Turkish Journal of Endocrinology and Metabolism, (2006) 1 : 21-24

CASE REPORT

Malignant Insulinoma and Gallbladder Agenesis: A Case Report

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Insulinoma and gallbladder agenesis are rare pathologies and co-existence of these two pathologies is not reported previously. A 74-year-old woman was admitted to our clinic with syncope brought on by fasting. After 4 hours of fasting, the patient's blood glucose level was 14 mg/dL (normal range: 70-105 mg/dL) and her insulin level was 89.9 µU/mL (normal range: 5-25µU/mL). The symptoms resolved after intake of high-sugar foods. Abdominal ultrasonography and computerized tomography revealed an approximately 1 cm-diameter lesion consistent with an insulinoma in the distal pancreas. Additionally gallbladder was not seen on these radiological examinations. During surgery, gallbladder agenesis was confirmed, and distal pancreatectomy and splenectomy were performed to remove the tumor, which was adhered to vessels. After surgery, the patient's blood glucose and insulin levels returned to normal, and her symptoms improved. Histopathological examination of the specimen revealed a 1.6×1.5×1-cm malignant neuroendocrine tumor and a peripancreatic lymph node metastasis. The article details this rare case of malignant insulinoma combined with gallbladder agenesis and reviews the literature.

Keywords: Insulinoma, malignancy, gallbladder agenesis

Introduction

The reported incidence rates of gallbladder and cystic duct agenesis range from 0.01% to 0.04% (1). Islet cell tumors of the pancreas are also rare (annual incidence 5 to 10 cases per million persons), and most of these are insulinomas (2). Insulinomas are usually small, benign intrapancreatic lesions. The documented malignancy rates for insulinomas range from 5% to 15% (3-5). Histopathological diagnosis of malignant insulinoma is difficult and can be accomplished by detection of neighbouring organ invasion or tumor metastasis to regional lymph nodes or distant organs (5-7).

Case Report

A 74-year-old woman was admitted to our emergency service with complaints of syncope brought on by fasting. The syncope's had initially occurred once every 10 to 15 days, but had become more frequent. The patient recovered from the symptoms after intake of high sugar foods. She weighed 76 kg and was 156 cm tall. The only abnormality on physical examination was mild obesity. The patient's postprandial blood glucose level was 55 mg/dL (normal range: 70-105 mg/dL). Her blood glucose level after 3 hours of fasting was 40 mg/dL, and this dropped to 14mg/dL after 4 hours. At the 4-hour stage, her insulin level was 89.9µU/mL (normal range: 5-25 µU/mL) and her C-peptide level was 7 ng/mL (normal range: 1-5 ng/mL). The results for the rest of her blood biochemistry profile were normal.

Abdominal ultrasonography (USG) and contrast enhanced abdominal computerized tomography (CT) showed multiple simple cysts in both lobes of the liver and a 5×3-cm hemangioma in the posteroinferior segment of the right liver lobe. No gallbladder was apparent on these radiological examinations. CT revealed a 1cm-diameter, markedly enhanced mass on distal pancreas that was consistent with an islet cell tumor (Figures 1A, 1B and

