



Videolaparoscopic Resection of Insulinomas: Experience in Two Institutions

Luis Gramática, Jr., M.D.,¹ Miguel F. Herrera, M.D.,² Andrés Mercado-Luna, M.D.,¹ Mauricio Sierra, M.D.,² Guillermo Verasay, M.D.,¹ Noemí Brunner, M.D.³

¹Department of Surgery, Clínica Sucre, Santa Rosa 770, B° Alberdi, Córdoba, Argentina

²Department of Surgery, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Vascode Quiroga 15, Tlalpan 1400, Mexico City, Mexico

³Department of Radiology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Vasco de Quiroga 15, Tlalpan 1400, Mexico City, Mexico

Published Online: September 4, 2002

Abstract. Laparoscopic resection of islet cell tumors has been performed in some selected cases. The aim of the study was to analyze the experience of two institutions in the laparoscopic management of insulinomas. In a 4-year period, videolaparoscopic resection of sporadic insulinomas was performed in 9 patients. All patients had hypoglycemia/hyperinsulinism and a solitary tumor demonstrated by image studies. Demographics, surgical findings, results, and complications were analyzed. Mean age of the patients was 43 years. One patient was male and eight were females. One tumor was located in the head of the pancreas, 4 in the body, and 4 in the tail. Laparoscopic resection was completed in all patients. Procedures included 4 enucleations and 5 distal pancreatectomies. Pancreatic resection with splenic preservation was achieved in 4 cases. Intraoperative ultrasound was used in 7 patients. Mean size of the tumors was 1.6 cm. All patients became normoglycemic after surgery. Complications included one pancreatic fistula, one pleural effusion, and one peripancreatic fluid collection. All resolved spontaneously. In a follow-up period between 3 and 48 months no evidence of recurrence has been observed. This series supports laparoscopic resection of preoperatively localized benign solitary insulinomas. The operation provides the advantages of minimally invasive surgery and can be safely performed in most cases.

Insulinoma is a neoplasm that arises from the pancreatic insulin-producing β cells. It is a rare tumor that occurs in approximately 1 to 6 persons per million of population per year [1]. Like other endocrine neoplasms, insulinomas can be sporadic or be part of the Multiple Endocrine Neoplasm syndrome type 1 (MENs-1).

Once the biochemical diagnosis of an insulinoma is established, surgical exploration is indicated. Surgeons can choose to localize the tumor with image studies before surgery or proceed directly with a pancreatic surgical exploration. Although the risk–benefit analysis of both approaches is still under debate [2, 3], with the current advances in imaging technology, most insulinomas can be accurately localized in the preoperative setting.

Insulinomas can be treated by enucleation or segmental resection of the pancreas. The choice of the surgical strategy depends on the size of the tumor, its relationship with the pancreatic duct, and its location within the pancreatic parenchyma. Considering

the particular characteristics of insulinomas and the fact that they are often located in the body and tail of the pancreas laparoscopic resection has been considered a reasonable alternative. In the last few years, some reports of laparoscopic resection of islet cell tumors have shown the feasibility of the technique, emphasizing the advantages that minimally invasive surgery can offer to these patients [4–7]. The aim of the study was to analyze the experience of two institutions in the laparoscopic management of insulinomas.

Patients and Methods

From 1996 to 2000, all patients with diagnosis of a sporadic insulinoma localized by imaging techniques were considered suitable candidates for laparoscopic exploration in both institutions. The disease was suspected in the presence of neuroglycopenia and sympathetic symptoms related to the autonomic nervous system. Biochemical confirmation was obtained by demonstration of fasting hypoglycemia and hyperinsulinemia and or by a supervised 72-hour fasting test. C peptide was measured when there was uncertainty about the cause of the hypoglycemia. Preoperative localization using several imaging techniques was strongly pursued; the goal was to have two concordant studies in each patient. The initial localizing study was computerized tomography. It was followed by an angiogram with or without Ca stimulation. Endoscopic ultrasound was routinely used in one of the two centers. When patients were referred for surgical treatment after a diagnostic work-up performed elsewhere, the sequence and number of the studies varied.

Surgical Technique

Patients were positioned in a 30-degree to 45-degree right lateral decubitus. To get wide exposure of the pancreas, the gastrocolic ligament was divided, the splenic flexure of the colon was fully mobilized inferiorly, the spleen was retracted superiorly, and the

Table 1. Presentation and localization of insulinomas in the nine patients.

