Case Report

A case of early morning abnormal behavior and refractory epilepsy

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Insulinomas are rare neuroendocrine tumors of pancreatic islet cells that retain the ability to produce and secrete inappropriately high insulin. The clinical symptoms of insulinoma are the subsequent to development of hypoglycemia. We herein present a case of one patient who had been symptomatic for 6 years with symptoms of early morning abnormal behavior and refractory epilepsy, which eventually was diagnosed as a case of Insulinoma and could be cured after successful removal of lesion. All patients with unexplained abnormal behavior and seizure disorder should have blood glucose level checked during the episode.

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Key words **: Epilepsy, hypoglycemia, insulinoma**

Case Report

A 54 year old lady was admitted for evaluation of refractory epilepsy. She had been symptomatic since last 6 years, when she started having episodes of abnormal behavior early in the morning. Her husband with whom she lived reported that her abnormal behaviors were in multiple forms like repeatedly cleaning the house at same place or many times she used to be confused and was reacting inappropriately to situations. During these episodes minimal sweating was noticed by her husband, otherwise she didn't have any other complaint during the episodes. Also, she could not remember these episodes. Earlier frequency of these episodes was approximately one episode once a week. Other than early morning frequent episodes, day time episodes were observed when she used to have fast for religious reasons. She was seen by a neurologist and was started on antiepileptic drugs after a diagnosis of seizure disorder. Her electroencephalography (EEG) and magnetic resonance imaging (MRI) of brain was normal. Because of no response even with multiple antiepileptics, she was referred to psychiatrist and was treated with antidepressant and antipsychotic drugs with no response. Frequency and severity of these episodes worsened gradually. Over the years, her husband had noted that the symptoms could be promptly relieved by giving the patient morning tea, which was a custom in the house to have with jaggery. Two years before hospitalization, she also started having episodes of generalized tonic-clonic seizures followed by unconsciousness almost daily early in the morning. Subsequently patient had consultation with many neurologists, with frequent change of antiepileptics and psychiatric medication. She was labeled as a case of refractory epilepsy and was hospitalized for evaluation. During one of episodes in hospital her blood sugar was found to be low. Subsequently, multiple episodes of hypoglycemia could be documented with corresponding inappropriately high insulin and c peptide levels. She had no personal or family history of diabetes mellitus, and was not taking oral hypoglycemics or insulin. Her episodes of hypoglycemia and corresponding laboratory values are summarized in Table 1.

Finally, a diagnosis of hyperinsulinemic hypoglycemia was made and for localization she underwent multiphasic computed tomography (CT) and MRI of abdomen, in which arterial enhancing lesion in body of pancreas was found. Meantime she was started on frequent complex carbohydrate based diet with two additional night time feedings, which failed to control her early morning and nocturnal hypoglycemic episodes. After that she was started on 5 mg prednisolone at bed time in view of inappropriately low cortisol response at many times during hypoglycemic episodes (Table 1), which is well described in literature in patients with Insulinoma[1,2]. After that her hypoglycemic episodes could be controlled and she didn't have any further episodes of hypoglycemia in next six weeks. All antiepileptics' were discontinued, with no recurrence of seizures. She was also detected to have hypertension and was controlled on amlodepine 10 mg/day and enalapril 5 mg/day preoperatively. Work up for secondary causes of hypertension, including for pheochromocytoma was negative. Subsequently patient was operated and 1 x 1 cm lesion was identified in body of pancreas during intraoperative palpation, and was also confirmed in intraoperative ultrasonography and successfully removed. Histopathology confirmed the lesion to be an insulinoma. Postoperative period was uneventful; she was rapidly tapered off steroids after that. After 10 months of surgery, the patient was symptom free, and has normal blood glucose values.

Discussion

Insulinomas are rare neuroendocrine tumors of pancreatic islet cells that retain the ability to produce and secrete insulin. The clinical symptoms of insulinoma are the subsequent development of symptoms of hypoglycemia. The leading symptoms establishing the diagnosis of endogenous hyperinsulinism comprise the Whipple's triad. This includes : (1) symptoms of neuroglycopenia, (2) documented hypoglycemia (plasma glucose levels <50 mg/dl), and (3) symptoms relief (often within 5-10 minutes) following glucose administration[3]. Clinical manifestations of an insulinoma can mimic central nervous system disorders, like epilepsy and psychiatric disturbances[4]. Dizon AN *et al*, reported that before the confirmation of diagnosis of insulinoma, 39% of the cases are diagnosed as epi-

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Table 1 — *Episodes of documented hypoglycemia in hospital and corresponding laboratory values*

BG (mg/dl) Glucometer value	BG (mg/dl) Laboratory value	Serum Insulin (µU/ml)	Serum C-peptide (ng/ml)	Serum cortisol (µg/dl)	Plasma ACTH (pg/ml)	Serum GH (ng/ml)
39	42	33.44	7.08	10.81	Not done	0.224
48	51	47.34	7.53	4.58	21.47	0.223
38	40	23.33	6.82	13.72	7.99	0.061

BG- Blood glucose; ACTH-Adrenocorticotropic hormone; GH- Growth hormone

lepsy, 12% of the cases are treated with antiepileptic drugs, and 89% of patients with insulinoma are confused while 64% of them have personality changes and abnormal behaviors[5]. Chronic hypoglycemic symptoms associated with hypoglycemia appear in patients with insulinoma and in many diabetic patients treated with excess insulin, and these symptoms are similar to schizophrenia, depression, and dementia.

Our patient typically had episodes of abnormal behavior and confusions in early morning before breakfast, and later had more severe episodes associated with generalized tonic clonic seizures. However typical history was overlooked and only after six years, correct diagnosis was made. In summary, the symptoms caused by hypoglycemia show great variability and hence the difficulty in the diagnosis. Higher brain dysfunction might become permanent if the diagnosis of insulinoma is delayed. Atypical seizure or abnormal behaviors, especially in the fasting state, are sometimes observed as hypoglycemic symptoms of insulinoma. Clinicians should take the history of symptoms carefully. Insulinoma should be considered in patients with no reason for having drug-resistant epilepsy, and blood sugar measurement should be a routine investigation at time of witnessed seizures. Another important point that our case highlights that transient hypothalamic- pituitary- adrenal axis suppression can be there in patients with insulinoma with its recovery after successful surgery[1,2]. In fact, our patient very well responded to 5 mg/day prednisolone daily at bed time, which is likely a good therapeutic option in these patients till they are waiting for surgery to take care for life threatening hypoglycemias. There are very few previous reports of short term successful use of steroids in patients with insulinomas[1,6]. Suzuki K *et al*[7], have also reported one patient of insulinoma presenting with stereotypical abnormal behavior of nocturnal paroxysmal arousals, including wild laughing and walking around early in the morning and complete amelioration of these symptoms on prednisolone 10 mg/day at bed time after the diagnosis.

Conflict of interests : None

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