

ISLET TUMORS — SURGICAL TREATMENT

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SUMMARY

Three patients with insulinoma have been presented. Accurate diagnosis, localization, and multiplicity are possible employing angiography, sonography, CAT, and insulin concentration determinations of specimens obtained by percutaneous, transhepatic simultaneous sampling of the portal, splenic and superior mesenteric veins. Meticulous exploration of the gland will permit enucleation rather than major resection to be a feasible solution and the operation of choice.

RESUMO

Tumores Insulares — Tratamento cirúrgico

Os autores apresentam três casos de insulinoma. O diagnóstico da situação clínica, a localização do tumor e a avaliação da sua eventual multiplicidade são possíveis mediante a utilização da angiografia, da sonografia, do TAC e da determinação das concentrações de insulina no sangue obtido por colheita simultânea nas veias porta, esplênica e mesentérica superior, por punção percutânea transhepática. A exploração meticulosa intraoperatória da glândula permite a enucleação do tumor, que constitui uma técnica exequível e de eleição, em vez da ressecção alargada.

INTRODUCTION

The diagnosis of hyperinsulinism may first be suspected by the demonstration of Whipple's triad (symptoms of hypoglycemia associated with low serum glucose and response to exogenous glucose). There are many non-beta-cell causes of organic fasting hypoglycemia in adults, including hepatic disorders, enzyme defects, counterregulatory defects (Addison's disease, hypopituitarism, glucagon deficiency), nonbeta-cell tumors (fibrosarcoma, leiomyosarcoma, mesothelima, etc.), etc. The most practical, safest, and most reliable test to differentiate insulinoma from other causes of hypoglycemia is the demonstration of inappropriately high serum insulin and synchronously low serum glucose levels after a prolonged fast.¹

Further confirmation of the diagnosis may be obtained by demonstrating an exaggerated response to secretagogues of insulin, such as tolbutamide or leucine. However, patients must be monitored very carefully during these tests since they can provoke sudden and severe hypoglycemic crisis. Furthermore, the tolbutamide test has been reported to have a 20 to 50% incidence of false negatives.²

Once the diagnosis of insulinoma has been established, an attempt should be made to localize the tumor within the pancreas prior to surgery. Celiac and superior mesenteric

arteriography should be performed routinely. When positive, the arteriogram serves an extremely useful purpose, following the surgeon to focus attention on the particular area of the gland where the tumor appeared on the arteriogram. However, arteriography is only positive in 40 to 60% of cases, and false positives have also been reported.³

Whether or not a tumor has been localized pre-operatively, the entire pancreas must be inspected carefully at the time of surgery since there is an 8% incidence of multiple tumors. A bi-lateral sub-costal incision is excellent for exploration. The lesser sac is entered by dividing the gastro-colic omentum. After mobilizing the splenic flexure of the colon downward and dividing the short gastric vessels, the stomach can be reflected superiorly and the body and tail of the gland carefully palpated. By mobilizing the hepatic flexure downward and performing a Kocher maneuver, the duodenum may be reflected medially and the head of the pancreas palpated. When a tumor is found, it can usually be enucleated without much difficulty. Tumors of the head and uncinat process can nearly always be enucleated or locally excised with reapproximation of normal pancreas and control of hemorrhage using non-absorbable sutures. Pancreatico-duodenectomy (Whipple operation) could never be necessary. Tumors of the body and tail of the gland, when they cannot be enucleated or easily excised, should be trea-

ted by distal resection, a procedure normally associated with a relatively low morbidity and mortality.⁴

In those cases where pre-operative localization has been unsuccessful and no tumor can be palpated at surgery after thorough exploration, there appears to be some controversy regarding the best surgical approach. Many surgeons agree that after meticulous exploration of the head and uncinate process the procedure of choice is distal sub-total pancreatectomy. The rationale for this approach dates back to Whipple's early reports that most tumors are located in the tail of the pancreas. However, Crain has reported that adenomas are evenly distributed throughout the gland.⁵ Mengoli and LeQuerne reviewed 50 case of *blind* distal resections and found that in only 11 patients was a tumor found in the resected specimen.⁶ Fonkalsrud, believing that most occult tumors are located in the head of the pancreas, has advocated blind pancreatico-duodenectomy.¹ Another alternative which has been suggested in patients where no tumor is palpable at the time of surgery, is to simply close the abdomen and control the hypoglycemia using diazoxide and diet. Then, after six months, angiography can be repeated to determine if the tumor has become angiographically visible.

Let us briefly review some cases which illustrate diagnostic procedure and surgical approach:

CASE 1

Mr. F.A. (Case 1), a 64-year-old white male, was admitted to the hospital because of confusion, disorientation, and *blackout* spells since the age of 16. The patient had been diagnosed as an epileptic and treated with dilantin. Physical examination and routine laboratory data were not remarkable.

In the hospital, the patient had an «attack» of confusion and slurred speech. Blood drawn during this attack showed the glucose to be 30 mg %. On a prolonged fast, after 12 hours, he became agitated and disoriented. Blood glucose at this time was found to be 28 mg %. The patient was given 20 mg of glucose intravenously and within five minutes was completely oriented and feeling well.