	Patients								
	1	2	3	4	5	6	7	8	9
Age (years)/Gender	25/M	70/F	40/F	36/F	40/F	57/F	42/F	27/F	56/
Hypoglycemia/Hyperinsulinemia	+	+	+	+	+	+	+	+	+
Fasting test	+	Np	Np	+	+	+	+	+	+
C peptide	Nl	Np	↑	↑	Np	↑	↑	Nl	↑
Ultrasound	Np	Np	Np	Np	Np	+	-	-	-
CT	+	+	+	+	-	-	-	+	+
Angiography	+	+	+	+	+	Np	+	+	+
Selective arterial Ca stimulation	Np	+	+	Np	+	Np	+	+	+
Endoscopic ultrasound	Np	Np	+	Np	Np	+	+	+	+
Octeotide scintigraphy	Np	Np	Np	Np	Np	Np	Np	-	-
IOUS	Np	+	+	+	+	Np	+	+	+

Np: not performed; Nl: normal; CT: computed tomography; IOUS: intraoperative ultrasound.

congenital adhesions between the posterior wall of the stomach and the pancreas were divided. Because all tumors had been preoperatively localized, we focused our attention on a specific anatomic region in each case. Laparoscopic ultrasound using an Acuson Aspen or a B-K Medical Ultrasound with a lineal 7.5 MHz transducer was used to identify non-visible lesions on the pancreatic surface and/or to assess the relationship of the tumor with the pancreatic duct. For superficial tumors located close to one of the pancreatic edges, enucleation was the selected technique, and for tumors located deep in the pancreatic parenchyma of the body or tail of the pancreas or for those in close relation to the pancreatic duct, distal pancreatectomy was preferred. When distal pancreatectomy was the chosen technique, special efforts were made to preserve the spleen. Splenic preservation was performed in two different ways. In some patients, splenic vessels were transected at both sides of the selected segment of the pancreas, leaving the short gastric and the inferior phrenic vessels as the main blood supply for the spleen. In the others, the small pancreatic vessels were individually sutured or clipped, detaching the splenic vein and artery from the pancreas. For the division of the major vessels and the pancreatic parenchyma, an endoliner stapler was used in most cases. Enucleation was performed using electrocoagulation and/or a harmonic scalpel. The cut edge of the pancreas was carefully inspected and additional sutures were placed on the main pancreatic duct was individually controlled when appropriate. A peripancreatic close suction drain was used in all patients.

Follow-up

Glucose levels were measured postoperatively up to normalization. Liquids were initiated the day after surgery and progressed to a normal diet according to patient tolerance. Drains were removed in the absence of fluid secretion, and patients were discharged when they were able to tolerate a normal diet. Patients were contacted at the latest follow-up for evaluation of their status.

Analysis

General characteristics, presentation, results of the biochemical diagnosis and imaging studies, surgical details, and outcome were prospectively recorded. Descriptive statistics were used for the final analysis.

Results

A successful videolaparoscopic resection of a sporadic insulinoma was completed in all 9 patients. Mean age was 44 years (range 25 to 70 years). One patient was a man; the rest were women. All patients had symptoms of neuroglycopenia. Fasting hypoglycemia with concomitant hyperinsulinemia was confirmed in all cases. A solitary tumor was demonstrated by at least two imaging studies in each case. The results of the preoperative evaluation studies are summarized in Table 1.

One tumor was located in the pancreatic head, four in the body, and four in the tail. Procedures performed included four enucleations and five distal pancreatectomies. Pancreatic resection with splenic preservation was achieved in four of the five cases. In two, the small pancreatic vessels from and to the splenic main vascular trunks were divided, and in the other two the splenic artery and vein were ligated at both sides of the resected specimen. Intraoperative ultrasound was used in seven patients. In all cases, intraoperative ultrasound aided in tumor localization and it was used to evaluate the relationship between the tumor and the pancreatic duct. Mean operative time was 2 hours for enucleations and 4 hours for pancreatic resections. Median hospital stay was 5 days. Pathology analysis and immunohistochemistry for insulin established the diagnosis of a benign islet cell tumor in all cases. Mean size of the tumors was 1.6 cm (range 1.0 to 3.0 cm).

All patients became normoglycemic immediately after surgery. No mortality was seen in the series. Complications included one pancreatic fistula, one pleural effusion, and one small peripancreatic fluid collection. All complications resolved spontaneously. In a follow-up period that lasted between 3 and 48 months, no evidence of recurrence has been demonstrated. A summary of the size of the tumors, their localization, the type of surgery, and complications is shown in Table 2.

