

Endoscopic ultrasound-guided ethanol ablation therapy for pancreatic insulinoma: an unusual strategy

Adriana de Sousa Lages¹, Patrícia Oliveira¹, Isabel Paiva¹, Francisco Portela², Daniela Guelho¹, Luís Cardoso¹, Nuno Vicente¹, Diana Martins¹, Diana Oliveira¹, Mara Ventura¹, Francisco Carrilho¹

¹ Endocrinology Department, Coimbra Hospital and University Center, Portugal
² Gastroenterology Department, Coimbra Hospital and University Center, Portugal



BACKGROUND

Insulinomas are the most frequent cause of endogenous hypoglycaemia. 90 to 95% of these tumours are benign. Occur in 1-4 people per million of the general population and represent 1%-2% of all pancreatic neoplasms. Surgical enucleation or resection is the standard treatment. Medical therapy focuses mainly on the use of diazoxide with few alternatives in patients with high surgical risk. Recent data has focused on the promise of Endoscopic ultrasound (EUS)-guided ethanol ablation as a safe and effective method for treating patients with small lesions or who are poor operative candidates.

CASE-REPORT

IDENTIFICATION:

♀
 89 years-old
 Retired
 Resident at Coimbra, Portugal

PAST MEDICAL HISTORY:

Acute myocardial infarction
 Stroke with motor sequelae
 Pacemaker carrier due to AV Block: 2nd degree, Mobitz II
 Severe aortic valve disease
 Hypertension
 Dyslipidemia
 Status post-adenocarcinoma of the sigmoid transition - pT4N0Mx

DAILY MEDICATION:

Clopidogrel 75mg id
 Enalapril 20 mg +
 Hydrochlorothiazide 12.5 mg id
 Pantoprazole 20mg id
 Trimetazidine 35 mg id
 Carvedilol 6.25mg id
 Simvastatin 20mg id

CASE PRESENTATION

1st visit to the Emergency Department (ED) in 21/5/2015 due to prostration and confusion → plasma glucose of 50mg/dl and prompt relief of symptoms following the administration of glucose → medical discharge with capillary blood glucose monitoring at home

2nd admission to the ED in 1/6/2015 due to recurrent hypoglycaemia, especially in fasting, with 3 weeks of evolution - capillary glucose measured at home ~ 30 mg / dl. There was no weight gain associated. No history of diabetes was known. No use and no access to hypoglycaemic drugs at home.

Plasma measurements in 21/5/2015		
Glucose	45mg/dl	<55mg/dl
Insulin	12 uUI/mL (<30)	>3 uUI/mL
C-peptide	1,6 ug/mL (1,0-7,6)	>0,6 ug/mL
HbA1c	5,1%	
TSH	1,1 (0,4-4)	
T4livre	1,1 (0,8-1,9)	

