CASE REPORT

Biliary Obstruction due to Pancreatic Insulinoma

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Pancreatic endocrine tumors are uncommon in clinical practice and the overall prevalence is as low as 10 per million population (1). Of these, insulinomas are probably the commonest, with a reported annual incidence of 0.9 cases per million per year. Most insulinomas are solitary, evenly distributed throughout the pancreas and benign; malignant insulinomas have been reported in only 5–16% and metastasis in only 5% at presentation. Common bile duct obstruction by insulinoma has not been previously reported. We describe here what we believe to be the first case of malignant insulinoma causing biliary obstruction.

CASE REPORT

A 50-year-old man without any significant past medical history presented with dull upper abdominal pain of six weeks' duration associated with anorexia and a recorded weight loss of 8 kg. This pain was continuous with intermittent exacerbations, unrelated to intake of food and without any specific radiation or postural variation. It was not associated with vomiting, upper abdominal distension, alteration in bowel habits, fever, or jaundice. Physical examination revealed mild pallor, absence of icterus, and no peripheral lymphadenopathy. The liver was palpably enlarged with a vertical span of 16 cm and had a firm feel, with an irregular surface. There was no intercostal tenderness or hepatic bruit or rub. Spleen was not enlarged and no peritoneal fluid could be detected. No other mass was felt in any quadrant.

Investigations revealed a hemoglobin of 13.8 gm/dl; a peripheral total leukocyte count of 14,800/mm³; a differential leukocyte count of 75% polymorphs, 20% lymphocytes, and 5% monocytes; an erythrocyte sedimentation rate of 6 mm (1st hour Westergren), platelets of 1.7 lac/mm³; a prothrombin index of 93%; and an activated plasma thromboplastin time of 39 sec. Biochemical profile showed a fasting blood sugar of 86 mg/dl, postprandial blood sugar of 110 mg/dl, urea of 26 mg/dl, creatinine of 0.8 mg/dl, total cholesterol 245 mg/100 ml, HDL cholesterol of 69 mg/100 ml, and triglycerides of 102 mg/100 ml. Liver function tests showed a bilirubin of 1.3 mg/dl, aspartate aminotransaminase (AST) of 68 IU/liter (normal < 15 IU/liter), alanine aminotransaminase (ALT) of 68 IU/liter (normal < 15 IU/liter), alkaline phosphatase of 473 IU (normal 70–140 IU), serum albumin of 3.3 mg/dl, and globulins of 3.0 gm/dl. Viral markers for hepatitis viruses B (HBsAg) and C (IgG anti-HCV) were negative. Ultrasoundography of the abdomen showed the liver to be enlarged with multiple anechoic cystic lesions with well-defined margins that were smooth with a 2- to 4-mm-thick wall, throughout the liver parenchyma. These cysts were of varying sizes, ranging from 3 to 6 cm, and the largest measured 5.2 × 5.9 cm. No abnormality in the biliary system was detected. The pancreas appeared normal, and there were no upper retroperitoneal lymph nodes. Both kidneys showed the presence of well-defined cortical cysts. The sonographic diagnosis was that of polycystic disease of the liver and kidneys, with a differential diagnosis of multiple hydatid cysts. Hydatid serology by indirect hemagglutination test (IHA) was less than 1:10, and an IHA for amebiasis was reported to be nonsuggestive. A computed tomogram of the abdomen confirmed the sonographic findings and did not detect any additional pathology (Figure 1).

Without having a reasonable explanation for his pain and significant weight loss, the patient was kept on a close follow-up and over the next three weeks, a further loss of 2 kg weight was noted. The radiology review after a month, together with the clinical profile, also prompted us to consider cystic metastatic deposits in the liver, and a fine-needle aspiration of the largest cyst was planned, which the patient did not agree to at this time. Over the next two months, the patient developed intense pruritus and liver function tests showed an elevation in the alkaline phosphatase value (mean 347 IU). A repeat ultrasonogram did not show any dilatation of the intra- or extrahepatic biliary ducts and an endoscopic retrograde cholangiopancreatog-
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Fig 1. Computed tomogram showing multiple hypodense areas in the liver, suggestive of cystic lesions and a normal head of the pancreas, without any evidence of tumor.

raphy (ERCP) was therefore deferred. A side-viewing du-odenoscopy revealed a normal papilla and biopsies from the papilla were negative for malignancy.

The patient subsequently developed symptoms of new-onset drowsiness and restlessness in the early hours of the morning associated with sweating and palpitations. He was admitted to the hospital and early morning blood sugar values were recorded as low as 40 mg/dl. His symptoms improved with oral glucose intake, and this appearance of fasting hypoglycemia prompted us to consider a clinical possibility of an endocrine pancreatic tumor such as an insulinoma. A repeat CT scan of the abdomen showed the liver cysts to be persisting with mild dilatation of the common bile duct; the pancreas was, however, reported to be normal. MRI of the abdomen (T1- and T2-weighted images) corroborated the findings of the CT scan with no additional information regarding the pancreas. A supervised in-hospital 72-hr fast showed blood sugar levels to drop to as low as 16–22 mg/dl with a corresponding plasma insulin level ranging from 54.4 to 79.9 μIU/ml (normal 0–30 μIU/ml). This further supported the clinical suspicion of hyperinsulinism due to an insulinoma.

At this time, the largest liver cyst was aspirated; clear fluid was obtained, which was negative for malignant cells by DNA flow cytometry. An ERCP together with endoscopic brush cytology of both the common bile duct (CBD) and the main pancreatic duct (MPD) was carried out. The CBD was narrowed at the lower end with proximal dilata-
tion, and the MPD was also narrowed in the head of pancreas with beading and dilatation of the duct in the body–tail region (Figure 2). A 7-cm-long, 10 Fr Teflon biliary endoprosthesis was placed in the common bile duct (Figure 3). Biliary and pancreatic brush cytology showed benign cells; no malignant cells were detected. Following stent placement, there was a fall in the alkaline phosphatase levels to normal, and ultrasonography showed nondilated biliary radicles.

The patient was then subjected to an “intention-to-treat” laparotomy for definitive treatment by pancreaticoduodenectomy and biliary bypass. However, a large 4 × 4-cm, hard, fixed mass was felt in the head of the pancreas, frozen section biopsy of which showed it to be a malignant neuroendocrine tumor of B-cell origin, likely to be an insulinoma. The liver had bluish cysts of varying sizes together with whitish metastatic nodules; a solitary metastatic nodule was also detected under the umbilicus. There were no peritoneal or pelvic deposits. The intraoperative finding was of an inoperable tumor, as it was fixed and could not be mobilized. The patient is currently undergoing palliative chemotherapy with 5-fluorouracil and mitomycin-C, but continues to be ill. Appropriate dietary therapy with frequent meals and a bedtime snack has been instituted to prevent symptomatic neurohypoglycemic episodes. He is on a regular monthly follow-up as an outpatient in the liver clinic.