Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 10, Issue, 06, pp.70219-70222, June, 2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

A CASE OF INSULINOMA PRESENTING AS SPELLS OF ALTERED CONSCIOUSNESS UNMASKED BY DRUGS

***Dr. Henna Naqash, Prof. Parvaiz Ahmad Shah, Dr. Ishrat Hussain Dar, Dr. Mohammad Hayat Bhat, Muzaffar Maqbool and Dr. Mohd Mansoor**

Senior Resident at GMC Srinagar, Department of General Medicine, R/o Aalikadal, Srinagar, J and K India

ARTICLE INFO

Article History:
Received 14th March, 2018
Received in revised form
29th April, 2018
Accepted 10th May, 2018
Published online 28th June, 2018

Key words:

Hypoglycemia, Personality,
Insulin, Neuroendocrine,
Pancreas.

****Corresponding author***

ABSTRACT

A 35 year old male, shopkeeper by occupation, presented to us with recurrent spells of altered consciousness with varying features for last 1 year. He was labelled as depression and was on velazodone for the same. He was finally diagnosed as insulinoma, likely unmasked by the drug. He was managed with surgery and is doing well. With this case, the importance of considering hypoglycemia in atypical neurological or psychiatric episodes is highlighted.

Citation: Dr. Henna Naqash, Prof. Parvaiz Ahmad Shah, Dr. Ishrat Hussain Dar, Dr. Mohammad Hayat Bhat, Muzaffar Maqbool and Dr. Mohd Mansoor. 2018. "A case of insulinoma presenting as spells of altered consciousness unmasked by drugs", *International Journal of Current Research*, 10, (06), 70219-70222.

INTRODUCTION

Insulinoma is a neuroendocrine tumor that is derived from the pancreatic islet cells. It is rare (1 to 5 per million persons per year), occurs more commonly in females and age above 50 years (Bliss, 1997). Due to its rarity and the paroxysmal occurrence of insulinoma-induced hypoglycemic symptoms, the diagnosis is often delayed (Wang *et al*., 2008; Graves, 2004; Bazil, 2001). Hypoglycemia can cause two types of symptoms namely adrenergic and neuroglycopenic. The adrenergic symptoms include diaphoresis, palpitations, tachycardia, hunger, visual disturbances, altered temperature perceptions and enhanced physiological tremors and are most pronounced with acute onset of hypoglycaemic episodes. The neuroglycopenic symptoms include headache, malaise, impaired concentration, confusion, slurred speech, disorientation, irritability, lethargy, stupor and even coma, generalized seizures, myoclonus, and psychiatric disturbances. Focal neurologic dysfunction, including focal seizures, hemiplegia, paroxysmal choreoathetosis, and patchy brain stem and cerebellar involvement sometimes resembling basilar artery thrombosis, have also been reported (Rother, 1992). With subacute onset, drowsiness, lethargy, decreased psychomotor activity, cerebellar ataxia and confusion may be observed (Jonathan, 2008), and when chronic, the insidious onset of memory, personality, and behavioral disturbances may suggest dementia (Hemalkumar *et al*., 2017). It occurs because of the re-setting of the glucosensor in the ventromedial hypothalamus (Cryer *et al*., 2003) and hypoglycaemia itself leads to autonomic unawareness. Hypoglycemia can cause insomnia and fearful dreams. Insulinoma can present as panic attacks, vague irrational behavioural disorders, episodic unresponsiveness and jerking of body parts, personality changes, and even dystonia and polyneuropathy. The differential diagnosis for symptoms suggestive of hypoglycemia includes many common neurologic and psychiatric disorders, seizures, hyperventilation, and anxiety attacks, syncope with exercise due to some cardiologic cause, episodic spells due to simple orthostatic hypotension or vasovagal syncope or the more disabling postural orthostatic hypotension syndrome .

According to Whipple, the following triad should exist before elaborate testing is performed for evaluating a rare insulinoma:

- Neuroglycopenic symptoms consistent with hypoglycaemia.

- Documentation of low plasma glucose with a reliable assay.
- Relief of symptoms after normalization of plasma glucose.