Suspicion of endogenous hyperinsulinism

Admitted to Endocrinology Department

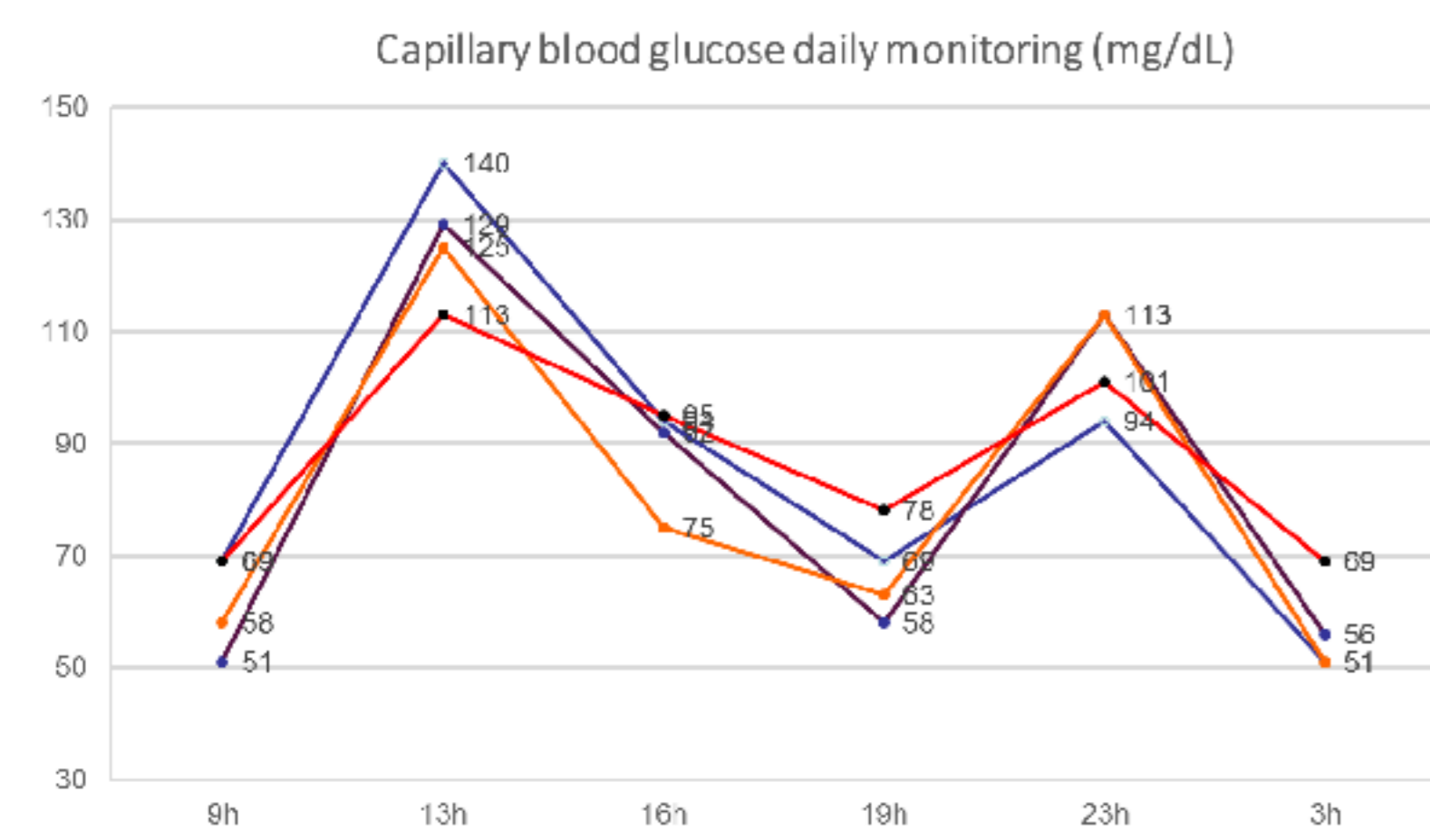
INVESTIGATION

LABORATORIAL INVESTIGATION

D1

Plasma measurements in 2/6/2015		
Glucose	38mg/dL	<55mg/dl
Insulin	10 uUI/mL	>3 uUI/mL
C-peptide	1,9 ug/mL	>0,6 ug/mL
ACTH	11 pg/mL	(VR 9-52)
Cortisol	14 ug/dL	(VR 5-25)
GH	0,3 ug/L	(VR <1)
IGF-1	100 ng/mL	(VR 81-225)
Atb anti-insulin	Negative	

Collected during an symptomatic hypoglycaemia (02.00h)