Discussion

In 1993, Pietrabissa and colleagues, from the Ninewells Hospital and Medical School of Scotland, described one of the initial steps in the laparoscopic treatment of islet cell tumors: identification of an occult insulinoma in the body of the pancreas by laparoscopic ultrasonography using a transomental approach [4]. Three years later, the initial reports of laparoscopic enucleation and distal pancreatectomy for the treatment of islet cell tumors began to

Table 2. Surgical details and outcome in the nine patients.

	Patients								
	1	2	3	4	5	6	7	8	9
Size (cm)	1.5	1.1	2.5	2.0	3.0	1,2	1	1	1,2
Localization	Body	Body	Tail	Body	Tail	Head	Body	Tail	Tail
Operation	E	DP + S	DP	DP	E	E	E	DP	DP
Morbidity	–	FC	–	–	PF	–	–	–	Left PE
Cure	+	+	+	+	+	+	+	+	+
Follow-up (months)	36	48	24	3	5	30	21	8	12

E: enucleation; DP: distal pancreatectomy; S: splenectomy; PE: pleural effusion; PF: pancreatic fistula; FC: fluid collection.

appear in the surgical literature [5–7]. Despite the hidden retroperitoneal location of the pancreas, some characteristics of insulinomas make it possible for them to be approached by laparoscopy in an adequate and safe way. Insulinomas are most often benign, with only a 10% malignancy rate. Less than 5% of patients have metastases at initial presentation. A single tumor is responsible for the disease in 90% of all patients. Multiple tumors are almost always related to the MEN-1 syndrome, and the vast majority of sporadic cases present a single lesion. Benign insulinomas are generally small, with approximately 70% of the tumors less than 1.5 cm in size at the time of diagnosis. Although tumors are distributed evenly throughout the pancreas, two-thirds of the lesions occur in the body and tail, which are the pancreatic regions easier to expose by laparoscopy. Additionally, their frequency in regions of difficult access such as the uncinate process is less than 5% [8]. Before laparoscopy, the need of preoperative image localization was debatable. Although some surgeons considered that preoperative localization played a critical role in the surgical treatment of patients with organic hyperinsulinemia, eliminating the need for blind pancreatic resection [2], others authors stated that the majority of these tumors were palpable at the time of pancreatic exploration and proposed the hand of an experienced surgeon as the most valuable localizing tool [3, 9, 10]. Several studies have focused on the value of imaging studies in the localization of insulinomas, and with few discrepancies, it was recognized that ultrasound and computerized tomography (CT) have low sensitivity and specificity [10]. Invasive studies such as angiography, portal venous sampling, and the arterial calcium stimulation test have significantly higher diagnostic accuracy [11, 12]. Endoscopic ultrasonography by an experienced radiologist has a sensitivity that ranges from 70% to 90% [13–15], and a careful surgical exploration assisted by intraoperative ultrasonography should lead to cure in virtually all patients with benign insulinomas [10].

Considering that the current series of patients represents the initial experience in the laparoscopic management of insulinomas in both institutions, we decided to include for laparoscopic resection only lesions identified by two independent imaging studies. In our experience, the most useful studies for the localization of insulinomas were angiography, endoscopic ultrasound, and the calcium stimulation test. Although the sensitivity we obtained with dynamic CT was not very high, we believe it is a useful study to rule out hepatic metastasis.

Despite the fact that not many surgeons have extensive experience in the surgical management of islet cell tumors and that many are not familiar with the use of intraoperative ultrasound, patient concentration in referral centers has made it possible for

some clinicians to acquire significant experience in the management of this disease. The use of the new laparoscopic technology in the management of insulinomas on the other hand has made it necessary to reassess some aspects of treatment that had been already solved using open surgery.

Main components of a surgical exploration in patients with benign insulinomas are (a) wide exposure of the pancreas, (b) careful visual exploration, (c) meticulous palpation, and (d) identification of the relationship between the tumor and the pancreatic duct, usually by ultrasound. Improvements in surgical skill and new technology have made possible the adequate exposure and visual exploration of the pancreas by laparoscopy, but palpation of the gland can only be performed using a hand-assisted technique. Palpation in laparoscopic surgery has been replaced by laparoscopic ultrasound. In 1985, Norton and colleagues reported the first location of an occult insulinoma by intraoperative ultrasound (IOUS) [16]. The reported sensitivity of IOUS in open surgery currently ranges from 75% to 100% [16–18]. Although in a smaller number of patients, similar results have been obtained using laparoscopic ultrasonography [4, 19, 20]. A thorough IOUS exploration can identify tumors immersed in the pancreatic parenchyma that are not visible on the surface and can establish the relationship between the tumor and the pancreatic duct.

