

Paroxysmal dystonic choreoathetosis with symptomatic seizures secondary to hypoglycemia caused by insulinoma

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Abstract

Neurological syndromes are not an uncommon presentation with insulinomas. Recurrent hypoglycemia associated with it can present with a variety of neurological symptoms that may include disturbances of consciousness, seizures, stroke-like presentation, movement disorder, dementia and chronic neuropathy. The myriad of presentations, resemblance with other neurological conditions and episodic nature often lead to misdiagnosis and a delay in definitive treatment. Rare cases of insulinoma presenting as combination of abnormal movements have been described. We report a patient who presented with both hypoglycemia induced symptomatic seizures and paroxysmal non-kinesiogenic dystonic choreoathetosis. Insulinoma is a potentially treatable disorder and early definitive intervention can prevent long term neurological disability in patients.

Key Words

Hypoglycemia, insulinoma, movement disorder, seizures

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Introduction

Paroxysmal non-kinesiogenic dystonic choreoathetosis (PDC) refers to attacks of dystonic posturing, chorea, ballismus or athetosis in varying combinations. The duration of these episodes ranges between few minutes to hours but are less frequent than paroxysmal kinesiogenic choreoathetosis. They are not precipitated by sudden movement or response to startle. Most reported cases of PDC are idiopathic or familial in etiology. Rare associations of paroxysmal dyskinesias secondary to hypoglycemia have been described. We describe a lady with symptomatic seizures and episodes of paroxysmal non kinesiogenic dystonic choreoathetosis caused by recurrent hypoglycemia secondary to an Insulinoma.

Case Report

A 24 year-old female, teacher by profession, with normal birth and developmental history, presented with a history of generalized tonic clonic seizures since three years and

frequent episodes of bizarre posturing of limbs followed by unresponsiveness since one and half years.

She was well until three years back when she had the first episode of sudden loss of consciousness with repetitive tonic clonic movements of all four limbs and tongue bite. This was not associated with any prodrome, aura or any postictal automatisms or autonomic symptoms. The episodes were short lasting (usually about a minute) and not followed by any focal neurological deficit and the frequency being two to three episodes per month. There was no history of myoclonic jerks or any definite relation to sleep deprivation or menstrual cycle and no family history of seizures. MRI of Brain and a routine EEG done prior to coming to this hospital were normal. At some other hospital, based on a diagnosis of Juvenile Myoclonic Epilepsy, sodium valproate with a maximum total dose of 1250 mg/day and clobazam with dose of 20 mg/day, was started. As per the patient the seizure frequency had not changed significantly on treatment. She had gained weight and also developed menstrual irregularities on medications and hence she left all her medications nearly an year ago.

Nearly one and half years ago, she started to have episodes which were more prolonged with a gradual progression of symptoms. She would start having bizarre, flinging movements of all four limbs and neck, without tonic clonic movements, jaw clenching, tongue bite or incontinence. At the onset of the episode she would be partially responsive but would lapse

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into drowsiness over the next few minutes. These would be precipitated whenever she would delay her meals or miss meals but had no relation to exercise or movement. Also the mother used to feed her in this state of reduced responsiveness and over next few minutes she would gradually improve. There was history of amnesia for these episodes. As a result the mother had started giving her meals every two to three hours and even wake her up at midnight to feed her. The duration of these would range from few minutes to about half an hour. She had also started feeling hungry more frequently and had gained weight in the last one year. During the same period she also continued to have generalized tonic clonic seizures.

A provisional clinical diagnosis of generalized tonic clonic seizures, probably idiopathic generalized epilepsy with Non epileptic attacks, was made.

She was admitted for evaluation. On examination she was found to be obese. Rest of her general physical examination including the vitals revealed no abnormality. Examination of her nervous system including higher mental functions, cranial nerves, sensorimotor system and extrapyramidal system were all normal.

The patient was instructed to miss her meals and concomitant video-EEG monitoring was done.