Case Report: A 35 year old male, shopkeeper by occupation, presented to us with recurrent spells of altered consciousness with polymorphic features for last 1 year. He was having one such episode at presentation. He was not fully unconscious but was confused and disoriented. There was no urinary incontinence, tongue bite or abnormal body movements. There were no palpitations, dizziness, sweating or hunger. There was no previous history suggestive of any substance abuse, hypertension, stroke or any hospital admissions. Patient was hemodynamically stable. ECG was normal. He remained in this state for about 20 minutes till his random serum glucose was available and reported 40 mg/dl. He was given dextrose parenterally and he recovered promptly and completely. Thus he fulfilled the Whipples triad and his repeat sugar was normal. He had partial amnesia of the event. Family history was not significant. On examination, patient was a well built male, confused, not fully oriented with time and place. His vitals were normal. Systemic examination was normal. There was no focal neurodeficit. Height was 170 cm, weight 66 kg and body mass index of 22.83.At normoglycemia, his mini mental status score was normal. Patient had similar complaints for last 1 year and consulted many practitioners for the same. He complained to have episodic spells of drowsiness, confusion, difficulty concentrating, sometimes unable to speak, numbness of body and memory impairment. His family members had also noticed intermittently bizarre behaviour and personality changes in him. He had these spells at a frequency of two to three times in a month initially. As per the patient, he could get the spells at any time during daytime with no noticed diurnal variation. However, these symptoms had progressed and occurred more frequently, about once a week for last 2-3 months. He reported no symptoms of shakiness, palpitations or perspiration. He was investigated with brain imaging with CT and MRI which were normal. He had undergone EEG of brain but that was normal.

Thus possibility of non epileptic seizures was provisionally ruled out. He was labelled as a case of depression and managed with anti depressants. However, he was very non compliant to his medications and had a poor follow up. Patient had been prescribed velazodone 10 mg initially with dose increments and was presently taking 40mg of this drug. A provisional diagnosis of hypoglycaemia was made and patient was evaluated for the same. Probably, velazodone had unmasked his symptoms and increased the frequency of hypoglycaemic episodes. During hospital stay, he had several documented episodes of hypoglycaemia with neuroglycopenic symptoms without any adrenergic ones. He had a normal hemogram, kidney and liver function tests and lipid profile. Serum electrolytes Na, K, Ca, P were normal. There was no acidosis or alkalosis on blood gas analysis. USG abdomen was reported normal except obscured body and tail of pancreas which could not be commented upon. An extended glucose tolerance test was planned, patient was given 75g oral glucose (and following results were obtained

Blood sugar level (in mg/dL):

F: 56
1h: 120
2h: 116
3h: 44
4h: 50
5h: 52

CECT Abdomen: A well defined soft tissue density nodule 14 x 11 mm noted at junction of pancreatic body and tail at inferior border, 40 HU on non contrast and 137 HU homogeneous enhancement on contrast. No calcification in the lesion. Rest of pancreas normal.Liver, Gall bladder, Portal vein, Spleen, Adrenals all normal. Triple Phase CT abdomen Figure 1. Relatively well defined hyperenhancing lesion (on arterial phase) measuring 18 x 14 mm in pancreatic tail region with well preserved surrounding fat planes, suggestive of Neuroendocrine tumour Rest of study normal.
At the time of fasting blood sugar 50 mg/Dl,

Serum Insulin: 9.4 microU/mL

Fasting C-Peptide (using CMIA):1.30 ng/mL. Critical diagnostic findings for diagnosing Insulinoma are

- Plasma Insulin concentration > 3 microU/Ml.
- Plasma C-peptide >0.6 ng/mL
- Plasma Peoinsulin >5.0 pmol/L
- At a plasma glucose <55 mg/dL
- With symptoms of hypoglycaemia.

Serum PTH: 18 ng/mL (normal).

Serum Ca: 9.7 mg/dL (nomal).

Serum Prolactin : 12ng/mL (normal)

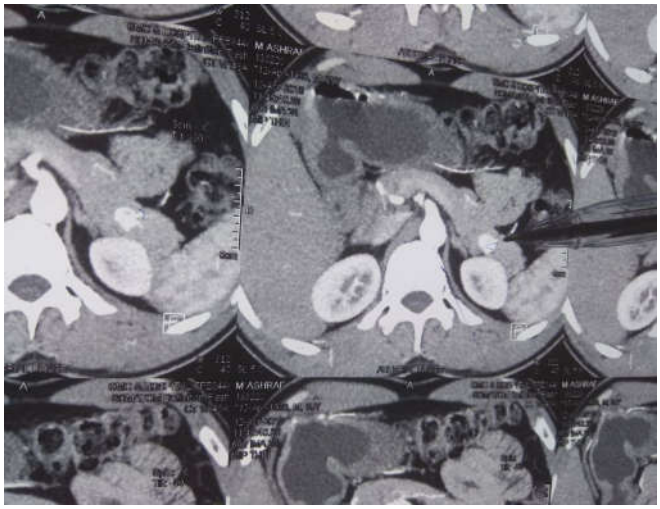

Figure 1.

