Case Report

NON INSULINOMA PANCREATOGENOUS HYPOGLYCEMIA

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ABSTRACT:
A middle age Saudi male patient presented with attacks of hypoglycemia for almost three years. Insulin and c- peptide levels were high with attacks of hypoglycemia. All investigations to localize the source of the insulin were normal which include CT scan and MRI of the abdomen and celiac angiography. Glucose tolerance test was normal. Selective catheterization of all arteries was done which supply the pancrease and injection calcium chloride was injected in each artery alone, and simultaneous samples from the portal vein were collected. The result revealed high insulin and c-peptide from gastro pancreatic artery which supply the head of the pancrease. The decision was made to resect the head of the pancrease. There was no tumor found on intraoperative examination. The surgery was uneventful and there was no hypoglycemia up to 3 weeks after surgery with normal insulin and c- peptide levels. The pathology of the resected part of the pancrease showed hyperplasia and no insulinoma.

KEY WORDS: Hypoglycemia, Non Insulinoma, Pancreatic hypoglycemia.

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INTRODUCTION

Hypoglycemia is an uncommon clinical problem in patients not being treated for diabetes. A prolonged supervised fast, which can be for as long as 72 hours, is the oldest, best established and probably most reliable test for the evaluation of hypoglycemic disorder. However this test is expensive and should be reserved for those patients in whom a reasonable diagnosis can not be made by other mean. Pancreatogenous hypoglycemia is diagnosed by high c- peptide and insulin with attacks of hypoglycemia.[1] The pancreato-genous hypoglycemia is usually caused by insulinoma. Over the past several years many patients were found to have hyperinsulinemic hypoglycemia with unusual clinical, diagnostic, surgical, and pathologic feature. Those patients were called Non Insulinoma Pancreatogenous Hypoglycemia Syndrome (NIPHS).[2] We are reporting a similar case who was suffering from reactive hypoglycemia for the last three years. The insulin and c- peptide were high with attacks of hypoglycemia but no tumor was localized by homographic CT scan and magnetic resonance image of the pancrease, or celiac angiography. Selective arterial stimulation test by calcium was done which showed insulin was high in gasteropancreatic artery. The head of the pancrease was resected and histopathology showed hyperplasia (nesidioblastosis) no tumor was found. Subsequently the patient improved and was followed up for almost 3 months after surgery. No hypoglycemia symptoms were encountered and insulin level was normal.

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CASE REPORT

Fifty two years old Saudi male patient was complaining of attacks of dizziness, sweating, and palpitation. Those symptoms used to occurs mainly 3 to 4 hours after eating but rarely occured during fasting. His symptoms resolved by ingestion of sugar. He was admitted in different hospitals because of same complaints, and was diagnosed to have hypoglycemia with high insulin level, but was not not investigated fully. He was not known diabetic or hypertensive. Systemic review was unremarkable. Examination revealed normal vital signs. Cardiovascular, chest, abdomen, and neurological examination were normal. Complete blood count, electrolytes, urea creatinine were also normal. Cortisol level and thyroid function tests were normal. Insulin level and c – peptide were high with attacks of hypoglycemia. (Table-I). The radiological investigations to localize the source of high insulin were all normal (Table- I). Pancreatic arterial stimulation test was done for the first time in our hospital. The procedure was performed in the radiological department after over night fasting and signing the consent Form by the patient. The risk and benefit of the procedure was explained very well to the patient. The catheterization of all arterial blood supply of the pancrease was done first followed by catheterization of hepatic portal vein. Blood samples for insulin and c-peptide levels were taken from each artery separately and calcium gluconate was injected directly to each artery. Blood sample for insulin and c-peptide levels from the portal vein were obtained simultaneously. The insulin and c-peptide levels were done by cheminolumenscent assay which showed higher levels more than double with stimulation of gastropancreatic artery. (Table-II). The stimulation test indicated the head of the pancrease is the source of high insulin level and it was decided to resect it. Intraoperative examination of the pancrease failed to find any pancreatic tumor. The surgery was performed successively where the head of the pancrease and part of the body was resected. The patient

