CASE REPORT

Insulinoma: rare yet important

Taha Hasan Al-Saigh

Nineveh Medical College,
Mosul University, Mosul, Iraq

Correspondence to
Dr Taha Hasan Al-Saigh,
taha_alsaiigh@yahoo.com

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SUMMARY

We report our experience with six cases of insulinoma that were managed at our hospital between 2009 and 2013. Four patients were women and two men, with mean age of 43 years and mean duration of symptoms before diagnosis of 5.7 years. Biochemical confirmation was made in all cases and preoperative localisation was successful in two cases only. In the other four, intraoperative localisation was made. Enucleation was performed in four patients and distal pancreatectomy in the other two. The tumour was proved benign in all patients by histopathology. Postoperatively, all patients were asymptomatic during a follow-up period ranging from 9 months to 4 years and both serum glucose and insulin were normal during that period. We think that careful preoperative workup and skilful surgical techniques can end the prolonged suffering of patients with insulinomas with excellent results.

BACKGROUND

Owing to the rare nature of insulinoma, it is of paramount importance to review and understand the clinical features, diagnosis, localisation and management of this tumour.

Insulinoma is the most common neuroendocrine tumour of the pancreas with an annual incidence of 4–10 in every 1 million persons.¹ It can be seen in every age but is mostly seen above 50 years and is more common in women than men.² The majority (90%) of insulinomas are benign and solitary, and only 10% are malignant. Ninety per cent of insulinomas are sporadic, and 10% are associated with the MEN-1 syndrome.³ Insulinomas are evenly distributed throughout the head, body and tail of the pancreas.⁴

The clinical features of insulinoma result from hypoglycaemia and autonomic nervous overactivity, as expressed by fatigue, weakness, hunger, tremor, sweating and tachycardia, or from neuroglycopenia leading to central nervous system (CNS) disturbance with apathy, confusion, excitement, loss of orientation, blurring of vision, delirium, stupor, coma or convulsions. The diagnostic criterion for insulinoma is Whipple triad: symptoms of hypoglycaemia, low blood glucose (40–50 mg/dL) and relief of symptoms after the intravenous administration of glucose.⁵ The pathognomonic finding is an inappropriately high (>5 mU/mL) level of serum insulin during symptomatic hypoglycaemia. If the high insulin level is suspected to be due to exogenous insulin use, C-peptide levels will be helpful in diagnosis. A diagnostic ratio of blood insulin to glucose of greater than 0.4 or C peptide levels higher than 2 nmol/L is helpful in the diagnosis.^{6 7}

The workup for preoperative localisation of insulinomas includes abdominal ultrasound (US), CT, MRI and endoscopic US (EUS) which is regarded currently the test of choice in most Western centres.^{8 9} Transhepatic portal venous sampling and angiography are other invasive tests that are rarely used for localisation.^{10–12}

Treatment of insulinoma is surgical. It can be carried out by either open or laparoscopic approaches. Surgical options include simple enucleation, distal pancreatectomy or pancreaticoduodenectomy.

CASE PRESENTATION

Our patients presented almost similarly with a long-standing history of vague symptoms, including excess sweating, palpitation and tremor. Some of them had CNS symptoms like confusion, behavioural and personality changes and visual disturbances. These symptoms were present for years before diagnosis (mean 5.7 years). We had two patients who were misdiagnosed as psychological cases, and another patient was receiving treatment for epilepsy. None of the patients had a family history of insulinoma or MEN-1, and all patients were overweight with a mean body mass index of 32.

INVESTIGATIONS

During routine laboratory investigations, our patients were found to have low fasting blood glucose, ranging between 2.9 and 4.6 mmol/L, so we requested serum insulin level which was very high, C-peptide levels were checked and all suggested the diagnosis. Preoperative localisation of the tumour was made in two cases only; by MRI in the first case (figure 1) and by EUS (endoscopic ultrasound) in the second one. In the remaining four cases, abdominal US, CT scan, MRI and EUS failed to localise the tumour. MEN-1 syndrome was excluded in all of the patients.

TREATMENT

All of our patients underwent open laparotomies, intraoperative localisation of the mass was easily made in all of them by simply palpating the gland (figure 2), except in one patient with a small tumour (0.8 cm), in whom intraoperative US localised it. Enucleation was carried out in four of the cases and distal pancreatectomy in the other two (figure 3). The tumour was found to be benign in all patients by histopathological examination (figure 4). Postoperatively, none of our patients had complications such as wound infection, leakage or collection. The glucose and insulin levels were normal at the postoperative period and all patients were asymptomatic during a follow-up period

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Figure 1 Preoperative MRI showing an ovoid mass in the neck of the pancreas with low signal intensity in T1-weighted image (upper left) and high signal intensity in: T2-weighted image (upper right) with early enhancement in T1-weighted image following intravenous gadolinium (lower).

ranging from 9 months to 4 years. None of the patients had recurrence of symptoms.