IMAGING INVESTIGATION

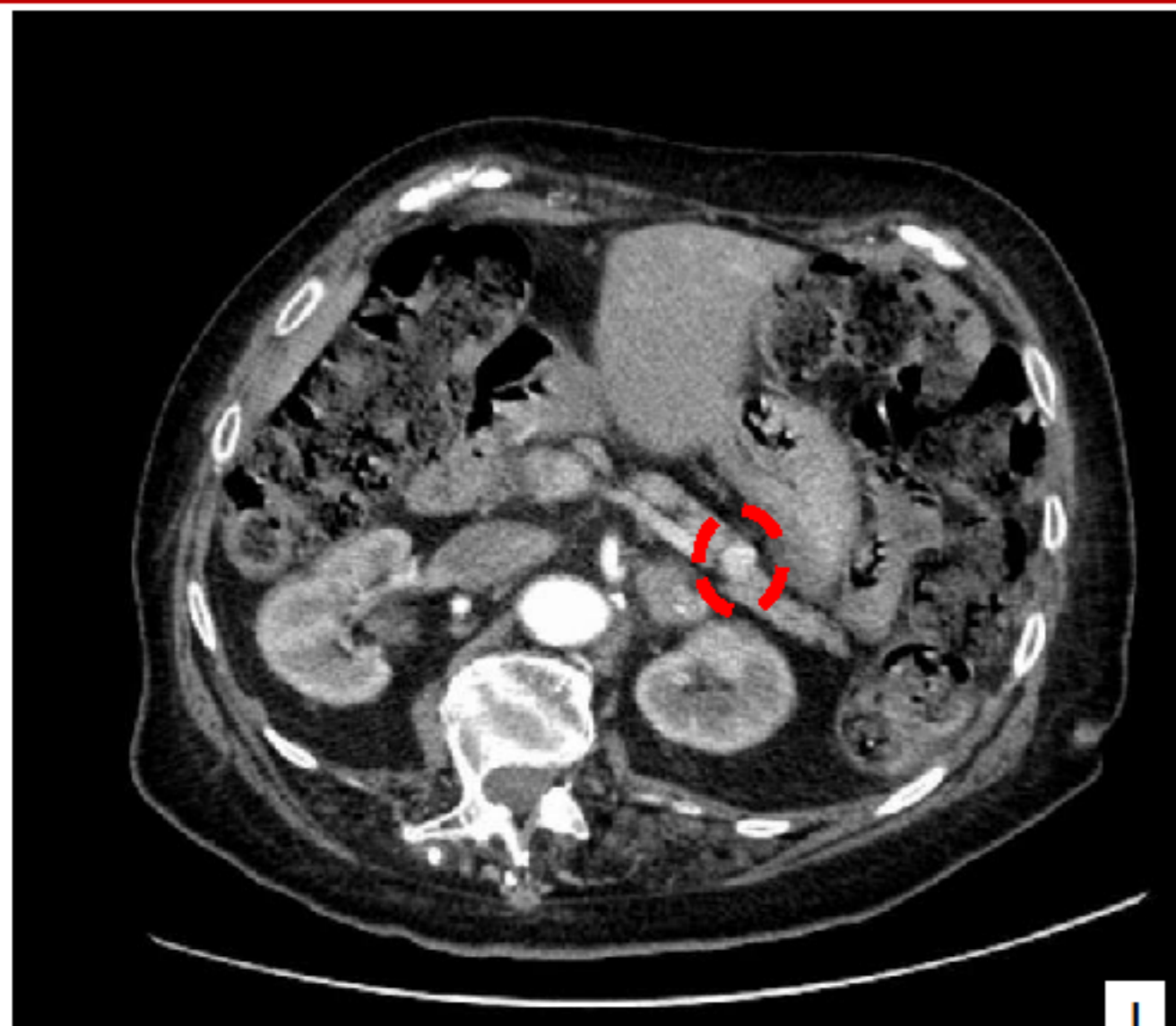


Figure 1 – Abdominal CT scan- (17/6/2015): "Nodular hypervascular lesion with 12mm suggestive pancreatic neuroendocrine tumor"

THERAPY

MEDICAL THERAPY

1st OPTION → DIAZOXIDE

Initial dose: 25 mg in 3 divided doses per day

Titrated to 100-200mg 2 a 3 times a day
 Maximum dose of 400mg/day

Edema
 Hypotension
 Symptomatic bradycardia

Gradual titration of diazoxide poorly tolerated

CONTACT WITH GASTROENTEROLOGY

EUS- GUIDED ETHANOL ABLATION THERAPY



Figure 2 – EUS- guided ethanol ablation therapy: A total of 0.6 ml 95% ethanol was injected in a transgastric approach - ¼ of the round structure changing from hypoechoic to hyperechoic appearance after ethanol injection.

24H POST-PROCEDURE EVALUATION

Amylase	31 U/L(28-100)	24H POST-PROCEDURE	Glucose	80mg/dL
Lipase	3 U/L(<67)	Insulin	7,3 uUI/mL (<30)	
		C-peptide	2,7 ug/mL (1,0-7,6)	