Velazodone was stopped from first day and patient was started on Verapamil 120mg .He was advised to take frequent meals with corn flakes included in the diet. Meanwhile he was planned for surgery. He underwent surgical removal of the tumour which was subjected to histopathologic examination. This was done on a distal pancreatectomy specimen measuring 6.5X 4X 2.5 cm with dark brown capsulated growth at tail measuring 2X2 cm. HPE revealed a tumour arranged in trabeculae, pseudoglandular, ribbons and nesting pattern. Individual cells minimally pleomorphic with round nuclri, prominent nucleoli and stippled chromatin with < 2/10 per hpf

mitosis suggesting a well differentiated neuro endocrine tumour (insulinoma). On immunohistochemistry marking (Ki 67), immunoreactive score 3+ in 15% neoplastic cells. The patient is now doing well, off any medication, and is on continuous follow up. His blood sugars are normal now and his symptoms have also subsided.

DISCUSSION

Insulinoma presentation is usually insidious with neuroglycopenia and fasting hypoglycemia. The median interval from onset of symptoms to the diagnosis of insulinoma is 2 years with a range of one month to 30 years as reported by Service F. and colleagues (Service *et al*., 1976). Drugs used to treat diabetes mellitus are the most common cause of hypoglycemia. Insulinoma is the most common cause of hyperinsulinemic hypoglycaemia. MEN associated insulinomas usually occur before 40 years of age. A careful search for other components of the MEN-1 syndrome (hyperparathyroidism, anterior pituitary tumours, positive family history) should be undertaken in all patients of insulinoma (Service *et al*., 1991; Machens *et al*., 2007). EEG can be misleading in insulinoma since hypoglycemia can affect it by causing diffuse or focal slow activity.Seizure disorder is described in a few cases of persistent hypoglycemia later on diagnosed as insulinoma like those reported by Akanji A. and colleagues in 1992 and by Basil C. and Pack A. in 2001(Akanji *et al*., 1992; Bazil, 2001). Wang S. and his colleagues have described recurrent episodes of automatism, confusion and convulsions with electroencephalography (EEG) findings resembling the pattern in complex partial seizures in a case of insulinoma (Wang *et al*., 2008). An interesting report by Jaladyan V. and Darbiyan V. described a girl presenting with drug-refractory myoclonus and generalized tonic-clonic seizure initially misdiagnosed as having juvenile myoclonic epilepsy before insulinoma was detected (Jaladyan *et al*., 2007).

O'sullivan S. and Redmond J. also presented a case of insulinoma misdiagnosed as late onset refractory epilepsy(O'Sullivan, 2005). In Daggett and Nabarro's review of 252 reported cases the most common neurological symptoms were confusion, coma, and seizures (Daggett, 1984). Newman and Kinkel have reported a diabetic woman who developed two episodes of limb choreoathetosis and opisthotonus associated with hypoglycaemia (Newman, 1984). Winer *et al.* described a woman with an insulinoma who, developed abnormal posturing of her body when recovering from hypoglycaemic attacks (Winer *et al*., 1990). Chronic neuropathic and dementing syndromes due to hypoglycemia have also been described by Danta G. and Snook J. and his colleagues (Danta, 1969; Snook, 1986). In a prospective survey by Harrington M., two of 25 patients referred to neurologists with "funny turns" were found to have an insulinoma (Harrington *et al*., 1983). With this case, the importance of considering hypoglycemia in atypical neurological or psychiatric episodes is highlighted. Neuroglycopenia should be considered in all such patients with seizures, and other neuropsychiatric symptoms, who do not conform to diagnostic criteria or respond to standard treatment. Taking a full history and clinical suspicion are the key to making a diagnosis of insulinoma. Once suspected, confirming the diagnosis with a 72 h fast is relatively simple. In various retrospective reviews, ≤64% patients with insulinoma presenting with neuropsychiatric symptoms were misdiagnosed with neurological disorders (Ding, 2010; Dizon, 1999). According to the literature, surgical resection of insulinoma is curative in ~90% of the cases (Service *et al*., 1991). Velazodone is a drug with combined selective serotonin-reuptake inhibitor and serotonin type 1-A receptor partial agonist activity. It is used for the treatment of major depressive disorder in adults. It is started at 10mg per day and dose is increased on weekly basis upto 40mg a day.Its mean terminal half-life is 25 hours. Hypoglycemia is found among people who take this drug, especially in those who are males, 50-59 year old , have been taking the drug for < 1 month, and are also using insulin or have Diabetes. Hypoglycemia due to this drug affects females and males equally. It causes very little traditional tricyclic, extrapyramidal side effects and tardive syndromes as compared to typical antipsychotics, so preferably used.