DISCUSSION

Insulinoma is a rare tumour, which makes the diagnosis difficult and usually cases of insulinoma remain undiagnosed for months or even years.

In our series, the mean duration of symptoms prior to diagnosis was 5.7 years. In other studies, it has been documented that the mean duration of symptoms prior to diagnosis ranges from several months to several decades.²⁻⁵ One of the most important causes of delay in the diagnosis is that these symptoms are not unique to insulinoma, that is why a high index of suspicion and a low threshold for confirmatory biochemical tests are mandatory.

In our review, we found a debate about the importance of preoperative localisation of the tumour. Some of the reports state that it is critical to localise the tumour before embarking on the surgery, on the other hand, other authors think that most insulinomas can be identified intraoperatively by an experienced surgeon and that preoperative localisation is not mandatory.^{13 14} From our experience with our patients, we are more inclined to the second opinion since preoperative localisation was possible in two of our patients only, nevertheless, intraoperative localisation was readily made by palpating the gland, except in one case in whom it was localised using intraoperative US, that is why we emphasise here on the role of intraoperative US, since it was the best solution in the only case that was bothersome between our cases. The role of intraoperative US is not only to localise insulinomas but also to have an idea about the relation of the tumour

Figure 2 Operative image showing the insulinoma in the pancreas. The lesser sac through the gastrosplenic ligament has been entered to expose the anterior surface of the pancreas. A Kocher manoeuvre has been performed to mobilise the duodenum and head of the pancreas to facilitate bimanual palpation of the head of the pancreas.

Figure 3 Operative image showing distal pancreatectomy being performed for an insulinoma in the body of the pancreas.

Figure 4 Pathological section with H&E staining (H&E, $\times 100$ on the left and H&E, $\times 400$ on the right) showing tubular and trabecular architecture. The cells have uniform round to oval nuclei with finely stippled and evenly distributed granular chromatin. Immunostaining for insulin was performed later on and was strongly positive.

to the pancreatic duct which of course will affect the options for the surgery.^{7 10 15 16}

Surgical resection is the treatment of choice for insulinomas. During the operation the entire abdomen must be explored, liver metastases should be excluded. The pancreas should be mobilised by dividing the gastrocolic ligament entering the lesser sac and the second part of the duodenum should be mobilised too (Kocher manoeuvre). The head of the pancreas should be palpated carefully and examined anteriorly and posteriorly; the body and tail of the pancreas should also be checked. After localising the tumour and excluding any features of metastases, enucleation is the best option since more than 90% of these tumours are benign and solitary; this option is justified since it preserves exocrine and endocrine functions of the gland. We were able to perform enucleation in four of our cases for tumours ranging between 0.8 and 2.2 cm and in all parts of the gland including the head in one case. In the other two cases, enucleation was not possible due to a close relation to the main pancreatic duct in one case and because the tumour was located deeply within the gland in the other case (which was located by intraoperative US), and since both tumours were located in the distal part of the body, distal pancreatectomy was performed in order to remove the tumour safely without the risk of pancreatic duct injury with resultant post operative leakage or fistula formation. It has been documented that partial pancreatectomy and pancreaticoduodenectomy are other options for neuro endocrine tumours when enucleation is not possible. In all cases blind pancreatic resection is not recommended.^{17 18}

We found few published articles regarding the applicability of laparoscopy to endocrine pancreatic tumours, especially insulinomas. Laparoscopy is especially useful for small solitary benign islet tumours in the body and tail.^{19–25} One critical point is that preoperative localisation is especially important if the surgeon prefers to use laparoscopic surgery. Four of our patients underwent the surgery without preoperative localisation of the tumour, and since the gland cannot be palpated during laparoscopy, it was not feasible for us to choose the laparoscopic approach especially in the absence of laparoscopic intraoperative ultrasonography. Unfortunately, the two patients in our series in whom preoperative localisation of the tumour was made were

poor candidates for laparoscopic approach because of previous abdominal surgeries.

The surgical cure rate in our series was 100%, that is the glucose and insulin levels were normal and all patients were asymptomatic during the follow-up period ranging from 9 months to 4 years. None of the patients had recurrence of symptoms, and all of the cases were benign solitary lesions. None of our patients developed complications like wound infection, pancreatic leakage, fistula or collection.

Learning points

- ▶ Owing to the rare nature of insulinoma, it is of paramount importance to review and understand the clinical features, diagnosis, localisation and management of this tumour.
- ▶ A high index of suspicion and a low threshold for confirmatory biochemical tests are mandatory because the clinical features are misleading and not unique.
- ▶ The preoperative localisation of insulinoma is critical; yet a good surgical experience in conjunction with intraoperative ultrasound can localise insulinomas in almost all cases.
- ▶ Surgery is the mainstay for treatment and offers the only hope for cure and a normal life span.

