Case Report

Localization of Occult Insulinoma by Super-Selective Pancreatic Venous Sampling for Insulin Assay through Percutaneous Transhepatic Catheterization

VICTOR G. MILLAN, CLAUDIO L. UROSA, MARK E. MOLITCH, HARRY MILLER, AND IVOR M. D. JACKSON

SUMMARY

Preoperative localization of insulinomas by arteriography is successful only 66% of the time. With small tumors, intraoperative localization is usually unsuccessful also. Because surgical morbidity and mortality are increased greatly when major, blind, pancreatic resections or reoperations are performed, additional preoperative localization procedures are needed. We now report the successful localization of an occult insulinoma by means of blood sampling for insulin radioimmunoassay, obtained by selective pancreatic vein sampling through percutaneous transhepatic catheterization.

Our patient had symptoms of fasting hypoglycemia for 11 months. Routine studies were normal and two fasting plasma glucose concentrations were 34 and 16 mg/dl to correspond with insulin values of 33 and 75 μU/ml. Celiac arteriography was normal. Percutaneous transhepatic portal and pancreatic venous catheterization revealed insulin concentrations (μU/ml) of between 23 and 36 in portal and splenic veins, 17 in the short, gastric vein, 17 in the dorsal pancreatic vein, 19 in the superior, mesenteric vein, and 61 and 288 in two pancreatic magna veins draining the tail. An insulinoma of 2 × 3 cm was resected from the tail.

On the basis of our experience with this patient, it is clear that selective venous sampling may facilitate the localization of occult insulinomas at surgery and thereby avoid extensive, blind, pancreatic resections and the need for reoperation. DIABETES 28:249–251, March 1979.

A variety of diagnostic tests have been devised to establish the clinical diagnosis of insulinoma in a patient. However, once this diagnosis is established, the insulinoma may be difficult to localize even using selective arteriography. On the average, only two thirds of the insulinomas can be localized by this method.[2] In a review of 1067 patients, Stefanini et al.[2] have shown that surgical morbidity and mortality are increased greatly when major, blind, pancreatic resections for such occult insulinomas are carried out, and the risk increases further should reoperation be necessary. Recently, Ingemansson et al.[3] demonstrated the feasibility of splenic and portal vein sampling for insulin by use of a transhepatic approach for entry into the portal system. A "step-up" of the assays for insulin was found in the area of a 4 × 5 cm insulinoma. This technique appears to be useful in the preoperative localization of occult islet cell tumors. We recently employed this approach successfully by use of super-selective sampling from the pancreatic veins for insulin in a patient with an insulinoma not visualized on arteriography.

CASE REPORT

A 32-year-old Chinese woman was admitted for the evaluation of morning dizziness, mental confusion, and weakness of 11 months' duration. Repeated fasting plasma glucoses, done before admission, were 45 mg/dl, 16 mg/dl, 35 mg/dl, and 15 mg/dl. She had a past history of Graves's disease, which was in remission at the time of admission. Physical examination on admission was normal except for a diffusely enlarged thyroid gland. No abdominal masses were palpated. Routine laboratory data showed normal liver, kidney, and thyroid function tests. Fasting plasma glucose concentrations with the corresponding simultaneous insulin levels by radioimmunoassay* were as follows: glucose 34 mg/dl—insulin 33 μU/ml; glucose 16 mg/dl—insulin 75 μU/ml. The normal fasting levels of insulin are between 5 and 25 μU/ml.

There was no clinical or laboratory evidence of liver disease or of malignancy. A liver-spleen scan was normal. Selective pancreatic arteriography was interpreted as not showing an insulinoma.

Percutaneous transhepatic portography and super-selective pancreatic vein catheterization for venography and blood sampling for insulin assays from the major pancreatic veins were performed. As shown in Figure 1 there were significantly higher insulin levels

A preliminary report of this work has been published in abstract form.[1]

From the Cardiovascular Radiology Service, Department of Radiology; Division of Endocrinology, Department of Medicine; and Division of Surgical Oncology, Department of Surgery; Tufts University School of Medicine, New England Medical Center, Boston, Massachusetts.

Address reprint requests to Mark E. Molitch, M.D., Endocrinology Division, New England Medical Center Hospital, 171 Harrison Ave., Boston, Mass. 02111.

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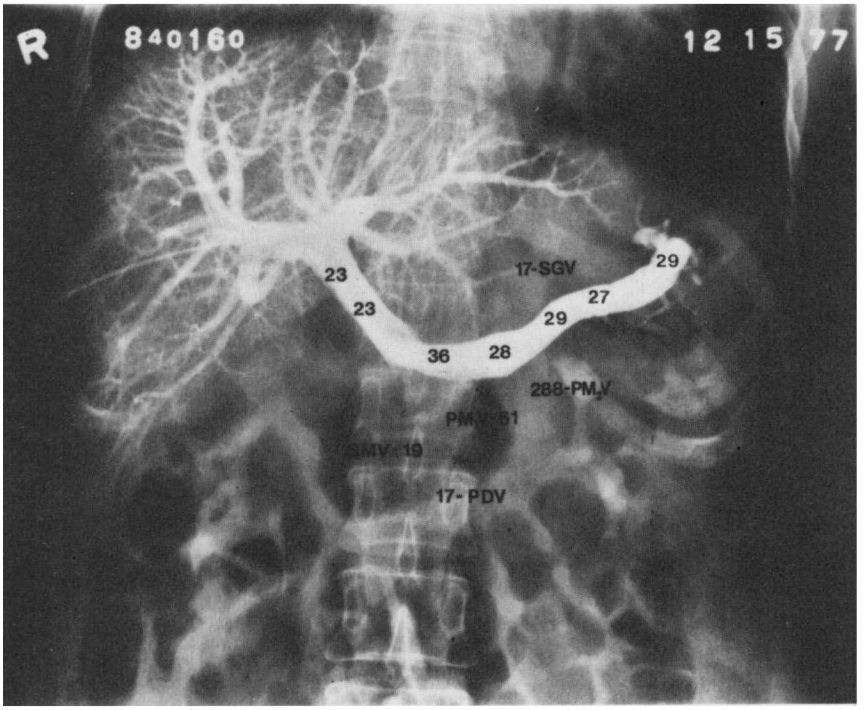

