http://rjdnmd.org
Rom J Diabetes Nutr Metab Dis. **26**(3):327-330
doi: 10.2478/rjdnmd-2019-0035

UNCOMMON MANIFESTATION OF HYPOGLYCEMIA IN A PATIENT WITH INSULINOMA – A CASE REPORT

Nicoleta Mihaela Mîndrescu [1], ***Georgeta Văcaru*** [2], ***Loreta Guja*** [3], ***Rucsandra Elena Dănciulescu Miulescu*** [3,4,✉]

[1] Nicodiab Private Practice, Bucharest
[2] EasyDiet Private Practice, Bucharest
[3] "Carol Davila" University of Medicine and Pharmacy, Bucharest
[4] "N.C.Paulescu" National Institute of Diabetes, Nutrition and Metabolic Diseases Bucharest

received: August 13, 2019 *accepted*: September 09, 2019
available online: October 21, 2019

Abstract

Insulinoma are insulin-secreting tumors of pancreatic origin that generates hypoglycemia by excessive secretion of insulin. Insulinoma is a rare disease ant the most tumors are benign, solitary and occur at intrapancreatic sites. ***Case report****. A 42-year old Caucasian women was hospitalized at the "Prof. N.C. Paulescu" National Institute of Diabetes, Nutrition and Metabolic Diseases Bucharest in April 2019 after an episode of hypoglycaemia remitted after intravenous glucose administration. Patient accused for about two weeks anxiety phenomena. At the time of admission in the hospital the patient was conscious in a good general condition. Paraclinical investigations revealed basal blood glucose 29 mg/dl, fasting insulin serum 87.7 µU/ml and pancreatic C-peptide-7.90 ng/ml. During hospitalization under strict glycaemic monitoring, the patient presented frequent asymptomatic hypoglycemic episodes that was remitted after intravenous glucose administration. Nuclear magnetic resonance highlighted a nodular lesion of the pancreas and in May 2019 the tumor resection was practiced. After surgery the blood glucose ranged between 86 mg/dl and 116 mg/dl. To mention that patient has a family history of diabetes and she's obese.* ***Conclusion.*** *This case suggests that lack symptoms of hypoglycaemia may be present in patients with insulinoma. Diagnostic of insulinoma requires high clinical suspicions, accurate biochemical investigations and imaging techniques for the localization of the tumor and may represent a challenge in certain situations.*

key words: *anxiety phenomena,* ***insulinoma,*** *hypoglycemia.*

Introduction

Insulinoma are insulin-secreting tumors of pancreatic origin that generates hypoglycemia by excessive secretion of insulin. Insulinoma is a rare condition with a incidence appreciated at 1-4 person per million per year (in the general population) [1]. Most insulinoma are benign, solitary and occur at intrapancreatic sites; extrapancreatic insulinoma are rare and are most commonly found in the duodenal wall [2]. Insulinoma may occur in familial form,

✉ 5-7 Ion Movila Street, Bucharest, District 2, Postal Code 11420, Tel: 0040748134500, Fax: 004021/2105575; *corresponding author e-mail*: rucsandra_m@yahoo.com

