

# Confusion of Insulinoma's Neuroglycopenic Symptoms with Epilepsy, Two Case Presentation and a Review of Literature

*İnsülinomada Nöroglikopenik Semptomların Epilepsi ile Karışıklığı, İki Olgu Sunumu ve Literatürün Gözden Geçirilmesi*

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## Keywords

Insulinoma, hypoglycemia, acute symptomatic seizure

## Anahtar Kelimeler

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## Abstract

Insulinoma is a pancreatic endocrine tumour which origins from beta cells and characterized by excessive insulin secretion and hypoglycemia due to this. Symptoms seen in hypoglycemia are due to brain's lack of glucose (neuroglycopenia) such as somnolence, irritability, confusion, abnormal behaviour, epileptic seizure and even coma. In this study, we presented two insulinoma cases who applied to our clinic with neuroglycopenic symptoms. Patients followed up with epilepsy diagnosis were referred to us because of low blood glucose rates. Hyperinsulinemic hypoglycemia in the prolonged fasting test and a mass in pancreas were detected in both patients and so they were diagnosed as insulinoma. The mass was excised by laparoscopic ways in surgical clinic and patients clinic were completely recovered post-operative. In conclusion, it is necessary to determine whether there is an underlying organic brain lesion or a metabolic condition in order to prevent long-term use of unnecessary antiepileptic in patients presenting with seizures.

## Öz

İnsülinoma, aşırı insülin salınımı ve buna bağlı hipoglisemi ile karakterli, beta hücrelerinden köken alan endokrin bir pankreas tümörüdür. Hipoglisemide ortaya çıkan semptomlar beynin glikozsuz kalması (nöroglikopeni) sonucu, somnolans, irritabilite, konfüzyon, anormal davranış, epileptik atak ve hatta koma görülebilir. Biz, burada, nöroglikopenik semptomlarla başvuran iki insülinoma olgusunu sunduk. Epilepsi hastalığı ile takip edilen hastaların kan şekeri düşük saptanması üzerine kliniğimize refere edilmiş. Her iki olguda insülinoma tanısı, uzun açlık testinde hiperinsülinemik hipoglisemi, pankreasta kitle tespit edilmesiyle kondu. Cerrahi kliniğinde pankreastaki kitle laparoskopik olarak eksize edildi, post-operatif takiplerde hastaların kliniği tamamen düzeldi. Sonuç olarak nöbet ile gelen hastalarda uzun süreli gereksiz antiepileptik kullanımını önlemek amacıyla altta yatan organik beyin lezyonu ya da metabolik bir durum olup olmadığını belirlemek gerekir.

## Introduction

Diagnosis of insulinoma is usually delayed because of non-specific indications. Adrenergic and neuroglycopenic symptoms are seen when hypoglycemia occurs. There may be a long period between the onset of symptoms and the diagnosis. Because of neuroglycopenic symptoms, patients can be followed-up and treated with misdiagnoses such as epilepsy or psychosis in neurology or psychiatry clinics (1).

In this case report we wanted to remind and emphasize the existence of two insulinoma cases who applied to the neurology and psychiatry clinics before diagnosis and who used long term unnecessary antiepileptic drugs due to misdiagnosis of epilepsy or psychiatric disorders.

## Case Reports

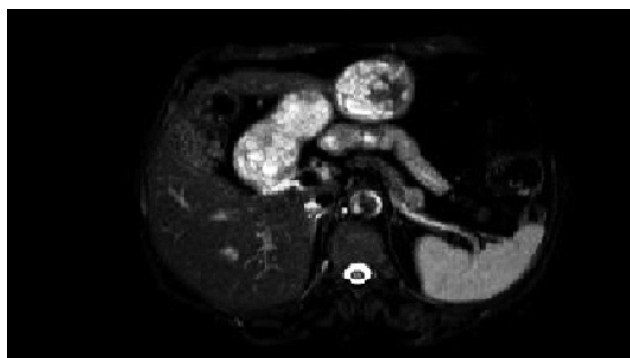
### Case 1

Sixty-six year old female patient, she had the complaints of getting fat, sweating, palpitation, seizure and fainting. The patient began to use antiepileptic drugs with the diagnosis of epilepsy, three years ago. The patient's seizure frequency had increased in the last 3-5 months and seizures become uncontrollable with the drugs. The patient was referred to our clinic with the prediagnosis of insulinoma after they measured fingertip blood glucose 26 mg/dL in the emergency service when she applied with neuroglycopenic symptoms. Her fasting blood glucose was measured as 60 mg/dL after biochemical tests. At the 4<sup>th</sup> hour of the prolonged fasting test the insulin value was determined as 28.4 (6-27) IU/dL and c-peptide: 5 (1.1-5) IU/dL while blood glucose was measured as 30 mg/dL. These findings were biochemically suitable with insulinoma. Pancreas ultrasonography, magnetic resonance imaging (MRI) and tomography were performed to the patient and tumour could not be localized in the pancreas. Endoscopic ultrasonography reported 11x7 mm mass in the tail zone of the pancreas (NET?). Patient underwent operation in our general surgery clinic. Immunohistochemical studies in the pathological examination of the fragment revealed that the resulting tumour was a well differentiated endocrine tumour insulinoma carrying low-grade malignancy potential. Post-operative follow-up showed a blood

glucose level of 110-150 mg/dL and there was no epileptic attack in the last 3 months. Informed consent was obtained from the patients.