Table-I: Investigation Results

Investigation	*Results*
Blood glucose during the symptoms	45mgdl, 40 mgdl, 55mg / dl
Insulin level during hypoglycemia	33 uIU, 39uIU,31uIUml*
C–Peptide level	9ng / ml, 17ng / ml, 11ng / ml**
TSH and FT4	Normal
Cortisol level	Normal
Urea, creatinine, CBC, Electrolytes	Normal
Chest x-ray and ECG	Normal
CT scan and MRI of the pancrease	Normal, no tumor detected
Celiac angiography	Normal

TSH: Thyroxin stimulating hormone, CBC: complete blood count, MRI: Magnetic resonance image
* Normal insulin levels 6.0 – 27.0 uiu / ml. ** C-peptide normal levels 0.8 – 4.0 ng / ml.

Table-II: The Results of Arterial Insulin Stimulation

The artery	*Insulin level before stimulation*	*Insulin level after stimulation*
Splenic artery	7 uiu / ml	8 uiu / ml
Superior mesenteric artery	4 uiu / ml	4.5uiu / ml
Gasteropancreatic artery	21 uiu / ml	47 uiu / ml

Significant positive test if the level of insulin increased more than twice after stimulation. The above result revealed positive test in gasteropancreatic artery which indicate that the head of the pancrease is the source of the inappropriate high insulin.

remained in the hospital for six days post operatively with no complication and no hypoglycemic episodes. The insulin and c-peptide levels were normal. On the second and sixth post operative day. The patient was followed in the out patients clinic up to three month post surgery with no more symptoms suggestive of hypoglycemia. The blood glucose profile and repeated insulin level were normal. The histopathology of the resected part showed hyperplasia of the pancreatic cells with no adenoma.

DISCUSSION

Low blood glucose concentrations were recognized as feature of several diseases in the 19th century. However, it was not until insulin became available for the treatment of diabetes mellitus in the early 1920s that clinical events similar to those arising from overtreatment with insulin were identified in nondiabetic persons. This observation led to the postulation of a new disease called hyperinsulinism.[3] Support for the existence of hyperinsulinism was provided by finding a malignant pancreatic islet – cell tumor in a patient who had episodes of sever hypoglycemia in 1927.[4] The first cure of hyperinsulinism by removal of an insulinoma was reported in 1929.[5] Over the last few years another disease has been identified with high endogenous insulin and hypoglycemia.[2] This disease was called Noninsulinoma Pancreatogenous Hypoglycemia Syndrome (NIPHS). The clinical features of this new disease are different from insulinoma at the time of occurrence of hypoglycemia. Patients having insulinoma hypoglycemia which usually occurs during fasting but in NIPHS it is usually reactive hypoglycemia.[6] All radiological investigation for localization of insulinoma will be normal in patients diagnosed to have NIPHS, as in our case. Arterial stimulation venous sampling involves selective injection into arteries supplying the pancrease calcium gluconate with subsequent sampling of the hepatic venous effluent.[7-10] This procedure is encouraging in localization of the source of high insulin secretion. One report evaluated 24 patients with proven hyperinsulinemia.[10] Seven of these patients had negative morphologic studies; at surgery, six had an insulinoma and one had nodular hyperplasia. In all seven patients, calcium infusion permitted localization of the source of insulin secretion. This procedure was first time done in our hospital where we were able to find the source of the insulin in our patient which was head of the pancrease. Surgery was done and the head of the pancrease resected. Intraoperatively no tumor was found. The pathology showed only hyperplasia of islet cell (nesidioblastosis).[11]

The treatment of NIPHS is surgery. The degree of surgery is determined by the result of the selective arterial calcium stimulation test. Partial pancreatectomy result in treatment and no more hypoglycemia in most reported cases. Some patients continued to have hypoglycemia which is most likely due to diffuse hyperplasia which required complete pancreatectomy.[12] Our patient improved with no more hypoglycemia after partial pancreatectomy. In future in all cases with similar problem we should localize the source of the insulin by the stimulation test and they should be treated by partial pancreatectomy rather than total pancreatectomy. This will reduce the incidence of developing diabetes mellitus after surgery.

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