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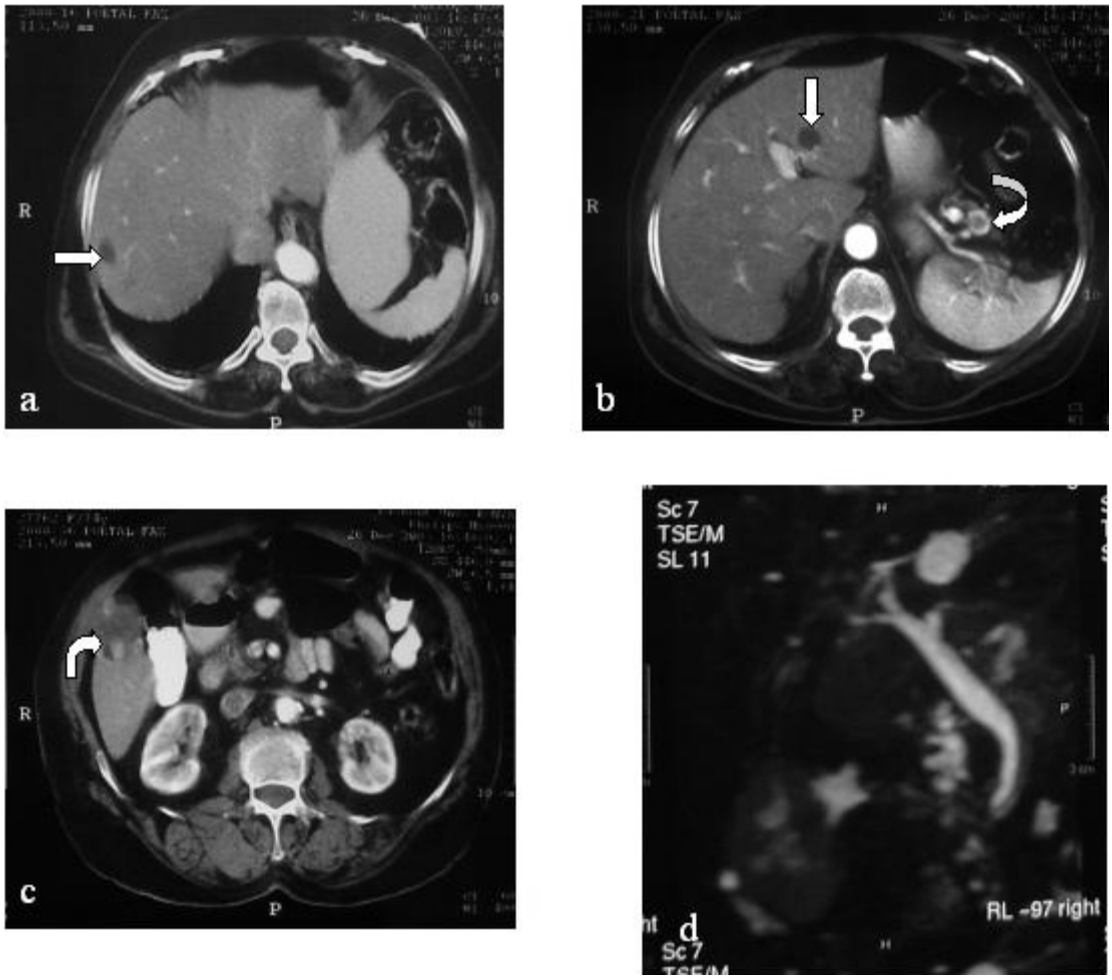

Figure 1: Multiple simple cysts were observed in both lobes of the liver on CT **(A, B)** (straight arrows); A strongly enhanced mass consistent with an islet cell tumor was noted in the tail of the pancreas (curved arrow), and a hemangioma was detected in the posteroinferior segment of the liver (arrow) **(C**); The gallbladder and cystic duct were not evident on MRCP **(D)**.

1C). Since no gallbladder was visible on abdominal USG or CT, magnetic resonance cholangiopancreatography (MRCP) was performed and showed agenesis of the gallbladder and cystic duct (Figure 1D).

The patient was diagnosed with islet cell tumor of pancreas and underwent surgery. No gallbladder was found intraoperatively. A simple 1-cm cyst was detected in the left liver lobe and a 4-cm hemangioma was detected in the anteromedial segment of the liver (Figure 2). In addition, there was a fixed, non-detachable mass measuring approximately 1.5cm in the pancreatic tissue. This lesion was attached to the splenic artery and vein, and thus had to be excised via distal pancreatectomy and splenectomy. The patient's postoperative course was uneventful, and her postoperative blood glucose, insulin and C-peptide levels were normal. She was discharged from hospital on the eighth postoperative day.

Histopathological examination of the lesion revealed a 1.6×1.5×1-cm mass that exhibited moderate pleomorphism, focal necrosis within its stroma, and invasion of vessels. The lesion's surgical margins were intact. There were two peripancreatic lymph nodes in the surgical specimen. One of the nodes contained tumor metastases, so the tumor considered as malignant neuroendocrine tumor (Figure 3). The patient did well on her sixth week follow up and she quitted coming controls.

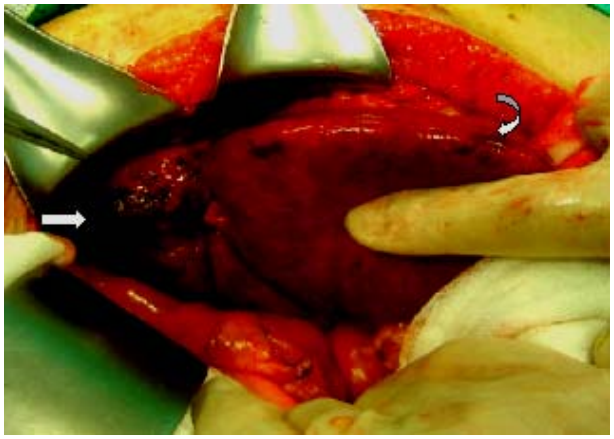

Figure 2. During surgery, a hemangioma was detected in the anteromedial segment of the right liver lobe (straight arrow) and a simple cyst was found in the anteromedial segment of the left liver lobe (curved arrow). Gallbladder agenesis was confirmed.

