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CASE REPORT

Ectopic renal insulinoma: case report

Insulinoma renal ectópico: informe de un caso

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Abstract

Insulinoma, the most common cause of hypoglycemia related to endogenous hyperinsulinism, is a rare neuroendocrine tumor. Its diagnosis is often delayed due to difficulties in identifying and localizing the functioning tumor. We report a case of a woman who suffered from an ectopic insulinoma, where the source of hormonal excess was not the pancreas as one might think, but the left renal mass. A 45-year-old female was admitted for evaluation of recurrent hypoglycaemic episodes she does not have diabetes mellitus. She referred a several-week history of symptoms :palpitations, tremors, sweating altered behavior, and anxiety (CT) scan of the chest and abdomen for localization of insulinoma with dimensions of 12x12 mm. In the left kidney, where a hypodense cortical lesion was observed in the middle part, well-limited, with necrotic areas inside, with dimensions of 62x81 mm which enhances after contrast After renal tissue pathology showed characteristics of a neuroendocrine tumor.

Key words: Insulinoma, Hypoglycemia, Whipple's triad Neuroendocrine tumor, renal mass.

Resumen

El insulinoma, la causa más frecuente de hipoglucemia relacionada con el hiperinsulinismo endógeno, es un tumor neuroendocrino raro. Su diagnóstico suele retrasarse debido a las dificultades para identificar y localizar el tumor funcionante. Presentamos el caso de una mujer que padecía un insulinoma ectópico, donde el origen del exceso hormonal no era el páncreas como podría pensarse, sino la masa renal izquierda. Una mujer de 45 años ingresó para evaluación de episodios hipoglucémicos recurrentes, no tiene diabetes mellitus. Refería cuadro de sintomatología de varias semanas de evolución: palpitaciones, temblores, alteración de la sudoración y ansiedad (TC) de tórax y abdomen para localización de insulinoma de 12x12 mm. En el riñón izquierdo, donde se observó una lesión cortical hipodensa en la parte media, bien delimitada, con áreas necróticas en su interior, con unas dimensiones de 62x81 mm que realza tras el contraste. Posterior a la patología del tejido renal, presenta características de tumor neuroendocrino.

Palabras clave: insulinoma, hipoglucemia, tríada de Whipple, tumor neuroendocrino, masa renal.

Background

Insulinoma, the most common cause of hypoglycemia-related to endogenous hyperinsulinism, is a rare neuroendocrine tumor with an annual incidence of 1-4 per million population per year[1]. Its diagnosis is often delayed due to difficulties in identifying and localizing the functioning tumor. We report a case of a young lady who suffered from an ectopic insulinoma, where the source of hormonal excess was not the pancreas as one might think, but the left renal mass.

Case presentation

A 45-year-old female was admitted for evaluation of recurrent hypoglycemic episodes in a person who does not have diabetes mellitus. She referred to suffering from a several-week history of symptoms that included: palpitations, tremors, hunger, sweating, altered behavior, and anxiety. Most of her symptoms occurred early in the morning (usually between 3-6 a.m.) and these symptoms improved spontaneously in 15 minutes or after intake of simple carbohydrates. Her clinical manifestations were consistent with Whipple's triad. The patient was admitted to the hospital and was subjected to a series of examinations.

The baseline blood results, including hemoglobin, white cell count, platelets, and renal and liver profiles were all within normal ranges. HbA1c was 4.5%. Laboratory test results showed an increase in C-reactive protein (CRP) levels to 9.06 mg/dL.

In conditions of an episode of hypoglycemia (venous glycemia-55 mg/dl), insulinemia, C-Peptide, and anti-insulin antibodies were obtained. The results were suggestive of insulinoma, with insulinemia 35.66 mcIU/mL (2.6-24.9) and C-Peptide 8.176 ng/ml(0.3-3.73). During another symptomatic episode of hypoglycemia, she had plasma glucose of 45 mg/dl while her plasma insulin and C-peptide were 42 mcIU/mL and 12 ng/ml (respectively) confirming the diagnosis of endogenous hyperinsulinemic hypoglycemia. The anti-insulin antibody test result was negative.

In terms of multiple endocrine neoplasia type 1(MEN-1) screening, anterior pituitary function, including levels of prolactin, thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), sex hormones, growth hormone(GH) and cortisol, all these were within normal range. The patient's PTH level was normal. As a result, there was no evidence for a diagnosis of MEN-1.

Later on, she underwent Computed tomography (CT) scan of the chest and abdomen for localization of insulinoma. It showed a small, isointense signal lesion at the level of the head of the pancreas that tends to be hyperattenuating on the arterial phase, with dimensions of 12x12 mm. Another finding was in the left kidney, where a hypodense cortical lesion was observed in the middle part, with mainly pararenal extension, well-limited, with necrotic areas inside, with dimensions of 62x81 mm, which enhances after contrast. There were no complaints of haematuria, frequent or burning micturition, or lumbar tenderness.

