US-guided ethanol ablation of insulinomas: a new treatment option

Michael J. Levy, MD,[1] Geoffrey B. Thompson, MD,[3] Mark D. Topazian, MD,[1] Matthew R. Callstrom, MD,[4] Clive S. Grant, MD,[3] Adrian Vella, MD[2]

Rochester, Minnesota, USA

Insulinomas account for the majority of functioning islet cell tumors of the pancreas. The diagnosis depends on documenting hypoglycemia as a cause of the patient's symptoms and demonstrating inappropriate endogenous insulin secretion at the time of hypoglycemia. Imaging and regionalization studies guide operative intervention. Surgical enucleation or resection is the standard treatment. Alternative treatment options may be necessary such as diazoxide or somatostatin for symptomatic patients with unresectable disease or for poor surgical candidates. Medical therapy is expensive and is characterized by tachyphylaxis and significant adverse effects such as hirsutism, nausea, and edema. We describe the technique and outcomes (1) after EUS and intraoperative US (IOUS)-guided fine-needle injection (FNI) of ethanol in symptomatic patients considered to be poor surgical candidates or (2) after incomplete surgical resection.

METHODS

Background information

Eight patients (mean age 66 years, range 34-82 years) underwent EUS- (n = 5) or IOUS- (n = 3) guided FNI of 95% to 99% ethanol for therapy of a sporadic (n = 7) or multiple endocrine neoplasia 1–associated (n = 1) insulinoma from August 2007 to December 2010 (Table 1, (Fig. 1). The diagnosis was based on our standard criteria, which include (1) symptoms of hypoglycemia provoked by fasting, (2) circulating glucose level less than 50 mg/dL at symptom onset, and (3) symptom relief with glucose administration. All patients met these criteria. The diagnosis was further confirmed by formal biochemical analysis. Patients were contacted and charts reviewed to determine the clinical, biochemical, and imaging outcomes. The study was approved by the Mayo Institutional Review Board. Descriptive statistics were computed for all variables including means and range for continuous factors and frequencies and percentages for categorical variables.

Surgery was not performed because of tumor location requiring pancreaticoduodenectomy (n = 3), significant comorbidities (n = 2), recent incomplete resection (n = 1), multiple abdominal operations with a frozen abdomen (n = 1), or intraoperative bleeding during attempted resection (n = 1). Patients experienced frequent and severe manifestations of hypoglycemia for a mean of 5.6 years (range 0.1-20 years) before treatment, with a venous glucose nadir of 23 mg/dL (range 9-38 mg/dL) (Table 2). Patients increased dietary consumption (n = 7) and/or restricted their physical activity (n = 7) in an effort to lessen or avoid hypoglycemic symptoms. Four patients were currently taking or had recently taken antihypoglycemic agents including diazoxide (n = 4), octreotide (n = 2), olanzapine (n = 1), prednisone (n = 1), acarbose (n = 1), or exenatide (n = 1). The insulinomas were located in the pancreatic head (n = 6), body (n = 1), or tail (n = 1) and initially measured 15 mm (range 9-23 mm) by helical CT versus 15 mm (range 8-21 mm) with EUS or IOUS (Table 3).

RESULTS

Technique

EUS FNI was performed by using a linear echoendoscope (GF-UC140P-AL5 or GF-UC 160P-AT8; Olympus America Inc, Center Valley, Pa) with a 22- or 25-gauge needle (Wilson Cook, Winston-Salem, NC). IOUS FNI was performed by using linear array imaging (Sequoia US platform, Siemens Medical Solutions, Malvern, Pa) with a 25- or 27-gauge needle (B-D Precision Glide, Franklin Lakes, NJ) (Table 4). Our decision to use alcohol was based on its long-standing percutaneous use to treat neuroendocrine tumors and other tumor types in the liver, thyroid, lymph nodes, and other sites. The injection was guided by EUS (n = 5) or IOUS (n = 3). A total of 14 treatment sessions was performed. For the 3 patients undergoing IOUS, 1 treatment was performed. For the 5 patients undergoing EUS FNI, a total of 3 (n = 1) and 2 (n = 4) treatment sessions were performed with 3.4 injections (range 2-6 injections) per session. A volume of 0.8 mL (range 0.12-3.0

Abbreviations: FNI, fine-needle injection; IOUS, intraoperative US; TUS, transabdominal US.

DISCLOSURE: *The authors disclosed no financial relationships relevant to this publication.*

0016-5107/$36.00
doi:10.1016/j.gie.2011.09.019

Received July 8, 2011. Accepted September 12, 2011.

Current affiliations: Divisions of Gastroenterology and Hepatology (1) and Endocrinology, Diabetes, Metabolism, and Nutrition (2), Departments of Surgery (3) and Radiology (4), Mayo Clinic College of Medicine, Rochester, Minnesota, USA.

Presented at Digestive Disease Week 2011 as an oral presentation (ASGE EUS Topic Forum) and an ASGE Video Forum (Gastrointest Endosc 2011;73: AB136-7).

Reprint requests: Michael J. Levy, MD, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Mayo Clinic, 200 First Street SW, Rochester, MN 55905.