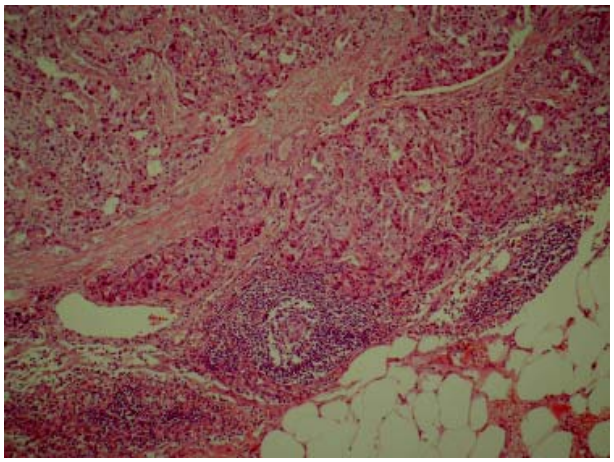

Figure 3. Examination of a pancreatic lymph node removed during surgery revealed insulinoma metastasis (H&E×200).

Discussion

Agenesis of the gallbladder can accompany various types of congenital anomalies. Gallbladder agenesis is an abnormality of embryologic development, and most affected individuals have bile duct anomalies as well (1,8,9). In our case, the patient's only anomalies were gallbladder and cystic duct agenesis, and these were evident on MRCP and confirmed at surgery.

The first step in diagnosing insulinoma is detection of Whipple's triad, which consists of fasting hypoglycemia, blood glucose level below 50 mg/dL, and alleviation of symptoms by ingesting sugar (3). Our patient presented with this triad. Her symptoms were being caused by hypoglycemia due to uncontrolled insulin secretion. Most individuals with insulinoma gain weight because they learn that their symptoms abate with food intake. Our patient, who was mildly obese, experienced syncope and reported that her symptoms subsided when she ingested sugar.

Before surgery precise determination of location of the lesion improves surgical outcome. In our case, the pancreatic tumor was detected on USG and CT. The recommended treatment for benign insulinoma is open or laparoscopic enucleation (3,10). Distal pancreatectomy or pancreaticoduodenectomy is advised for individuals with malignant lesions or those who cannot undergo enucleation for some reason (3). In our patient, distal pancreatectomy and splenectomy were performed because enucleation was not possible due to vessel invasion. The diagnosis of malignant insulinoma is based on the detection of neighbouring organ invasion and metastasis. Our patient was also diagnosed by detection of peripancreatic metastatic lymph nodes during surgery. Although we did not have the long-term follow-up of our patient, we thought distal pancreatectomy provided an effective treatment for this patient. To our knowledge, this is the first report of a patient with the combination of gallbladder agenesis and insulinoma.

References

1. Belli G, D'Agostino A, Iannelli A, Rotondano G, Ceccarelli P: Isolated agenesis of the gallbladder. An intraoperative problem. *Minerva Chir* **52:** 1119-1121, 1997.
2. Azimuddin A, Chamberlain RS. The surgical management of pancreatic neuroendocrine tumors. *Surg Clin North Am* **81:** 511-525, 2001.
3. Reber HA. Pancreas. In: Schwartz SI, Shires T, Spencer FC, Daly JM, Fischer JE, Galloway AC, eds. *Principles of Surgery* 7th ed. Singapore: McGraw Hill Co; **1999:** 1493-1494.
4. Bieligk S, Jaffe BM. Islet cell tumors of the pancreas. *Surg Clin North Am* **75:** 1025-1040, 1995.
5. Kobayashi M, Kawa S, Kobayashi M, Imai Y, Sodeyama T, Kiyosawa K. Malignant insulinoma presenting a non-functioning metastatic liver tumor 14 years after resection of the primary tumor. *J Gastroenterol* **33:** 891-894, 1998.
6. Thompson NW, Eckhauser FE. Malignant islet-cell tumors of the pancreas. *World J Surg* **8:** 940-951. 1984.

7. Eriguchi N, Aoyagi S, Hara M, Imayama H, Okuda K, Hashino K, Kanazawa N, Tamae T, Fukuda S, Jimi A. Insulinoma occurring in association with fatty replacement of unknown etiology in the pancreas: report of a case. *Surg Today* **30:** 937-941, 2000.
8. Turkel SB, Swanson V, Chandrasoma P. Malformations associated with congenital absence of the gallbladder. *J Med Genet* **20:** 445-449, 1983.
9. Gotohda N, Itano S, Horiki S, Endo A, Nakao A, Terada N, Tanaka N. Gallbladder agenesis with no other biliary tract abnormality: report of a case and review of the literature. *J Hepatobiliary Pancreat Surg* **7:** 327-330, 2000.
10. Tagaya N, Kasama K, Suzuki N, Taketsuka S, Horie K, Furihata M, Kubota K. Laparoscopic resection of the pancreas and review of the literature. *Surg Endosc* **17:** 201-206, 2003.