovir alone, is not associated with pancreatitis. One author reviewed cases of pancreatitis in patients receiving didanosine, which is antiretroviral plus tenofovir; co-administration of both drugs versus each of them individually was an independent risk factor for pancreatitis. These results suggest that the risk of pancreatitis is heightened when didanosine and tenofovir are given together.16 In this case, the patient is not on treatment with this combination.

Chemotherapy agents are one of many drugs that may be associated with pancreatitis in malignant patients. TACE procedure with doxorubicin is one cause of acute pancreatitis in malignancy patients, but its incidence is rare. The proposed mechanism involves regurgitation of the embolic beads from the hepatic artery into an artery supplying the pancreas, resulting in ischemia, especially in the head pancreas via pancreaticoduodenal arteries. The incidence of acute pancreatitis following TACE ranges from 1.7 to 15.2%. Acute pancreatitis can develop within 24 hours or up to 15 days after the TACE procedure. In this case, pancreatitis developed after more than a month.17–19

Significant hyperamylasemia was linked to prolonged blockage of the hepatoduodenal ligament after liver resection. In an experimental situation, hyperamylasemia can cause pancreatitis by completely occluding the pancreatic drainage veins. The gold standard for arterial occlusion in this patient, however, is intermittent clamping for 15 minutes, followed by 5 minutes of reperfusion. This method is secure for up to three hours of operation. In this instance, the total clamping time is under 3 hours.20,21

After liver resection, bile leakage is a dangerous consequence that can increase from 3% to 10% and could reach 30% in severe cases that include three or more segments of the liver.2 Following liver resection, biliary complications increase mortality, length of hospital stay, and likelihood of developing intraabdominal infection and liver failure. Recent studies have demonstrated the advantages of a leak test in certain conditions that lead to post-operative bile leaks.

Bile leakage tests are beneficial in reducing bilious complications following liver resection in several studies and randomized control trials. The agent that seems to be least effective is saline solution. The ability to identify bile leakage using a blue methyl test or an indocyanine green test is widespread; however, the test cannot be repeated due to liver segment color contamination. The advantages of fat emulsion, commonly known as the “white test,” which is frequently used for parenteral nourishment and is accessible and repeatable after being washed away with saline solution, have also been demonstrated in recent studies.22,23

The White test has many advantages compared with other bile leak tests, it can detect precisely, regardless of the defect. It doesn't stain the surface of the resection site, allowing it to be washed off, and it can be repeated. This test is safe, quick, and inexpensive.24 A white test is performed at the end of liver resection, and pediatric tube 5F is inserted in the cystic duct via incision. The diluted fat emulsion (about 5% diluted with normal saline) is injected slowly at low pressure after releasing the Pringle maneuver and clamping the common bile duct to prevent it from entering distally. Under direct vision on the resection surface, look for any leak of fat emulsion, which may be repeated. If any major fat emulsion leaks, suture the leak site and retest. The minor leak may be closed spontaneously or covered with fibrin glue. After performing this test, remove the tube and close the cystic duct (cholecystectomy). The literature mentions that at the end of the white test, we should wash out the remaining fat emulsion within the duct with saline solution.

We are confident that a white test to screen for bile leakage after liver resection in our case is connected to severe pancreatitis in the postoperative period. The steps in this method are all ambiguous. During the operation, we didn't pay attention to the amount of fat emulsion present; the product is also available in 10% and 20% concentrations. It must be diluted with a regular saline solution since, according to the literature, 5% is the safe concentration. Due to this, attention is essential. We also neglected to clear the bile duct after the exam. High-concentration solutions that are allowed to sit because of a duct obstruction at the level of the common channel might induce acute pancreatitis. More study is needed to show a relationship between constriction and duct obstruction.

**CONCLUSION**

The white test is beneficial for detecting bile leakage following liver resection; however, we do not advise frequent use of this test since there is a chance that it can trigger acute pancreatitis, which can have a substantial negative impact on the patient's morbidity or death.

**ETHICAL STATEMENT**

The patient received signed written informed consent regarding publication of medical data in scientific medical journals before any data collection with confidentiality of personal information.

**CONFLICT OF INTEREST**

The authors declare that there is no competing interest regarding the manuscript.
FUNDING

The authors are responsible for the study’s funding without the involvement of a grant, scholarship, or any other funding resource.

AUTHORS CONTRIBUTION

MSF responsible for concepts and design of the study, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, and manuscript review. DS responsible for concepts and design of the study, manuscript review, and guarantor. RN responsible for definition of intellectual content, literature search, clinical studies, manuscript preparation, manuscript editing, and manuscript review.

REFERENCES