respectively in multiple endocrine type 1 syndrome (MEN 1) in which tumors are usually multiple. Abboud B and Boujaoude J mention in an article published in 2008 that "*insulinoma may occur throughout life, the mean age at presentation is 45 (range 8-82) years, and there is a female preponderance (female to male ratio 1.4:1). In MEN 1 the mean age at presentation is younger, at 25 years or less*"[2]. In most cases patients present symptoms of hypoglycemia which are typically evident in the morning and are often precipitated by exercise [2,3]. Symptoms of hypoglycemia include neurogenic and neuroglycopenic symptoms. The first symptoms are generated by an autonomic discharge caused by hypoglycemia and are represented by hunger, sweating, paraesthesia (cholinergic symptoms), anxiety, tremor, palpitations (adrenergic symptoms). Neuroglycopenic symptoms are the results of brain glucose deprivation and are represented by fatigue, confusion, seizure, transient motor deficits, visual changes, severe cognitive failure, coma [2,4,5]. Diagnosis of insulinoma requires clinical observation and biochemical tests. After biochemical diagnosis, the next step is preoperative localization of tumor which can be performed by noninvasive or invasive method. Noninvasive imaging techniques include abdominal ultrasound, computer tomography (CT), nuclear magnetic resonance (MRI) and somatostatin receptor scintigraphy. Invasive method are represented by selective selective angiography, endoscopic ultrasonography and selective calcium stimulation [6,7]. After localization of the tumor, surgery is indicated for all localized insulinoma. A systematic review by Okabayashi T and coworkers mention that "*the choice of procedure will depend on the features of the tumor mass, such as type, size, and localization. Atypical resection, including enucleation, partial pancreatectomy, or middle pancreatectomy, has the advantage of preserving the pancreatic parenchyma as much as possible, thereby reducing the risk of late exocrine/endocrine insufficiency"* [8]. There have been described other medical methods for the management of benign insulinomas such: somatostatin analogues, radiofrequency ablation, embolization of tumor, if surgery is not feasible [9-11].

Case report

A 42-year old Caucasian women was hospitalized at the "Prof. N.C. Paulescu" National Institute of Diabetes, Nutrition and Metabolic Diseases Bucharest in April 2019 after an episode of hypoglycaemia (43 mg/dl) remitted after intravenous glucose administration. Patient accused for about two weeks anxiety phenomena. At the time of admission to the hospital the patient was conscious in a good general condition. Paraclinical investigations revealed basal blood glucose 29 mg/dl (normal range: 65-115 mg/dl), fasting insulin serum 87.70 µU/ml (normal range: 2.60-24.90 µU/ml), pancreatic C-peptide-7.90 ng/ml (reference values: 1.10–4.40 ng/dl). Abdominal ultrasound revealed: liver with homogeneous structure, discreet hyperecogen-hepatic steatosis, gallbladder with microcalculi infundibulari, slightly hyperecogenic pancreas without focused processes. During hospitalization under strict glycaemic monitoring the patient presented frequent asymptomatic hypoglycemic episodes regardless of the amount of blood glucose (33 mg/dl, 56 mg/dl, 37 mg/dl, 33 mg/dl, 48 mg/dl) that was remitted after intravenous glucose administration. According to Whipple's triad the diagnosis of insulinoma was suggested by elevated insulin levels in the presence of hypoglycaemia remitted after glucose administration [12,13]. It was recommended CT which did not highlight any

replacement of intrapancreatic space of an insulinoma and subsequently MRI. MRI highlighted a nodular lesion of 15/14 mm at the anterior corporate versant of the pancreas. In May 2019 the enucleation of tumor was practiced. The diagnosis of an insulinoma was histopathologically confirmed later. After surgery the blood glucose ranged between 86 mg/dl and 116 mg/dl. To mention that patient has a family history of diabetes (mother) and it's obese (height: 160 cm, weight; 90 kg, body mass index: 35.1 kg/m^2).

Discussion

This case suggests that lack of hypoglycaemia symptoms may be present in patients with insulinoma. Mejía D and coworkers reported a 50-year old Hispanic men with anxiety, agitation and decreased visual acuity. Paraclinical investigations confirmed an insulinoma was the cause of the symptoms. Authors mention that it "*is of critical importance to rule out organic causes of altered mental status prior to consideration of psychiatric disorders, as unusual diseases may be overlooked by physicians and be detrimental to the patient's progress*"[14]. Sharma P and collaborators have reported two cases of patients with insulinoma which were initially presented with neuro-psychiatric symptoms and were treated for anxiety, depression, seizures; the diagnosis of these patients was delayed for years [15]. Piccillo GA *et al* have described the clinical cases of two men respectively 41 and 73 years old affected with insulinoma but misdiagnosed for many years as psychiatric conditions [16]. Van Eyken P, Bex M and Vandenberghe W have described a 39-year old women suffered from paroxysmal nonkinesigenic dyskinsias which resolved after removal of an insulinoma. To mention that during an emergency admission for involuntary movements of arms and legs, the patient did not present any characteristic symptoms of hypoglycaemia although blood glucose levels were consistently below 35 mg/dl [17].