A typical attack was induced after 2 hours. Her extremities became cold and she started sweating profusely. She was confused but able to respond to questions. Almost simultaneously she started having involuntary, unpurposeful, non-rhythmic, asynchronous bizarre movements of her limbs, abnormal posturing, opisthotonus posturing, tongue darting, facial grimacing and limb thrashing. There were no tonic or clonic components. A random blood glucose level was done by finger prick method and was found to be 24 mg% (normal 55-100 mg%). She was infused intravenous dextrose and within a few minutes she regained consciousness and the movements subsided.

Regular monitoring of her blood glucose revealed spontaneous asymptomatic hypoglycemia at several occasions per day (as low as 35 mg%), precipitated by fasting. However, the attacks occurred only when her blood sugar decreased to < 25 mg%.

One episode of generalized tonic clonic seizure with tongue bite, lasting for a minute was witnessed in the ward during the morning hours. A random blood sugar done at that time was 45 mg%.

In view of the abnormal movements being a combination of chorea, ballism and dystonia with prolonged duration, no temporal relation to movement or any form of startle, we diagnosed them as being Paroxysmal non-kinesiogenic dystonic choreoathetosis. As a possible etiology for symptomatic recurrent hypoglycemia and weight gain, Insulinoma was suspected. Serum fasting insulin levels were done and were found to be markedly elevated in the range of 106 IU/L (Normal lab values 2.6-24.9 IU/L). MRI of abdomen with contrast revealed a hypoechoic mass lesion in the distal pancreas, size 2 × 3 cm with no evidence of local or distant metastasis, possibly Insulinoma Figures 1 and 2.

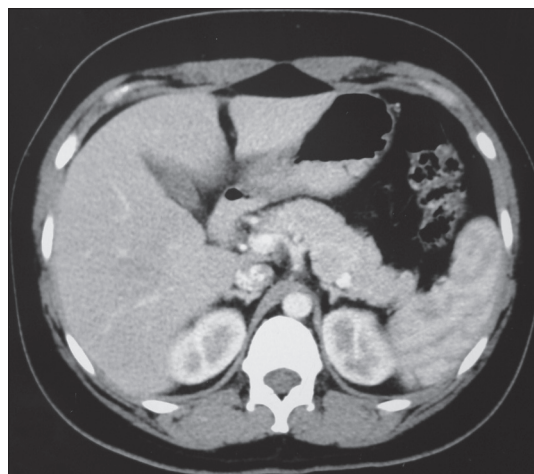


Figure 1: Axial section CECT Abdomen showing hyperechoic mass in distal pancreas and head of pancreas

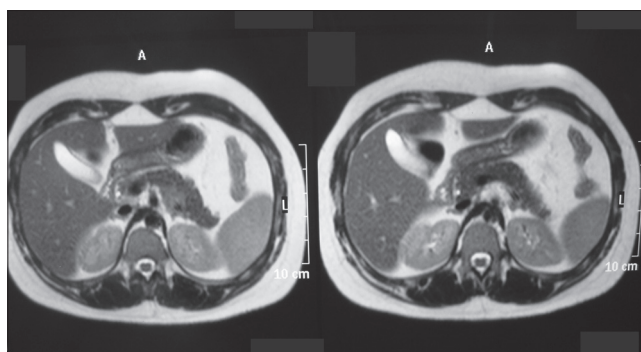


Figure 2: Axial section MRI Abdomen showing hypoechoic mass in distal pancreas

EEG done during the episode showed intermittent sharp waves and spike and wave discharges in the period preceding the episodes. Blood sugar levels were also done simultaneously and the electrographic discharges were found to appear only during hypoglycemic periods and subside when normoglycemia was restored. Interictal EEG record, however, was normal.

She was given frequent small meals and was given intravenous dextrose only if she became symptomatic. She underwent a laparotomy and was found to have a 3 × 3 cm firm tumor in the postero-superior aspect of distal pancreas adherent to the splenic vein, without any distant metastasis. A distal pancreatectomy with splenectomy was performed. Histopathology of the mass confirmed the diagnosis of insulinoma with an uncertain malignant potential, with the pancreatic resection margin and lymph nodes free of the tumor.

Presently she is doing well after the surgery and has been totally symptom-free since last 6 months. She has been off all antiepileptic drugs with no recurrence of seizure or abnormal movements.