No abdominal pain
 No hypoglycaemic episodes

HOSPITAL DISCHARGE

FOLLOW-UP

1 MONTH

Clinical evaluation

No symptomatic episodes of hypoglycaemia
 No medical therapy with diazoxide

Schedule of laboratorial and imaging reassessment

5 MONTHS

Re-admitted to Endocrinology Department

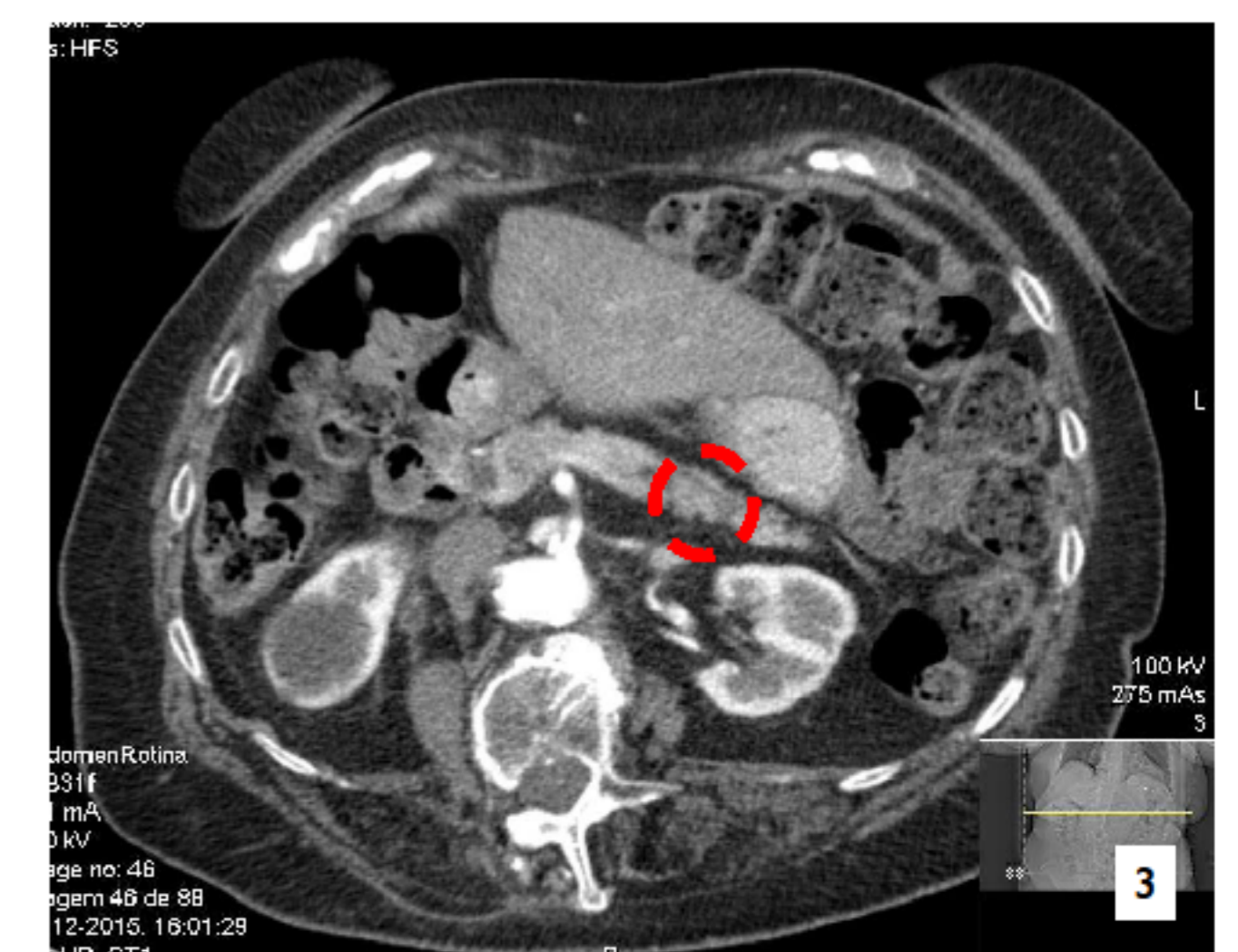
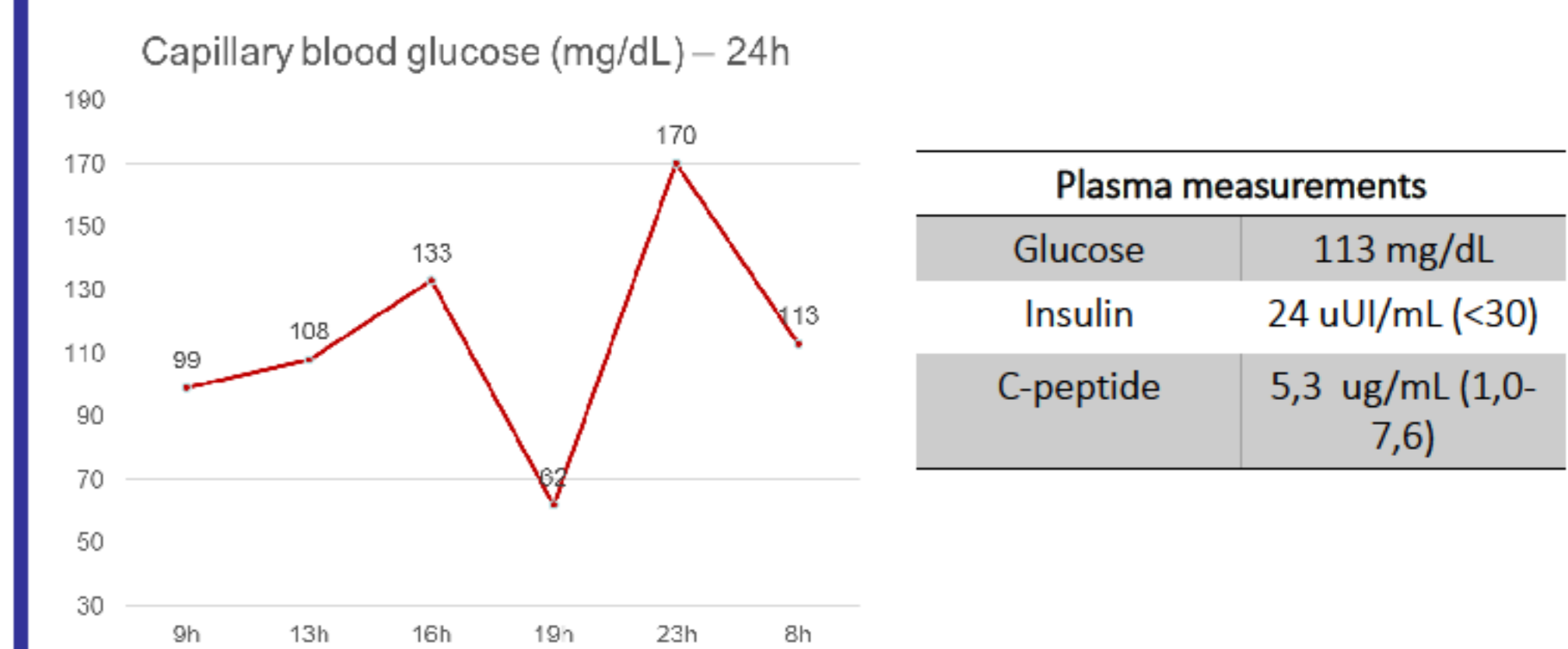