She underwent open surgical abdominal exploration. Pancreatic nodule enucleation and left nephrectomy were performed. Immediately after surgical treatment, the glucose level increased to the normal range. She became euglycemic without the need for dextrose infusion.

At first, we considered the diagnosis of incidentally detected left renal cell carcinoma in a patient with insulinoma. The histopathological findings disproved this idea. Microscopically, the pancreatic tumor was composed of a conglomerate of cysts lined by simple cuboidal epithelium. The nuclei were small, round to oval with dense, homogenous chromatin, thus suggesting the diagnosis of a Solid Serous Adenoma.

On the other hand, renal tissue pathology showed characteristics of a neuroendocrine tumor. Immunohistochemical staining revealed intense staining for pancytokeratin, insulin, chromogranin A, and neuron-specific enolase (NSE), confirming the left-sided renal mass to be the source of ectopic insulin secretion.

Discussion, Conclusions

Clinical hypoglycemia is, by definition, a plasma glucose concentration low enough to cause symptoms or signs, including impairment of brain function. Hypoglycemia is most convincingly documented by the Whipple triad. Documentation of the Whipple triad is particularly important when hypoglycemia is suspected in a person who does not have diabetes mellitus because hypoglycemic disorders are rare[2].

Insulinomas, the most common cause of hypoglycemia-related to endogenous hyperinsulinism, occur in 1-4 people per million of the general population[1]. Common autonomic symptoms of insulinoma include diaphoresis, tremor, and palpitations, whereas neuroglycopenenic symptoms include confusion, behavioral changes, personality changes, visual disturbances, seizures, and coma[3]. More than 90% of insulinomas are benign and usually small, well-encapsulated, solitary tumors[4].

Diagnosis of insulinomas can be challenging. The classical diagnosis of insulinoma depends on satisfying the criteria of Whipple's triad, which remains the cornerstone of the screening process: 1) hypoglycemia (plasma glucose < 50 mg/dL); 2) neuroglycopenic symptoms; and 3)

prompt relief of symptoms following the administration of glucose. In adults with symptoms of neuroglycopenia or documented low blood glucose levels, the gold standard for biochemical diagnosis remains measurement of plasma glucose, insulin, C-peptide, and proinsulin during a 72-h fast. This prolonged fasting test can detect up to 99% of insulinomas[2].

Ectopic insulin-secreting tumours are rare, comprising only 1% to 2% of all insulinomas, and are commonly located in the peripancreatic or periduodenal region where most heterotopic pancreatic tissue is located[5]. Ectopic insulin-producing tumours located away from pancreatic beds are infrequently reported in the literature[6,7].

Also its seems that like rare tumours Ectopic insulinoma to have a lower incidence four cases in million potion in years. Are diagnosis case ectopic insulinomas in the pelvis secondary to rectum[8], also in jejunum[9] and liver from metastasic pancreas.

Our patient had presented with a pancreatic lesion and a left renal mass lesion in imaging examinations and in the laboratory panel as hyperinsulinemic hypoglycemia. We initially considered the possibility of incidentally detected left renal cell carcinoma in a patient with insulinoma. The neuroendocrine and insulin-secreting nature of the renal tumor was confirmed by histopathological examination and immunohistochemistry, rejecting our initial hypothesis of pancreatic insulinoma.

Our case emphasizes the difficulty of the preoperative diagnosis of insulinoma. The localization diagnosis is the key to the success of surgical treatment. In general, the sensitivity of the noninvasive examinations commonly used in the diagnosis is approximately 56-70% for CT and 63-86% for MRI[10]. The imaging findings cannot determine the relationship between the lesion and hypoglycemia. Lesions found solely on CT or MRI can only be identified as insulinomas that cause hypoglycemia by postoperative pathology and the glycemic response. Nuclear medicine examinations including somatostatin receptor imaging and ^{68}Ga-NOTA-Exendin-4 PET/CT have greater advantages in determining the types and function of tumors[11]. However, the sensitivity rate of somatostatin receptor imaging is very low; the rate reported in the literature is only 19.5-50%. ^{68}Ga-NOTA-Exendin-4 PET/CT is currently the most sensitive noninvasive test, with a sensitivity rate of 97.7%, and is of great value for the diagnosis of ectopic insulinoma[12]. Surgical removal of the lesion is the main treatment and long-term close follow-up is needed for the malignant behavior of these ectopic lesions[13].

Conclusions

Ectopic insulinoma is a rare entity that is difficult to diagnose before surgery. This case emphasizes some of the challenges posed in the detection and management of insulinoma.

Conflict of interest

The authors declare no conflict of interest.

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