Discussion

Our patient had presented with a paroxysmal abnormal movements and seizures due to recurrent symptomatic

hypoglycemia and hence a diagnosis of Insulinoma was suspected. The atypical and bizzare nature of the episodes, the change in the semiology compared with the previous episodes led us to initially consider a diagnosis of non-epileptic attacks.

Only after the direct observation of the attacks combined with Video EEG monitoring, these could be diagnosed as Paroxysmal non-kinesiogenic dystonic choreoathetosis including combination of chorea, ballism and dystonia. The interval between the onset and diagnosis in our case was 18 months. After the removal of the tumor and off all antiepileptic drugs, she did not have recurrence of generalized seizures hence proving that those seizures were probably secondary to hypoglycemia.

Insulinomas are the commonest pancreatic endocrine tumors, derived from the pancreatic islet beta cells that ectopically secretes insulin and result in hypoglycemia.^[1] The most common age of presentation is between 30 and 60 years, with a female preponderance.^[2,3] They are generally small (>90%, <2 cm), usually not multiple (90%), and only 5–15% are malignant. These almost invariably occur only in the pancreas, distributed equally in the pancreatic head, body and tail.^[4] Most insulinomas are sporadic in origin, although 5–10% may occur in association with multiple endocrine neoplasia type I syndrome.^[5,6]

When clinically suspected, a supervised prolonged fast (up to 72 hours) under close monitoring should be performed to demonstrate hypoglycemia. A glucose level <45 mg/dL (2.5 mmol/L), a C-peptide level >0.2 nmol/L and an insulin level <6 mU/mL (36 pmol/L) can confirm the diagnosis of insulinoma.^[7]

Neurological and psychiatric symptoms are common manifestations of patients with insulinomas. Hypoglycemic episodes can mimic as disorders of awareness, consciousness, epilepsy, transient ischemic attacks or psychosis and if uncontrolled can result in cognitive impairment. In a retrospective study of 59 patients with histologically confirmed islet cell adenomas, the most common presenting diagnoses included neurological disorders (64%), especially seizure disorder (39%) while 8% patients were diagnosed as psychiatric disorder. All patients had neuroglucopenic symptoms including confusion, personality change or bizarre behavior. Autonomic symptoms including diaphoresis and tremulousness were seen in 83% patients. Food ingestion relieved symptoms in three quarters of patients and 39% reported weight gain.^[8]

Although cases of insulinoma presenting with seizures or intractable epilepsy have been described in literature, abnormal movements with hypoglycemia, are rare as presenting symptoms. Marsden *et al.*, have described a lady with islet cell tumor, with dystonic posturing of limbs and trunk during recovery from hypoglycemic episode.^[9] Shaw *et al.*, also reported a case with paroxysmal non-kinesiogenic dystonic choreoathetosis in a young female with Insulinoma-induced hypoglycemia, precipitated by exercise and fasting.^[10] In another recent report by F Debruyne *et al.*, a young female with episodes of paroxysmal non-kinesiogenic dyskinesias with documented hypoglycemia has been described, who had a biopsy proven insulinoma and had remission following surgical resection of the lesion.^[11] The exact mechanism for

these movements is unknown but it has been postulated that recurrent hypoglycemia may cause a temporary striatal dysfunction, which in turn may lead to defective pallidal and subthalamic inhibitory outflow to the thalamus, with overactivity of thalamocortical excitatory projections resulting in hyperkinesias.^[10]

Very few cases of insulinoma presenting with either seizures or as paroxysmal complex movements have been described in the literature, most of them from the West. Thus, we report an uncommon neurological presentation of insulinoma complicated by presence of coexistent symptomatic seizures.

Hypoglycemia secondary to insulinoma due to its episodic nature and a wide variety of neurological manifestations has been often misdiagnosed. However, a detailed clinical history, its relation to meals/exercise and high index of clinical suspicion can help in its diagnosis. Early definitive treatment can help prevent further attacks, avoid unnecessary use of antiepileptics and prevent permanent neurological deficits in these patients.

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