A tolbutamide test confirmed the diagnosis of insulinoma (Table 1). At operation a small Module was located in the uncinate process of the pancreas (Figure 1). The Module was enucleated by blunt and sharp dissection. Blood sugar and carbohydrate tolerance returned to normal, confusion and attacks ceased.

TABLE 1 Positive Tolbutamide Test Case #1

| Time | Blood Sugar % | Symptoms |
|---------|---------------|-----------------|
| Fasting | 28 mg | |
| 15 min. | 28 mg | |
| 30 min. | 20 mg | Became confused |
| 45 min. | 20 mg | Passed out |

CASE 2

Mr. A.G. (Case 2), a 42-year-old Indian male, was admitted to the Mount Sinai Hospital for hypoglycemic attacks. The patient was in good health until three years prior to admission when he began to have episodes of stammering, diaphoresis, and dizziness. These episodes would typi-

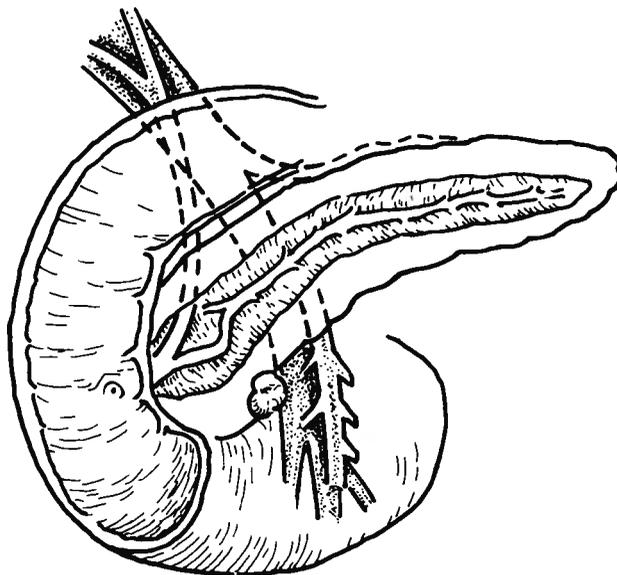


Figura 1

cally occur in the morning and would be relieved by intake of food. During one attack, the blood glucose was 42 mg %.

Physical examination and laboratory investigation including liver function were normal. The patient was stressed by a prolonged fast with serial glucose and insulin determinations made hourly (Table 2). A 2 hour glucose tolerance and tolbutamide test were also abnormal (Table 3,4).

Localization of the insulinoma by celiac and mesenteric arteriography as well was unseccessful. The patient then underwent trans-hepatic catheterization of the portal superior mesenteric and splenic veins. Samples were aspirated from different sites and sent for determination of insulin concentration. The insulin concentrations indicated a tumor in the head of the pancreas (Table 5).

After complete mobilization of the pancreas, initial palpation revealed no tumor. Persistent exploration of the head, where in the tumor was predicted finally resulted in localization of the insulinoma (Figure 2). The body and tail of the gland were resected. The tumor was enucleated from the head.

TABLE 2 Blood sugar and serum insulin determinations after a prolonged fast (case #2).

| Time | Serum Glucose % | Insulin (µU/ml) |
|---------|-----------------|-----------------|
| 0 | 57 mg | 41 |
| 1 hr. | 57 mg | 41 |
| 2 hrs. | 54 mg | 36 |
| 3 hrs. | 59 mg | 44 |
| 4 hrs. | 61 mg | 39 |
| 5 hrs. | 62 mg | 36 |
| 6 hrs. | 52 mg | 26 |
| 7 hrs. | 45 mg | 28 |
| 8 hrs. | 40 mg | 24 |
| 9 hrs. | 37 mg | 50 |
| 10 hrs. | 31 mg | 33 |
| 11 hrs. | 32 mg | 50 |

TABLE 3 Two hour glucose tolerance test (case # 2).

| Time | Serum Glucose % | Insulin (μ U/ml) |
|---------|-----------------|-----------------------|
| Fasting | 46 mg | 25 |
| 30 min. | 98 mg | 49 |
| 1 hr. | 103 mg | 33 |
| 1 ½ hr. | 126 mg | 13 |
| 2 hrs. | 70 mg | 20 |

TABLE 4 Tolbutamide tolerance test (case # 2).

| Time | Serum Glucose % | Insulin (μ U/ml) |
|----------|-----------------|-----------------------|
| Fasting | 44 mg | 43 |
| 5 min. | | 139 |
| 10 min. | | 217 |
| 15 min. | | >100 |
| 30 min. | | 196 |
| 45 min. | | 157 |
| 1 hr. | 26 mg | 129 |
| 1 ½ hrs. | 36 mg | 99 |
| 2 hrs. | 42 mg | 76 |

TABLE 5 High insulin concentrations in the portal but not splenic or superior mesenteric vein indicate a tumor of the head of the pancreas.

| Location | Insulin (μ U/ml) |
|------------------------|-----------------------|
| Portal v. | 290 |
| Splenic | 24 |
| Superior Mesenteric v. | 28 |

Serum glucose levels had been monitored throughout the operation in the unfulfilled expectation that massaging the gland at different sites would reveal its location by a sudden elevation of blood glucose. After removal of the tumor, the serum glucose was found to be 260 mg %, compared with a pre-operative serum glucose of 82 mg %. Histopathologic examination of the tumor demonstrated it to be an islet cell adenoma.