### Case 2

Fifty-seven year old female patient was admitted to the emergency center clinic with the complaints of palpitation and weakness. She was referred to our endocrinology clinic because of low blood glucose level (45 mg/dL) during the examinations. About three years ago patient was diagnosed as epilepsy in the neurology center due to the complaints of fatigue, loss of concentration, excessive nervousness, trembling in hands, glazed eyes, cold sweating, fainting, palpitations and treated with levatiracetam 2x500 mg, lamotrigine 1x25 mg. There was no decrease in complaints and seizure frequency of the patients on the follow-up. We made prolonged fasting test to the patient. We detected insulin: 68 uIU/mL, c-peptide: 5.1 mg/mL, cortisol: 15.3 mg/dL, at the third hour of the test while blood glucose level was 45 mg/dL. These findings were biochemically compatible with insulinoma. Pancreas MR showed approximately 15x13 mm hypervascular mass lesion in the tail section of the pancreas extending partially out of the pancreas contour, which was hypointense in T1 weighted series. Pancreatic mass was laparoscopically excised in general surgery clinic. In tissue pathology tumour was defined as neuroendocrine tumour grade 1, immunohistochemically positive for chromogranin and synaptophysin, proliferation index was 1%. There were no hypoglycemia and seizures in post op follow-ups. Informed consent was obtained from the patients (Figure 1).



**Figure 1.** The pancreas MRI shows a hypervascular mass of 15x13 mm in size, hypointense in T1-weighted series, hyperintense in the T2-weighted series in the tail of the pancreas, extending partially out of the contour of the pancreas.

MRI: Magnetic resonance imaging

## Discussion

Insulinoma is a rare neuroendocrine tumour originating from the Langerhans islet cells of the pancreas (2). Epileptic attacks due to hypoglycemia can be seen in these patients. Acute symptomatic seizure is associated with a systemic or neurological condition. These seizures are not as repetitive as epilepsy. The recurrence of acute symptomatic seizures is not expected unless the underlying event is repeated (3). Both two cases were followed-up in neurology and psychiatry clinics due to epileptic seizures.

In insulinoma, clinical symptoms occur due to hypoglycemia, sweating, tremor, anxiety, starvation and palpitation feelings due to hypoglycemia after exercise or eating, determine the clinical picture. Central nervous system findings occur when blood glucose falls below 50 mg/dL. Confusion, seizure, abnormal behaviours can be seen in patients (4). Patients may be followed up and treated with false diagnoses such as epilepsy or psychosis in clinics due to non-specific symptoms, like our cases.

In our cases, hypoglycemia is probably masked by frequent eating for about three years, neuroglycopenic symptoms may come out after hypoglycemia. But in last months the number of referrals to the doctor because of uncontrolled seizures has increased although high doses of drugs. Patients were referred to our clinic because of the low blood glucose levels observed during seizures in emergency. We made prolonged fasting test to the patients with a close follow-up and the serum glucose, insulin, c-peptide and insulin glucose ratio detected at the third and 4<sup>th</sup> hours of the test were biochemically suitable with insulinoma.

Insulinomas are usually small (<2 cm), solid, 90% benign tumours; they are small and it is hard to localize preoperatively. Conventional computerized tomography (specificity 12-73%) and transabdominal ultrasonographic examinations (specificity 62%) are relatively insensitive methods in the localization of these tumours and using dual phase computerized

spiral tomography can be used to show smaller insulinomas not seen with other radiological methods (6-18 mm). First studies with MR are not promising. Pancreatic Endoscopic ultrasound (EUS) is a non-invasive technique for the localization of pancreatic neuroendocrine tumours and reported sensitivity of 75-96% (5). We performed pancreatic tumour localization with MRI in one of the cases and with pancreatic EUS in other case.

As a result seizures associated with acute metabolic disturbance can be separated from epilepsy by lack off the tendency to recurrence and an identifiable cause of seizure. Forth is reason in a patient applying with seizure we should determine if there is a metabolic status or an organic brain lesion underlying to avoid long term unnecessary antiepileptic drug use.

## Ethics

**Informed Consent:** Informed consent was obtained from the patients.

**Peer-review:** External and internal peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: M.H.A., Concept: R.Ç., Design: F.G., Data Collection or Processing: F.G., M.H.A., Analysis or Interpretation: F.G., R.Ç., Literature Search: M.H.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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