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REFERENCES

- 1 Moss NH, Rhoads JE. Hyperinsulinism and islet cell tumours of the pancreas. In: Howard JM, Jordon GL Jr, eds. *Surgical diseases of the pancreas*. Philadelphia: JB Lippincott, 1960:321–70.
- 2 Brentjens R, Saltz L. Islet cell tumors of the pancreas. *Surg Clin North Am* 2001;82:527–42.

- 3 Mukai K, Greider MH, Grottin JC. Pancreatic endocrine tumors. *Pathol Res Pract* 1988;183:155–68.
- 4 Howard TJ, Stabile BE, Zinner MJ, *et al.* Anatomic distribution of pancreatic endocrine tumors. *Am J Surg* 1990;159:258.
- 5 Whipple AO, Frantz VK. Adenoma of islet cells with hyperinsulinism: a review. *Ann Surg* 1935;101:1299–335.
- 6 Virally ML, Guillausseau PJ. Hypoglycaemia in adults. *Diabetes Metab* 1999;25:477–90.
- 7 Doherty GM, Doppman JL, Shawker TH, *et al.* Results of a prospective strategy to diagnose, localize, and resect insulinomas. *Surgery* 1991;110:989–97.
- 8 Sotoudehmanesh R, Hedayat A, Shirazian N, *et al.* Endoscopic ultrasonography (EUS) in the localization of insulinoma. *Endocrine* 2007;31:238–41.
- 9 Richards ML, Gauger PG, Thompson NW, *et al.* Pitfalls in the surgical treatment of insulinoma. *Surgery* 2002;132:1040, discussion 1049.
- 10 Abboud B, Boujaoude J. Occult sporadic insulinoma: localization and surgical strategy. *World J Gastroenterol* 2008;14:657–65.
- 11 Boukhman MP, Karam JH, Shaver J, *et al.* Insulinoma—experience from 1950 to 1995. *West J Med* 1998;169:98–104.
- 12 Goh BK, Ooi LL, Cheow PC, *et al.* Accurate preoperative localization of insulinomas avoids the need for blind resection and reoperation: analysis of a single institution experience with 17 surgically treated tumors over 19 years. *J Gastrointest Surg* 2009;13:1071–7.
- 13 Hashimoto LA, Walsh RM. Preoperative localization of insulinomas is not necessary. *J Am Coll Surg* 1999;189:368–73.
- 14 Daggett PR, Goodburn EA, Kurtz AB, *et al.* Is preoperative localisation of insulinomas necessary? *Lancet* 1981;1:483–6.
- 15 Grover AC, Skarulis M, Alexander HR, *et al.* A prospective evaluation of laparoscopic exploration with intraoperative ultrasound as a technique for localizing sporadic insulinomas. *Surgery* 2005;138:1003–8.
- 16 Grant CS, van Heerden J, Charboneau JW, *et al.* Reading CC. Insulinoma: the value of intraoperative ultrasonography. *Arch Surg* 1988;123:843–8.
- 17 Nikfarjam M, Warshaw AL, Axelrod L, *et al.* Improved contemporary surgical management of insulinomas. *Ann Surg* 2008;247:165–72.
- 18 Stefanini P, Carboni M, Patrassi N, *et al.* β -islet cell tumors of the pancreas: results of a study on 1,067 cases. *Surgery* 1974;75:597–609.
- 19 Stabile BE, Morrow DJ, Passaro E Jr. The gastrinoma triangle: Operative implications. *Am J Surg* 1984;147:25–31.
- 20 Sweet MP, Izumisato Y, Way LW, *et al.* Laparoscopic enucleation of insulinomas. *Arch Surg* 2007;142:1202–4.
- 21 Arbuckle JD, Kekis PB, Lim A, *et al.* Laparoscopic management of insulinomas. *Br J Surg* 2009;96:185–90.
- 22 Berends FJ, Cuesta MA, Kazemier G, *et al.* Laparoscopic detection and resection of insulinomas. *Surgery* 2000;128:386–91.
- 23 Lo CY, Chan WF, Lo CM, *et al.* Surgical treatment of pancreatic insulinomas in the era of laparoscopy. *Surg Endosc* 2004;18:297–302.
- 24 Jaroszewski DE, Schlinkert RT, Thompson GB, *et al.* Laparoscopic localization and resection of insulinomas. *Arch Surg* 2004;139:270–4.
- 25 Gagner M, Pomp A, Herrera MF. Early experience with laparoscopic resections of islet cell Tumors. *Surgery* 1996;120:1051–4.

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