



# Insulin Washout in Fine-Needle Aspiration Fluid for Preoperative Diagnosis of Suspicious Lesion in Patients with Insulinoma: A Case Report

## İnsülinoma Hastalarında Şüpheli Lezyonun Preoperatif Tanısı İçin İnce İğne Aspirasyon Sıvısında İnsülin Yıkama: Bir Olgu Sunumu

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### Abstract

Insulinomas, the most common neuroendocrine tumors of the pancreas, are usually solitary in nature. Yet, they may be difficult to localize. A 29-year-old female patient with neurologic complaints including drowsiness, meaningless speech and temporary dementia (not recognizing her relatives), was evaluated for hypoglycemia. According to the critical laboratories investigations, the patient was found to be having hyperinsulinemic hypoglycemia. After diagnosing insulinoma by biochemical tests, the tumor was localized using endoscopic ultrasonography and fine needle aspiration biopsy was performed on the insulin washout material to obtain a prompt confirmation. After localization of the tumor, subtotal pancreatectomy was performed. The patient's symptoms were relieved and did not re-occur. Thus, this case report suggests that the insulin washout from fine needle aspiration biopsy can be successfully employed during endoscopic ultrasonography to obtain a hasty diagnosis since it delivers faster results and is a much more convenient approach than the pathological examinations. It promptly confirms the tumor site and may, therefore, be employed in cases of difficult tumor localization.

**Keywords:** Insulinoma; hypoglycemia; endoscopic ultrasonography; washout method

### Özet

Pankreasın en sık görülen nöroendokrin tümörleri olan insülinomalar, genellikle tek bir soliter tümöre bağlı olmalarına rağmen lokalizasyonları zor olabilmektedir. Uyku hâli, anlamsız konuşmalar ve geçici demans (yakınlarını tanıma) gibi nörolojik şikâyetleri olan 29 yaşındaki kadın hasta hipoglisemi nedeni ile değerlendirildi. Kritik laboratuvar tetkiklerine göre hastanın hiperinsülinemik hipoglisemisi olduğu saptandı. İnsülinomanın biyokimyasal tanısını takiben, tümörü endoskopik ultrasonografi ile lokalize edildi ve hızlı konfirmasyon için ince iğne aspirasyon biyopsi materyalinde insülin yıkama yapıldı. Tümörün lokalizasyonundan sonra subtotal pankreatektomi yapıldı; hastanın şikâyetleri düzeldi ve yeniden oluşmadı. Bu olgu sunumu, endoskopik ultrasonografi sırasında ince iğne aspirasyon biyopsi materyalinde insülin yıkama yönteminin hızlı tanı almak için başarılı bir şekilde uygulanabileceğini, çünkü daha hızlı sonuç verdiğini ve patolojik incelemeden çok daha uygun bir yaklaşım olduğunu düşündürmektedir. İnsülin yıkama yöntemi tümör bölgesini hızlı bir şekilde konfirme etmektedir ve bu nedenle tümör lokalizasyonunun zor olduğu vakalarda kullanılabilir.

**Anahtar kelimeler:** İnsülinoma; hipoglisemi; endoskopik ultrasonografi; yıkama yöntemi

### Introduction

Insulinomas form the most common neuroendocrine tumor of the pancreas. The annual incidence of these tumors has been reported to be about 1 to 4 people per one million people years (1). It is most common

in individuals between the age group of 40 to 50 years and shows a slightly higher female predilection (2). Insulinomas are mostly solitary benign tumors, with only less than 10% of the cases being malignant. The great majority of insulinomas are sporadic,

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with 10% occurring as multiple and as a component of Multiple Endocrine Neoplasia syndrome type 1 (MEN-1).

The typical Whipple triad of insulinoma comprises hypoglycemia symptoms when the blood glucose level is less than 50 mg/dL and improvement of these symptoms with glucose intake. It is diagnosed by hyperinsulinemia and elevated C-peptide level at the time of hypoglycemia. The most reliable test used for its diagnosis is a prolonged supervised fasting test as a majority of patients develop hypoglycemia within the first 24 h of this test (3, 4).