Because all tumors had been preoperatively localized in our series, we cannot comment on the value of laparoscopic ultrasound as a localization test, but we found it highly useful in the identification of deep non-visible tumors and in the assessment of their relationship with the pancreatic duct. In theory, familiarization of surgeons with this fairly new tool, may lead to its use as a localizing device in patients with no preoperative tumor identification.

Using open surgery, an overall complication rate of 32% has been reported [2, 21]. The most common complication in the surgical treatment of insulinomas is a pancreatic fistula that usually resolves spontaneously. One of our patients developed a pancreatic fistula, and a small peripancreatic collection was found in one additional patient. The incidence of pancreatic fistulas may be reduced by suture closure of the transected pancreatic duct and application of fibrin glue.

Both operative time and hospital stay were prolonged in this series. This two aspects are strongly affected by the learning curve. In particular, we decided to keep the patients hospitalized long enough to assure complete surgical recovery in the absence of complications or to confirm that each particular complication had been resolved. Advantages and disadvantages of the laparoscopic approach in comparison with conventional surgery cannot be assessed from this perspective. A randomized clinical trial would

be needed to define the actual role of laparoscopy in this setting. This study supports the fact that laparoscopic enucleation and distal pancreatectomy are feasible and safe, and that the conversion rate is very low. We feel that the advantages of laparoscopic surgery that have been persistently shown in other areas—reduction in pain, early recovery and short hospital stay—will also be demonstrated in comparative studies of patients with islet cell tumors. At the same time we recognize that the unusual nature of the disease and the small number of surgeons with the combination of advanced surgical skill and interest in endocrine surgery might limit widespread use of this technique.

Conclusions

Laparoscopic resection of preoperatively localized benign solitary insulinomas is safe and feasible.

Résumé. La résection par laparoscopie des tumeurs des îlots de Langerhans a été réalisée dans quelques cas bien sélectionnés. Le but de cette étude a été d'analyser l'expérience de deux institutions dans la prise en charge laparoscopique des insulinomes. Pendant une période de quatre ans, la résection vidéolaparoscopique des insulinomes sporadiques a été réalisée chez neuf patients. Tous les patients avaient une hypoglycémie combinée à une hypersécrétion insulinaire et une tumeur solitaire démontrée par l'imagerie. Les données démographiques, chirurgicales, les résultats et les complications ont été analysés. L'âge moyen des patients a été de 43 ans. Un patient était masculin alors que huit étaient de sexe féminin. Une tumeur a été localisée dans la tête, quatre dans le corps, et quatre dans la queue du pancréas. La résection laparoscopique a pu être menée à bien dans tous les cas. Les interventions comprenaient quatre énucléations et cinq pancréatectomies distales. La résection pancréatique avec conservation splénique a pu être réalisée dans quatre cas. L'échographie a été utilisée dans sept cas. La taille moyenne des tumeurs a été de 1.6 cm. Tous les patients sont devenus normoglycémiques après chirurgie. Les complications comportaient une fistule pancréatique, une pleurésie, et une collection liquidienne péripancréatique; toutes ces complications se sont résolues spontanément. Pendant le suivi de 3 à 48 mois, on n'a observé aucune récurrence. Cette série est en faveur de la faisabilité de résection par laparoscopie des insulinomes bénins solitaires, localisées en préopératoire. L'intervention comporte les avantages de la chirurgie mini-invasive et peut être réalisée avec sécurité dans la plupart des cas.