Conclusion

Diagnostic of insulinoma requires high clinical suspicions, accurate biochemical investigations and imaging techniques for the localization of the tumor and may represent a challenge in certain situations.

REFERENCES

1. **Service FJ, McMahon MM, O'Brien PC, Ballard DJ.** Functioning insulinoma--incidence, recurrence, and long-term survival of patients: a 60-year study. *Mayo Clin Proc* 66(7): 711–719, 1991.

2. **Abboud B, Boujaoude J.** Occult sporadic insulinoma: Localization and surgical strategy. *World J Gastroenterol* 14(5): 657-665, 2008.

3. **Suzuki K, Miyamoto M, Miyamoto T, Hirata K.** Insulinoma with early-morning abnormal behavior. *Intern Med* 46(7): 405–408, 2007.

4. **Cryer PE.** Symptoms of hypoglycemia, thresholds for their occurrence, and hypoglycemia unawareness. *Endocrinol Metab Clin North Am* 28(3): 495–500, 1999.

5. **DeRosa MA, Cryer PE.** Hypoglycemia and the sympatho-adrenal system: neurogenic symptoms are largely the result of sympathetic neural, rather than adrenomedullary, activation. *Am J Physiol Endocrinol Metab* 287(1): E32–E41, 2004.

6. **Mehrabi A, Fisher L, Hafezi M, et al**. A systematic review of localization, surgical treatment options and outcome of insulinoma. *Pancreas* 43(5): 675-686, 2014.

7. **Taye A, Libutti SK**. Diagnosis and management of insulinoma: current best practice and ongoing developments. *Res Rep Endocr Disord* 5: 125-133, 2015.

8. Okabayashi T, Shima Y, Sumiyoshi T, et al. Diagnosis and management of insulinoma. *World Gastroenterol* 19(6): 829-837, 2013.

9. Kishikawa H, Okada Y, Hirose A, Tanikawa T, Kanda K, Tanaka Y. Successful treatment of insulinoma by a single daily dose of octreotide in two elderly female patients. *Endocr J* 53(1): 79–85, 2006.

10. Limmer S, Huppert PE, Juette V, Lenhart A, Welte M, Wietholtz H. Radiofrequency ablation of solitary pancreatic insulinoma in a patient with episodes of severe hypoglycemia. *Eur J Gastroenterol Hepatol* 21(9): 1097–1101, 2009.

11. Rott G, Biggemann M, Pfohl M. Embolization of an insulinoma of the pancreas with trisacryl gelatin microspheres as definitive treatment. *Cardiovasc Intervent Radiol* 31(3): 659–662, 2008.

12. Whipple AO, Frantz VK. Adenoma of the islet cell with hyperinsulinism. *Annals of Surgery* 101: 1299-1304, 1935.

13. Kong MF, Lawden M, Dennison A. Altered mental state and Whipple triad. *BMJ Case Rep* 2010. pii: bcr08.2009.215, 2010.

14. Mejía D, Contreras R, Molina G, Alcántara M. Altered behavior with an organic cause: a case report. *J Med Case Rep* 13(1):192, 2019.

15. Sharma P, Sharma S, Kalhan S, Singh BP, Sharma S. Insulinoma: A Comprehensive Summary of Two Cases. *J Clin Diagn Res* 8(9): FD05–FD06, 2014.

16. Piccillo GA, Musco A, Manfrini S, Modati E, Guastella T. Two clinical cases of insulinoma misdiagnosed as psychiatric conditions. *Acta Biomed* 76(2): 118-122, 2005.

17. Van Eyken P, Bex M, Vandenberghe W. Paroxysmal nonkinesigenic dyskinsias due to recurrent hypoglyvemia caused by an insulinoma. *Movment Disorders* 24(3): 460-461, 2008.