Once hyperinsulinism is confirmed on the basis of biochemical tests, localization of the tumor becomes a challenging task as the known pre-operative imaging methods may pose difficulties. Here, the authors present a case of insulinoma wherein tumor localization was done using FNAB with insulin washout method via Endoscopic Ultrasonography (EUS) after confirmation of biochemical hyperinsulinism.

### Case Report

A 29-year-old female patient, with a blood glucose level of 50 mg/dL, reported to the neurology polyclinic with complaints including drowsiness, meaningless speech and temporary dementia (unable to recognize her relatives). The patient's symptoms improved soon after administration of oral carbohydrates and no neurological pathology was detected. Subsequently, similar complaints repeated several times during the same day, and the patient was referred to the endocrinology polyclinic. The patient was admitted to the endocrinology department for further examination of the etiology of hypoglycemia. The patient's past medical history was nil, she was not on any medications and gave no history of illicit drug use. Physical examination revealed that all the vital functions were normal. Systemic examination of the patient was normal. At the time of admission, routine laboratory test results were as follows: serum glucose- 60 mg/dL, TSH-1.37  $\mu$ IU/mL, HbA1c-5%, cortisol- 18  $\mu$ g/dL. Complete blood count, liver function tests, and kidney function tests were all normal. The patient was subjected to a prolonged supervised fasting test. At the 6<sup>th</sup> hour of the test, blood glucose was observed to be 50 mg/dL and at

the same time, the C-peptide and insulin levels were 2.66 ng/mL and 25.7  $\mu$ IU/mL, respectively. The insulin/glucose ratio was 0.51. Anterior pituitary hormones, calcium, PTH and gastrin levels were examined to rule out MEN-1 syndrome and were found to be normal.

No pancreatic mass was detected by abdominal magnetic resonance imaging (MRI). EUS revealed a hyperechoic homogeneous lesion, measuring 17 $\times$ 10 mm with unclear boundaries, present between the pancreatic body and the tail. Fine-needle aspiration of this lesion was performed under EUS guidance and insulin wash-out was performed on the biopsy material. The insulin level in washout material was observed to be 254  $\mu$ IU/mL. FNAB revealed pathologic findings that were consistent with those of a pancreatic neuroendocrine tumor (insulinoma). Immunohistochemical staining was positive for pancytokerin, cd56 and chromogranin. Immunohistochemical staining for insulin was, likewise, positive. All these findings confirmed the neuroendocrine nature of the lesion. The proliferation index Ki-67 was positive in 1-2% of the tumor cells. The patient underwent subtotal pancreatectomy. The pathology result was reported as follows: pancreatic neuroendocrine tumor, functional (insulinoma), chromogranin (+), insulin (+), Ki 67 index was 4%. In the postoperative follow-up, the patient's blood glucose levels were found to be normal with no hypoglycemia.

Informed consent from the patient was taken prior to the treatment procedures.

### Discussion

Surgery appears to be the only potential method of curing patients with insulinomas (5). Therefore, radiological localization of the lesion after clinical and biochemical diagnosis of insulinoma holds great importance. Insulinomas are usually solitary lesions, measuring less than 2 cm, thereby making its localization difficult (5). Insulinomas demonstrate their characteristic features in both CT and MRI, with a reported sensitivity of 33-64% and 40-90%, respectively, for CT and MRI (6, 7). In the present case, the lesion could not be visualized in MRI and subsequently, the EUS method was employed. EUS is reported to have excellent sensitivity (85-95%) (8, 9). In the study of

Kann et al., 10 insulinoma patients underwent FNAB with EUS and the diagnostic accuracy of FNAB was observed to be 70% (10). In the present case, after localization of the lesion with EUS, insulin wash-out from FNAB was performed at the same session. The insulin level, in the wash-out sample, was found to be 254  $\mu$ IU/mL, thus prompting that localization of the tumor with EUS can be confirmed by insulin washout. Earlier studies have shown that the correct combination of pre-operative localization methods for insulinomas helps choose a pancreas-sparing approach such as enucleation in the treatment plan (11, 12). The authors deliberate that better results can be obtained with the combined use of FNAB and insulin wash-out technique during EUS. Furthermore, the detection of insulin levels in the washout sample is sufficiently faster than that in the pathological result, which may make the washout method a much more convenient procedure. Further studies involving a large number of patients must be performed in this field so that a cut-off value for the insulin washout method may be presented. Thereafter, insulin washout may become a method that can be applied in cases where the tumor localization is difficult.