Resumen. La resección laparoscópica de tumores insulares ha sido realizada en unos pocos casos seleccionados. El propósito del estudio fue analizar la experiencia de dos instituciones en el manejo laparoscópico de insulinomas. En un periodo de 4 años se efectuó la resección laparoscópica de insulinomas esporádicos en 9 pacientes, todos con hiperinsulinismo hipoglicémico y tumor solitario demostrado por imágenes. Se analizaron los datos demográficos, los hallazgos quirúrgicos, los resultados y las complicaciones. La edad promedio de los pacientes, un hombre y 8 mujeres, fue 43 años. La resección laparoscópica fue exitosamente realizada en todos los casos: 4 enucleaciones y 5 pancreatectomías distales; en 4 se logró la resección pancreática con preservación del bazo. Se utilizó ultrasonido intraoperatorio en 7 pacientes. El tamaño promedio de los tumores fue 1.6 cm. Todos los pacientes retornaron a normoglicemia con la cirugía. Las complicaciones

incluyeron una fístula pancreática, un derrame pleural y una colección líquida peripancreática; todas se resolvieron en forma espontánea. En un seguimiento entre 3 y 48 meses, no se registra recurrencia. Nuestra serie da apoyo al empleo de la técnica laparoscópica para la resección de insulinomas benignos y solitarios cuya localización haya sido determinada preoperatoriamente. La operación ofrece las ventajas de la cirugía mínimamente invasora y puede ser realizada con seguridad en la mayoría de los casos.

References

- Norton JA. Neuroendocrine tumors of the pancreas and duodenum. *Curr. Prob. Surg.* 1994;31:77
- Pasieka JL, McLeod MK, Thompson NW, et al. Surgical approach to insulinomas. *Arch. Surg.* 1992;127:442
- Proye C, Boissel P. Preoperative imaging versus intraoperative localization of tumors in adult surgical patients with hyperinsulinemia: multicenter study of 338 patients. *World J. Surg.* 1988;12:685
- Pietrabissa A, Shimi SM, Vander Velpen G, et al. Localization of insulinoma by laparoscopic infragastric inspection of the pancreas and contact ultrasonography. *Surg. Oncol.* 1993;2:83
- Gagner M, Pomp A, Herrera MF. Early experience with laparoscopic resections of islet cell tumors. *Surgery* 1996;120:1051
- Sussman LA, Christie R, Whittle DE. Laparoscopic excision of distal pancreas including insulinoma. *Aust. N.Z. J. Surg.* 1996;66:414
- Cuschieri A. Laparoscopic pancreatic resections. *Semin. Laparosc. Surg.* 1996;3:15
- Mozell E, Stenzel P, Woltering EA, et al. Functional endocrine tumors of the pancreas: clinical presentation, diagnosis, and treatment. *Curr. Probl. Surg.* 1990;27:301
- Van Heerden JA, Edis AJ, Service FJ. Surgical aspects of insulinomas. *Ann. Surg.* 1979;189:677
- Böttger TC, Junginger T. Is preoperative radiographic localization of islet cell tumors in patients with insulinoma necessary? *World J. Surg.* 1993;17:427
- Doppman JL, Miller DL, Chang R, et al. Intraarterial calcium stimulation test for detection of insulinomas. *World J. Surg.* 1993;17:439
- Doppman JL, Chang R, Fraker DL, et al. Localization of insulinomas to regions of the pancreas by intra-arterial stimulation with calcium. *Ann. Intern. Med.* 1995;123:269
- Thompson NW, Czako PF, Fritts LL, et al. Role of endoscopic ultrasonography in the localization of insulinomas and gastrinomas. *Surgery* 1994;116:1131
- Rosch T, Lightdale CJ, Botet JF, et al. Localization of pancreatic endocrine tumors by endoscopic ultrasonography. *N. Engl. J. Med.* 1992;326:1721
- Chapuis Y, Bigourdan JM, Massault PP, et al. Videolaparoscopic excision of insulinoma. A study of 5 cases. *Chirurgie* 1998;123:461
- Norton JA, Sigel B, Baker AR, et al. Localization of an occult insulinoma by intraoperative ultrasonography. *Surgery* 1985;97:381
- Böttger TC, Junginger T. Is preoperative radiographic localization of islet cell tumors in patients with insulinoma necessary? *World J. Surg.* 1993;17:427
- Zeiger MA, Shawker TH, Norton JA. Use of intraoperative ultrasonography to localize islet cell tumors. *World J. Surg.* 1993;17:448
- Lo CY, Lo CM, Fan ST. Role of laparoscopic ultrasonography in intraoperative localization of pancreatic insulinoma. *Surg. Endosc.* 2000;14:1131
- Berends FJ, Cuesta MA, Kazemier G, et al. Laparoscopic detection and resection of insulinomas. *Surgery* 2000;128:386
- Rothmund M, Angelini L, Brunt LM, et al. Surgery for benign insulinoma: an international review. *World J. Surg.* 1990;14:393