Simultaneous diagnosis of type 2 diabetes mellitus and insulinoma. Diagnostic pitfalls.

Authors: ***Grzegorz Świder, Joanna Sztembis*** Hospital: St.Queen Jadwiga District Hospital No 2, Rzeszów, Poland Dept. of Internal Medicine, Nephrology and Endocrinology with Nuclear Medicine Unit

Introduction:

Type 2 diabetes mellitus (DM t.2) is common disease of civilization while insulinoma is very rare. Co-morbidity of DM t 2 and insulinoma is extremely rare. There are only some case reports of diagnosing insulinoma but they concern patients already diagnosed with DM t. 2. We present case report of female patient diagnosed at the same time with DM t. 2 and insulinoma, and discuss diagnostic challenges and pitfalls that may accompany clinical co-existence of both.

Case report:

A 69-year-old female patient was admitted to hospital because of high blood pressure accompanied by dizziness and weakness since 3 days. Blood pressure was normalized within 24 hours what was accompanied by remission of symptoms. Patient's hypertension diagnosed 10 years before after hysterectomy with appendages due to myomes, was well controlled with drugs. Since 2 years the patient reported attacks of weakness, tachycardia and sweating within the day, usually several hours after food intake or directly after physical effort or rarely while fasting. The food intake resolved the symptoms. That caused change of dietary habits and since patient used to have food more often she gained 7 kilograms. 2 months before admission to hospital the patient experienced syncope in the afternoon with documented hypoglycemia of 40mg/dl. After that episode she was referred to outpatient diabetic clinic where she was diagnosed with diabetes mellitus type 2 by oral glucose tolerance test (OGTT). The patient was recommended to take metformine which she did not do as she was concerned with anticipated hypoglycemia.

Physical examination revealed blood pressure 200/100mmHg, BMI 26kg/m2, abdominal obesity, waist circumflex 89cm.

By prolonged 5-hours OGTT (75g) diabetes with reactive hypoglycemia at hour 5 of test was diagnosed. Table 1 presents glycaemia, insulinaemia and C peptide concentration values. The mean value of HOMA index was 4.53, abdominal US revealed hepar steatosis. Antibodies: anti-GAD, ICA, IAA were negative. During hospitalization fasting glycaemia levels were within range of 3,22 -6,33 mmol/l (range: 3.9-5.6 mmol/l) and postprandial glicaemia levels were: 3,61 – 8,94 mmol/l. Hypothyroidism, adrenal insufficiency as well as kidney and hepar failures were excluded. Screening cancer exams were negative. We performed fasting test. After 14 hours symptomatic hypoglycaemia: 2,44 mmol/l (range: 3.9-5.6 mmol/l) was observed with inadequately high levels of insulin: 31.4 uIU/ml (range: 2.6 - 24.9 uIU/ml) and C-peptide: 3.89ng/ml (range: 0.78 - 5.19 ng/ml). Endogenic hyperinsulinaemia was diagnosed. CT scans revealed highly attenuated (up to 140 H.U.) tumor diameter 17mm with regular margins at the border of pancreatic body and tail, suspected to be neuroendocrine tumor.

The patient underwent distal pancreas's resection. The tail and part of pancreatic body were excised.

Histopathological examination confirmed well differentiated endocrine pancreatic tumor, Ki67<2%, IM: 0/10HPF. Within 7 days after operation the patient needed small doses of short-acting insulin that was stopped and replaced by metformine. C-peptide level on day 10 after procedure was 4.32ng/ml, 6 weeks after procedure 2.56ng/ml and was within normal range after. HOMA index was 2.39 six weeks after operation. The patient remains euglicaemic and is well.

Table 1: Prolonged oral glucose tolerance test (75g)

Time [minutes]	glicaemia [mmol/l] range 3.9-5.6 mmol/l	insulinemia [uU/ml] range 2.6 - 24.9 uIU/ml	C peptide [ng/ml]range 0.78 - 5.19 ng/ml
0	3.6	20.7	2.8
60	12.3	94.8	8.8
120	12.2	78.8	10.2
180	6.2	44.7	8.6
240	4.1	34.8	6.2
300	1.9	21.3	4.7

Discussion:

Co-existence of diabetes mellitus and insulinoma is very rare. There are only 6 reported cases of previously diagnosed diabetes when unexpected, non-treatment related hypoglycaemic episodes led to insulinoma suspision. They were further confirmed [1-6]. Our case report is example of simultaneous diagnosis of type 2 diabetes mellitus and pancreatic insulinoma. It would seem that postprandial hypoglycaemias are only reactive as a signs of clinical symptomatologia of DM t. 2. This fact was suggested also by prolonged OGTT. However that was not the true. Extremely interesting was that putative hypoglycaemic episodes were too often, there was one episode of severe hypoglycaemia with syncope and levels of insulinaemia in OGTT were inadequately high. Of course clinical history and persistent symptoms played crucial role in undertaking broader diagnostic efforts. Assessment of insulinaemia during standard OGTT in not a routine diagnostic tool of course. It should be stressed that after recognition of DM t.2 by routine 2-hours OGTT whenever there is hypoglicaemiain history, some diseases like adrenal insufficienty, hypothyroid state, kidney or liver failure, cancers, should be excluded. The most important diagnostic tool was fasting test. It confirmed endogenic hiperinsulinism in our patient. Previously quantified HOMA index proved not to be reliable considering autonomic insulin excretion. Case report discussed here proves that diagnosis of DM t 2 should not be followed by abandoning diagnosis of fasting hypoglycaemia when there are morning or frequent postprandial hypoglycemia episodes within the day. In conclusion, hypoglicaemia must not be always typical sign of the early stage o the diabetes mellitus. Other causes should be considered even insulinoma.

References:

1. Cander S, Gül OÖ, Yildirim N, Unal OK, Saraydaroglu O, Imamoglu S, A rare cause of hypoglycemia in a type 2 diabetic patient: insulinoma. J Diabetes Complications. 2012; 26(1): 65-7.
2. Heik SC, Klöppel G, Krone W, Iben G, Priebe K, Kühnau J. Hypoglycemia caused by insulinoma in diabetes mellitus. Dtsch Med Wochenschr. 1988;113(44):1714-7
3. Abbasakoor NO, Healy ML, O'Shea D et al. Metastatic Insulinoma in a Patient with Type 2 DiabetesMellitus: Case Report and Review of the Literature, Int J Endocrinol. 2011; 2011:124078. doi: 10.1155/2011/124078.
4. Lei W.Y, Wang T.E, Chen T.L, Chang W.H, Yang T.L, Wang C. Y, Insulinoma causing hypoglycemia in a patient with type 2 diabetes. Journal of the Formosan Medical Association 2007;106: 392–396,.
5. Kane L.A, Grant C.S, Nippoldt T.B Service F. J, Insulinoma in a patient with NIDDM. Diabetes Care 1993; 16:1298–1300
6. Ishii H., Ito T., Moriya S., Horie Y., Tsuchiya M. Insulinoma - a statistical review of 443 cases in Japan. Nippon Rinsho 1993; 51 supplement: 199–206