TABLE 1. Background information

Pt	Age, y	Sex	Initial symptom duration, mo	Antihypoglycemic therapy (before injection)	Rationale for foregoing resection
1	67	M	14	None	Desire to avoid pancreaticoduodenectomy
2	72	F	240	Diazoxide (100 mg tid); prednisone 2.5 mg/d; olanzapine 5 mg/d	Desire to avoid pancreaticoduodenectomy
3	60	M	65	None	Desire to avoid pancreaticoduodenectomy
4	82	M	48	Diazoxide 60 mg/d	Presence of significant comorbidities
5	80	F	1	Diazoxide 150 mg tid; octreotide 50 μg tid	Presence of significant comorbidities
6	57	F	72	None	Desire to avoid pancreaticoduodenectomy
7	34	M	96	Diazoxide, exenatide, octreotide, precose; doses unspecified	Multiple previous abdominal operations with a frozen abdomen
8	79	F	1	None	Intraoperative bleeding during attempted resection

Pt, Patient; *tid*, 3 times daily.

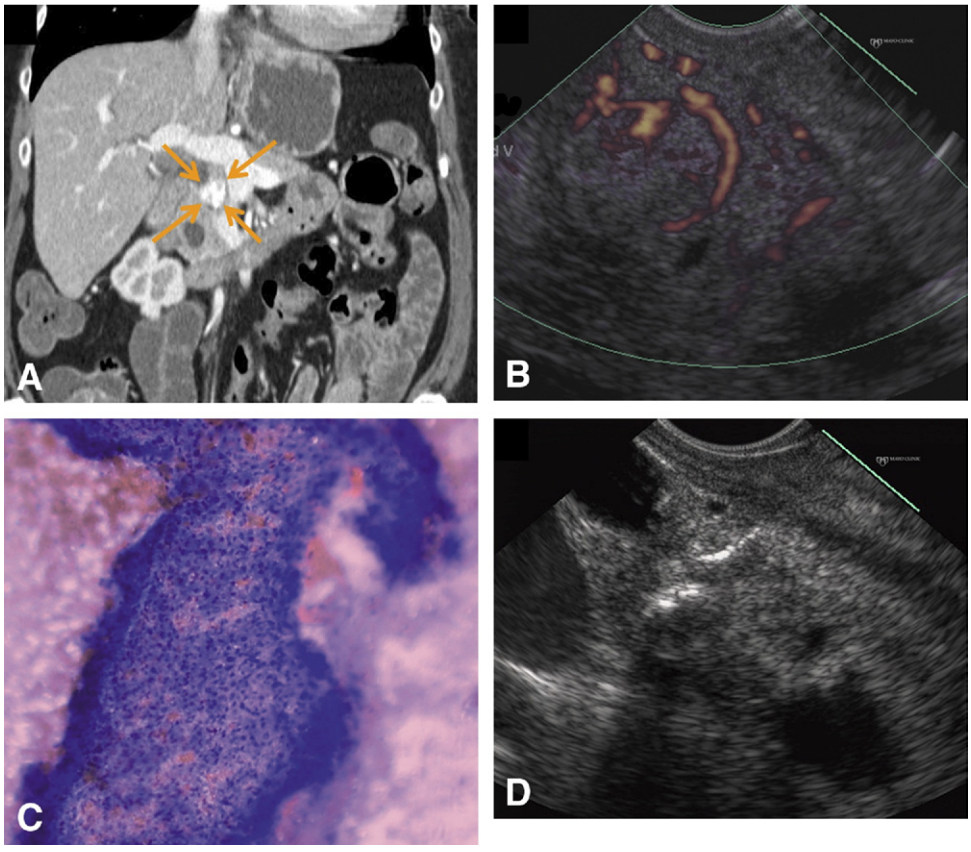

Figure 1. The images pertain to a 72-year-old woman with thyroid cancer and chronic obstructive pulmonary disease. She had symptoms of hypoglycemia for approximately 20 years with worsening symptoms over the past 2 years. Nursing home admission was planned because of clinical deterioration. She had a recent diagnosis of an insulinoma and was deemed a poor surgical candidate. Enucleation was considered technically challenging, and the patient was not a candidate for pancreaticoduodenectomy. **A,** CT of the abdomen revealed a 15 × 17-mm enhancing mass lesion (*arrows*) located in the pancreatic head. **B,** EUS from the duodenal bulb reveals the insulinoma. **C,** On-site FNA yielded cytology (Diff Quick, ×20) compatible with a neuroendocrine tumor. **D,** A 25-gauge needle was inserted and a total of 0.12 mL of 98% alcohol was injected with 2 needle passes. The alcohol produced a hyperechoic infiltrate. After withdrawing the needle, the pattern of alcohol spread can be appreciated. A second needle pass was performed to treat the untreated region of the tumor. The patient underwent a total of 3 EUS sessions. Follow-up at 11 months revealed that the diazoxide dose could be tapered to 50 mg/d. The patients' mean blood sugar was a mean of 140 mg/dL and usually 110 to 160 mg/dL, and there had been complete resolution of all clinical manifestations.