The patient had an uneventful post-operative course, and was discharged on the 15th post-op day. Blood sugars at the time of discharge ranged between 100 to 150 mg % without exogenous insulin.

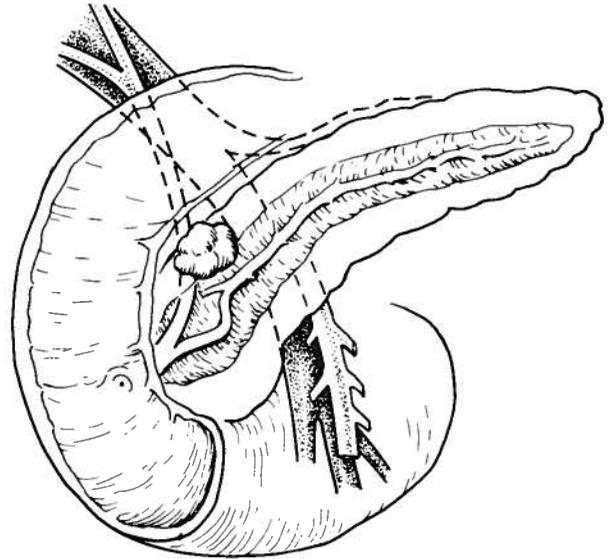


Figura 2

CASE 3

Mrs. A.V. (Case 3), was referred to Mount Sinai from Lisbon, Portugal. She had been well until 2 years prior to admission when she noted increasing periods of dizziness and disorientation. Her symptoms were most marked in the mornings upon arising and relieved by eating. Indeed the patient gradually gained 40 lbs. having noted that her complaints responded to chocolate.

The fasting blood sugar was 22 mg %. Glucose tolerance and prolonged fasting yielded are given in Tables 6 and 7. The x-ray revealed an area of staining at the upper border of the body of the pancreas just to the left of the spine. A small vessel branching from the splenic artery fed the stained area.

At operation a small nodule was immediately apparent at the site predicted by angiography. The tumor was easily enucleated without mobilization of the gland (Figure 3).

Hemostasis was obtained with a few silk sutures. The postoperative course was complicated by the development of a transient pancreatic fistula which ceased spontaneously within a month. Fasting blood sugars and glucose tolerance reverted to normal. All symptoms subsided and the patient rapidly lost 35 lbs. returning to normal weight and normal activity.

TABLE 6 Glucose tolerance test (Case # 3).

| Time (hrs) | Serum Glucose (mg) |
|------------|--------------------|
| Fasting | 60 mg |
| 30 min. | 88 mg |
| 1 hrs. | 110 mg |
| 1 ½ hrs. | 116 mg |
| 2 hrs. | 74 mg |
| 3 hrs. | 50 mg |

TABLE 7 Serum glucose levels following prolonged fast (Case # 3).

| Time | Serum Glucose % | Symptoms |
|---------|--------------------|----------|
| 0 | 64 mg | |
| 1 hr. | 60 mg | |
| 2 hrs. | 62 mg | |
| 3 hrs. | 57 mg | |
| 4 hrs. | 52 mg | |
| 6 hrs. | 52 mg | |
| 7 hrs. | 49 mg | headlock |
| 8 hrs. | 42 mg | dizzy |
| 9 hrs. | 39 mg | |
| 10 hrs. | 37 mg | |
| 12 hrs. | 30 mg | confused |

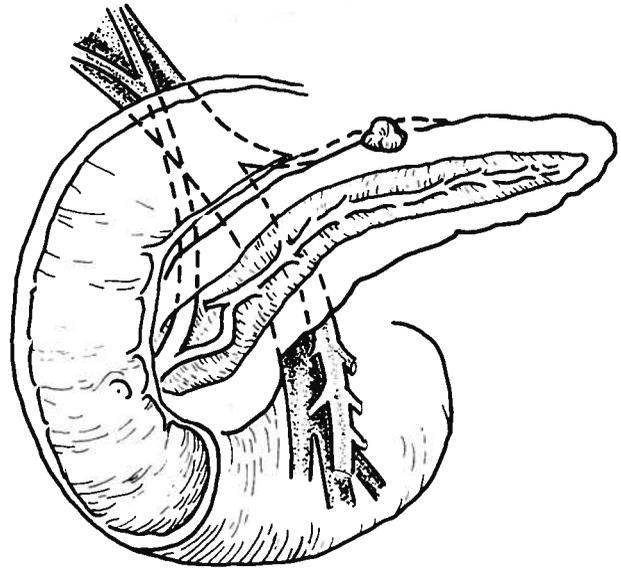


Figura 3

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