Case Report

Glucagonoma Presenting with Obstructive Jaundice : A Case Report

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Abstract : **A case report of a 2-cm glucagonoma at head of pancreas in 48-year old woman presented with obstructive jaundice. She had no manifestation of the glucagonoma syndrome. She underwent pylorus preserving pancreaticoduodenectomy (PPPP). Immunohistochemical studies revealed that this tumor was a malignant glucagonoma. She made an uneventful recovery after the operation and was discharged from the hospital without complication. Six months later, she was found to have multiple liver metastases which did not response to chemotherapy and died 11 months after the operation with liver failure.**

Key words : malignant glucagonoma, obstructive jaundice, pancreaticoduodenectomy

เรื่องย่อ : **ผู้ป่วยก้อนกลูคากอนที่มาด้วยอาการทางเดินน้ำดีอุดตัน : รายงานผู้ป่วย 1 ราย**

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รายงานการศึกษาผู้ป่วยหญิงไทยอายุ 48 ปีที่มีก้อนกลูคากอนขนาด 2 เซนติเมตร ที่หัวของตับอ่อนที่มาโรงพยาบาลด้วยอาการทางเดินน้ำดีอุดตัน ไม่พบอาการแสดงของกลุ่มอาการก้อนกลูคากอนในผู้ป่วยรายนี้ ผู้ป่วยได้รับการผ่าตัดตับอ่อนและลำไส้ดูโอดีนั่มโดยเก็บรักษาหูรูดไพโลรัสไว้ การตรวจชิ้นเนื้อทางอิมมูโนเคมี พบว่าก้อนกลูคากอนนี้เป็นชนิดเนื้อร้าย ภายหลังการผ่าตัดผู้ป่วยมีอาการดีขึ้นตามลำดับ และสามารถกลับบ้านได้โดยปราศจากผลแทรกซ้อน 6 เดือนต่อมาพบมีการกระจายไปที่ตับหลายตำแหน่ง ซึ่งไม่ตอบสนองต่อการรักษาด้วยเคมีบำบัด และผู้ป่วยเสียชีวิต หลังผ่าตัด11 เดือนด้วยภาวะตับวาย

INTRODUCTION

Glucagonoma is a rare pancreatic tumor of the islet cells with distinct clinical manifestations, including necrolytic migratory erythema (NME), stomatitis, weight loss, anemia, diabetes mellitus, and hypoaminoacidemia[1,2]. Fewer than 200 cases have been reported worldwide, with an estimated incidence of 1 in 20 millions[3]. They are predominantly located in the body and tail of the pancreas, and are malignant in about 70% of cases[4].

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We report a case of a 2-cm glucagonoma in the pancreatic head that caused obstructive jaundice. The patient had no manifestation of the glucagonoma syndrome. ERCP showed dilatation and stenosis at the distal end of the common bile duct. The patient underwent pylorus preserving pancreaticoduodenectomy (PPPP). Immunohisto-chemical studies revealed that this tumor was a malignant glucagonoma. Six months later, she was found to have multiple liver metastases which did not respond to chemotherapy. The patient died 11 months after the operation with liver failure.

CASE REPORT

A 48-year-old lady, owner of a private school, living near-by in Bangkok, presented to the surgical clinic with abdominal discomfort and progressive jaundice for one week. She had previously been well without any preexisting illness or regular medication.

Physical examination revealed an acutely ill patient with markedly jaundice and moderate abdominal pain. There were no particular skin or mucosal lesions. Routine examination of blood and urine revealed no evidence of hyperglycemia or glycosuria. Serum total bilirubin was 50 mg/dl. Serum levels of CEA, CA 19-9 and CA 125 were within normal limits.

Abdominal ultrasonography (US) and CT scan failed to reveal a pancreatic mass. Endoscopic retrograde cholangiography (ERC) demonstrated marked dilatation of the common bile duct and a stricture at the distal end (Figure 1).

At operation, a firm mass was seen on the anterior side of pancreatic head. There were no findings suggestive of malignancy; no liver, peritoneal or lymph node metastases were found at operation. PPPP were performed using a dunking technique pancreaticojejunostomy.

Histopathologic examination confirmed the diagnosis of a malignant islet cell tumor. Angiolymphatic tumor emboli were present. The tumor stained positive for glucagon (Figure 2A, 2B), and negative for synaptophysin, chromogranin, somatostatin and insulin. No marked fibrosis or calcification was found in the pancreatic parenchyma.

This patient was discharged without any postoperative complications. Follow-up study (abdominal CT scan) showed evidence of liver metastases 6 months after the operation (Figure 3). She died of liver failure 11 months after operation.

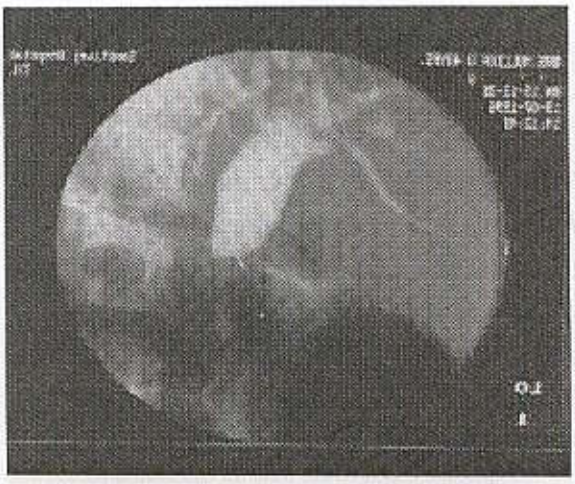

Figure 1. Endoscopic retrograde cholangiogram shows distal bile duct obstruction due to a pancreatic tumor.