FIGURE 1. An angiogram of the portal and splenic veins. Insulin values (in μU/ml) are superimposed on the sampling locations. Note the "step-up" in the pancreatica magna veins. [Abbreviations: SGV—short gastric vein, SMV—superior mesenteric vein, PDV—inferior pancreaticoduodenal vein, PM_1V—pancreatica magna vein (no. 1), PM_2V—pancreatica magna vein (no. 2).]

on sampling of the pancreatica magna veins in the tail of the pancreas. Selective sampling from the intrinsic pancreatic veins was needed to localize the tumor since insulin levels in the splenic and portal veins showed no gradient.

The patient underwent pancreatic exploration, which showed a mass measuring 2.5 by 2.5 cm in the tail of the pancreas. Splenectomy and distal resection of the pancreas were performed. Pathologic examination revealed an islet, beta cell tumor that was encapsulated and showed no vascular invasion or other evidence of malignancy. During operation the patient was maintained initially at elevated levels of blood glucose by intravenous glucose administration. After pancreatic resection she received no glucose for the next 48 h. The blood glucose returned to normal during operation, and after operation she had a mild, transient hyperglycemia without glycosuria that required no treatment. The patient remained asymptomatic after discharge. On reevaluation of the arteriogram after surgery it is likely that what was interpreted as a splenic cyst, deriving all of its blood supply from intrasplenic branches, was the insulinoma.

DISCUSSION

With the ready availability of the insulin radioimmunoassay, beta islet cell neoplasms can now be diagnosed with increased accuracy. Inappropriately elevated insulin levels in the face of abnormally low blood glucose levels is considered to be diagnostic for an insulin-secreting tumor.

Selective pancreatic arteriography is a useful procedure for the localization of these tumors, but the reported success in demonstrating the tumor varies from 20 to 86%.[2] Of the 1012 cases of insulinoma reviewed by Stefanini et al.[2] that were operated, only 772 (76.3%) were found on first operation, 111 (11%) on second, and 58 (5.7%) were found on subsequent operations, and 71 (7%) were never found. In this series, a variety of procedures were performed including enucleation, distal resection, subtotal resection, pancreatoduodenectomy, and total pancreatectomy. The larger procedures were performed more frequently on reintervention.

The strikingly high (three to five times) morbidity and mortality associated with extensive surgical procedures and reoperation when the tumor is not found initially emphasize the importance of preoperative localization of an insulinoma. It appears that the technique of selective venous sampling first used by Ingemansson et al.,[3] showing an insulin gradient in a patient with a radiographically demonstrable insulinoma, can be used successfully in localizing an occult insulinoma as shown in our patient. With occult tumors it is probably necessary, as it was in our patient, to catheterize the major pancreatic veins super-selectively to demonstrate the site of the augmented insulin secretion within the pancreas, because the larger blood flows of the splenic and portal veins may obscure a small gradient of assayed insulin values. Turner et al.[4] demonstrated gradients within the portal and splenic veins in seven patients with arteriographically demonstrable tumors using intraoperative (in six) and percutaneous transhepatic (in one) venous sampling for insulin and, in one patient with an occult insulinoma, using a percutaneous transhepatic approach. In one of these patients, portal and splenic sampling did not demonstrate a gradient, and a second catheterization with selective pancreatic vein sampling was needed to demonstrate an insulin gradient with localization of the tumor.

The technique of transhepatic portography consists of inserting a needle-catheter-guidewire combination into an intrahepatic portal vein branch from a percutaneous puncture in the right midaxillary line at the level of the porta hepatis (usually T12). After the portal vein is so catheterized, any of the small pancreatic veins or other branches of the portal system can be sampled selectively by angiographic manipulation. In the past this technique has been used primarily in patients with hepatic cirrhosis and a variety of other liver diseases, who often had varying degrees of portal hypertension. In such patients, intraperitoneal hemorrhage and bile leak, symptomatic portal vein thrombosis, pneumo-

thorax and pleural effusions, hemobilia, accidental puncture of the colon and renal failure secondary to contrast media injection have occurred uncommonly. In the series of nine patients in the literature with hormone-secreting islet cell tumors who have undergone transhepatic selective portal vein catheterization and sampling in this fashion, no complications have occurred.[4–7] Overall the procedure appears to have quite a low morbidity, especially in patients without a significant degree of cirrhosis.

Utilization of the technique of transhepatic selective pancreatic venous catheterization for venous sampling for insulin assay in patients with insulinomas not localizable preoperatively by arteriography should eliminate much of the uncertainty associated with the surgical management of these tumors. Ingemansson and associates have extended this technique to patients with gastrin-producing[5] and glucagon-producing[6] islet cell tumors as well as to patients with a restricted, insulin-secreting islet cell hyperplasia,[7] with successful localization in these circumstances. We hope that use of this technique will contribute to the reduction of morbidity and mortality and simplify the operative procedures in the management of functioning islet cell abnormalities.

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