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### Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

### Authorship Contributions

Idea/Concept: Melia Karaköse, Hüseyin Ataseven; Design: Melia Karaköse, Hüseyin Ataseven; Control/Supervision: Feridun Karakurt; Data Collection and/or Processing: Muhammet Kocabaş; Analysis and/or Interpretation: Mustafa Kulaksızoğlu; Literature

Review: Muhammet Kocabaş; Writing the Article: Melia Karaköse, Muhammet Kocabaş, Mustafa Can; Critical Review: Melia Karaköse, Mustafa Can; References and Fundings: Mustafa Can; Materials: İlker Cordan.

### References

- Okabayashi T, Shima Y, Sumiyoshi T, Kozuki A, Ito S, Ogawa Y, Kobayashi M, Hanazaki K. Diagnosis and management of insulinoma. *World J Gastroenterol*. 2013;19:829-837. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Zhao YP, Zhan HX, Zhang TP, Cong L, Dai MH, Liao Q, Cai LX. Surgical management of patients with insulinomas: result of 292 cases in a single institution. *J Surg Oncol*. 2011;103:169-174. [[Crossref](#)] [[PubMed](#)]
- Grant CS. Insulinoma. *Best Pract Res Clin Gastroenterol*. 2005;19:783-798. [[Crossref](#)] [[PubMed](#)]
- Vaidakis D, Karoubalis J, Pappa T, Piaditis G, Zografos GN. Pancreatic insulinoma: current issues and trends. *Hepatobiliary Pancreat Dis Int*. 2010;9:234-241.
- Christ E, Wild D, Ederer S, Béhé M, Nicolas G, Caplin ME, Brändle M, Clerici T, Fischli S, Stettler C, Eil PJ, Seufert J, Gloor B, Perren A, Reubi JC, Forrer F. Glucagon-like peptide-1 receptor imaging for the localisation of insulinomas: a prospective multicentre imaging study. *Lancet Diabetes Endocrinol*. 2013;1:115-122. [[Crossref](#)]
- Sotoudehmanesh R, Hedayat A, Shirazian N, Shahraeeni S, Ainechi S, Zeinali F, Kolahdoozan S. Endoscopic ultrasonography (EUS) in the localization of insulinoma. *Endocrine*. 2007;31:238-241. [[Crossref](#)] [[PubMed](#)]
- McAuley G, Delaney H, Colville J, Lyburn I, Worsley D, Govender P, Torreggiani WC. Multimodality preoperative imaging of pancreatic insulinomas. *Clin Radiol*. 2005;60:1039-1050. [[Crossref](#)] [[PubMed](#)]
- Masciocchi M. Pancreatic imaging. *Endocrinol Metab Clin North Am*. 2017;46:761-781. [[Crossref](#)] [[PubMed](#)]
- Nockel P, Babic B, Millo C, Herscovitch P, Patel D, Nilubol N, Sadowski SM, Cochran C, Gorden P, Kebebew E. Localization of insulinoma using 68 Ga-DOTATATE PET/CT scan. *J Clin Endocrinol Metab*. 2017;102:195-199. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Kann PH, Moll R, Bartsch D, Pfützner A, Forst T, Tamagno G, Goebel JN, Fourkiotis V, Bergmann SR, Collienne M. Endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNA) in insulinomas: indications and clinical relevance in a single investigator cohort of 47 patients. *Endocrine*. 2017;56:158-163. [[Crossref](#)] [[PubMed](#)]
- Goh BK, Ooi LL, Cheow PC, Tan YM, Ong HS, Chung YF, Chow PK, Wong WK, Soo KC. Accurate preoperative localization of insulinomas avoids the need for blind resection and reoperation: analysis of a single institution experience with 17 surgically treated tumors over 19 years. *J Gastrointest Surg*. 2009;13:1071-1077. [[Crossref](#)] [[PubMed](#)]
- Zhang T, Mu Y, Qu L, Wang X, Lv Z, Du J, Guo Q, Ba J, Dou J, Lu J. Accurate combined preoperative localization of insulinomas aid the choice for enucleation: a single institution experience over 25 years. *J Hepatogastroenterology*. 2012;59:1282-1285. [[Crossref](#)] [[PubMed](#)]