Figure 3 – Abdominal CT scan – "Pancreatic nodular lesion currently with 6mm and less enhancement"

Size evolution: 12mm → 6mm

ENDOCRINOLOGY CONSULTATION

CONCLUSIONS

Ethanol ablation therapy of insulinomas is a minimally invasive alternative treatment with low complication rates although with little clinical experience. In high risk patients, this may be one of the only feasible options with satisfactory clinical results and significant impact on quality of life and survival. There is a possibility to repeat the procedure in patients who maintain symptomatic hypoglycaemic episodes. Prospective, large trials should be performed to better evaluate this technique: its indications and complications before it is recommended for widespread use in clinical practice.

REFERENCES

- Zhang WY et al. Endoscopic ultrasound-guided ethanol ablation therapy for tumors. *World J Gastroenterol* 2013; June 14, 19(22): 3397-3403
- D'Maino CJ, Swartz JM, Bragge WR. Ablation of pancreatic cystic lesions: the use of multiple endoscopic ultrasound-guided ethanol large sessions. *Pancreas* 2011; 40: 664-668
- Jørgensen C, Schuppan D, Nesser F, Ernberger J, Jungheuer U, Stöbel U. EUS-guided alcohol ablation of an insulinoma. *Gastrointest Endosc* 2006; 63: 1058-1062
- Masciello N, Sakurai A, Macari L, Cignarelli M, Principe S, di Maggio M, Castronza M, D'Agnese V, Ierardi E. Treatment of a pancreatic endocrine tumor by ethanol injection guided by endoscopic ultrasound. *Endoscopy* 2008; 40 Suppl 2: E258-E259
- Deprez PH, Claessens A, Borbath I, Giger JF, Maier D. Successful endoscopic ultrasound-guided ethanol ablation of a sporadic insulinoma. *Acta Gastroenterol Belg* 2008; 71: 333-337
- Vaigyan PP, Bhale-Vaite EA, Yalk GD, Legitt RJ, Siemema PD. Endoscopic ultrasound-guided ethanol ablation of a symptomatic sporadic insulinoma. *Endoscopy* 2011; 43 Suppl 2: UC19-E259
- Levy MJ, Thompson GB, Topczian MD, Callstrom MR, Grant CS, Vella A. US-guided ethanol ablation of insulinomas: a new treatment option. *Gastrointest Endosc* 2012; 75: 200-209