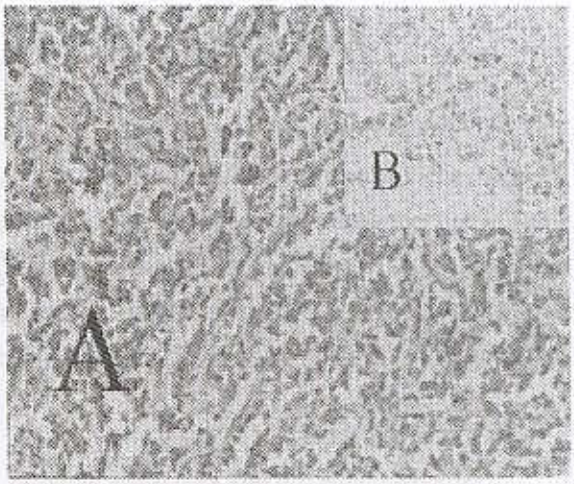

Figure 2. **A:** Photomicrograph of the resected tumor (H&E, mag. x 400)
B: Immunohistochemical staining demonstrates immunoreactivity to glucagon (x 400).

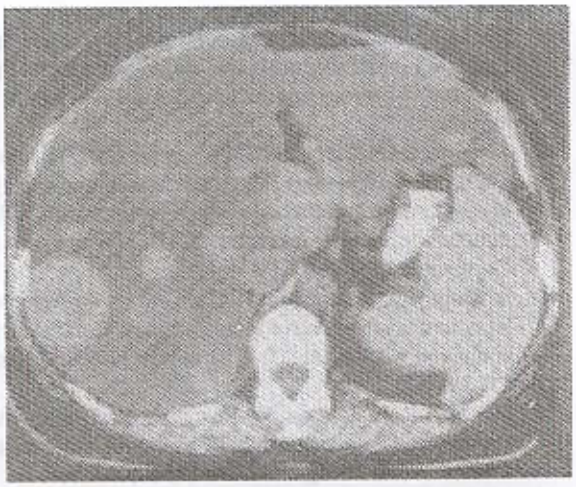

Figure 3. Abdominal CT scan 6 months after the operation shows multiple liver metastases.

DISCUSSION

A glucagonoma is a very rare tumor of the pancreatic islet cells. The prevalence of glucagonoma is 1 in 20,000,000 people. The peak incidence is between 40 and 60 years of age. There is no sex difference in incidence[3]. Because the tumor can excrete excess glucagon, which antagonizes the effect of insulin, glucagonoma is characterized by a high blood glucose, which may include necrolytic migratory erythema (NME), stomatitis, weight loss, anemia and hypoaminoacidemia[5]. The tumors arise more often in the body and tail of the pancreas and are generally larger than 4 cm in diameter[6]. Unfortunately, 70% of tumours are malignant, as determined by the presence of local invasion, spread to regional lymph nodes or distant metastases. They metastasize most commonly to the liver, less often to bone and adrenal glands[7]. About a half of cases tend to have liver metastases at presentation. As in other islet cell tumors, morphological atypia, angioinvasion, and perineural infiltration, are often lacking in metasta-sized glucagonomas[8].

Localization of the tumor is sometimes difficult. Transabdominal US and CT scan are noninvasive and are the first choice of imaging modalities. In this patient, the tumor could not be demonstrated. ERCP has a specificity and sensitivity of about 90% for the diagnosis of pancreatic ductal carcinoma[9]. Although glucagonoma does not arise from ductal cells, ERCP can detect a distortion or stenosis of the pancreatic duct in glucagonoma[10]. Endoscopic ultrasonography (EUS) can provide the best appraisal of pancreatic anatomy and has the highest rate of detection of pancreatic tumor[11]. EUS has been found to be more sensitive than angiography for localization of lesions not detected by transabdominal US or CT[12,13]. When the technique becomes more widely available, it may replace angiography in the work-up of small tumor of the pancreas.

The treatment of choice is surgical excision. Most glucagonomas are large and malignant; and since they are usually located in the body and tail of the pancreas, distal pancreatectomy is required. Enucleation is not recommended because of the malignant potential of these tumors. Resection is recommended even for large or metastatic tumors because the tumors tend to grow slowly and resection may provide prolonged palliation[14].

The surgery is difficult, since anemia and blood clotting problems require careful monitoring and management during the operation. Post-operatively, prophylaxis against blood clotting is required.

If the liver has been extensively infiltrated with metastases then resection of the primary tumor with liver transplant is the only chance of cure. In recent years, 4 glucagonoma patients with hepatic metastases have undergone total pancreatectomy and liver transplantation[8]. Early results have been promising with three of the four patients living and disease-free after 3 years[15]. However, the role of hepatic transplantation in patients with metastatic disease remains to be elucidated.

Alternatives include cytoreductive surgery plus adjunctive chemotherapy[16] and embolisation (where small arteries feeding the tumours are blocked off, killing the cells)[17].

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