Conflict of Interest: None.

Financial support: None.

REFERENCES

Akanji AO, George AO, Olasode BJ, *et al*. 1992. Insulinoma in pregnancy presenting as a seizure disorder: a case report. *East Afr Med J.*, 69(2):117–119.

Bazil CW, Pack A. 2001. Insulinoma presenting as seizure disorder. *Neurology*.56:817–8.

Bliss RD, Carter PB, Lennard TW. 1997. Insulinoma: A review of current management. *Surg Oncol.,* 6:49–59.

Cryer PE. 2003. Hypoglycaemic disorders. In: Larsen PR, Kronenberg HM, Shlomo M *et al* (eds). Williams Textbook of Endocrinology. *Philadelphia, Saunders*. pp 1585- 1618.

Daggett P, Nabarro J. 1984. Neurological aspects of insulinomas. *Postgrad Med J.* , 60(707):577–581.

Danta G. 1969. Hypoglycemic peripheral neuropathy. *Arch Neurol.* 21(2):121–132.

Ding Y, Wang S, Liu J, Yang Y, Liu Z, Li J, Zhang B, Chen Y and Ding M. 2010. Neuropsychiatric profiles of patients with insulinomas. Eur Neurol 63: 48-51.

Dizon AM, Kowalyk S and Hoogwerf BJ. 1999. Neuroglycopenic and other symptoms in patients with insulinomas. Am J Med 106: 307-310.

Graves TD, Gandhi S, Smith SJ, Sisodiya SM, Conway GS. 2004. Misdiagnosis of seizures: Insulinoma presenting as adult-onset seizure disorder. *J Neurol Neurosurg Psychiatry.* 75:1091–2.

Harrington MG, McGeorge AP, Balantyne JP, *et al*. 1983. A prospective survey for insulinomas in a neurology department. *Lancet.* 1(8333):1094–1095.

Hemalkumar B Mehta, Vinay Mehta, James S Goodwin. 2017. Association of Hypoglycemia with Subsequent Dementia in Older Patients with Type 2 Diabetes Mellitus. *The Journals of Gerontology*: Series A ,Volume 72, Issue 8.1110-1116.

Jaladyan V, Darbinyan V. 2007. Insulinoma misdiagnosed as juvenile myoclonic epilepsy. *Eur J Pediatr.* 166(5):485–487 .

Jonathan P B Berz and Jay, D. 2008. Orlander. Prolonged Cerebellar Ataxia: An Unusual Complication of Hypoglycemia. *J Gen Intern Med*., Jan; 23 (1):103-105.

Machens A, Schaaf L, Karges W. *et al*. 2007. Age related penetrance of endocrine tumors in multiple endocrine neoplasia type 1: a multicentre studyof 258 gene carriers. Clin Endocrinol (Oxf) 67:613-622.

Newman RP, Kinkel WR. 1984. Paroxysmal choreoathetosis due to hypoglycemia. *Arch Neurol.,* 41(3):341–342 .

O'Sullivan SS, Redmond J. 2005. Insulinoma presenting as refractory late-onset epilepsy. *Epilepsia* 46(10):1690–1691.

Rother, J., Schreiner, A., Wentz, K.U. and Hennerici, M. 1992. Hypoglycemia presenting as basilar artery thrombosis. *Stroke*., 23:112-113.

Service FJ, Dale AJ, Elveback LR, *et al*. 1976. Insulinoma, clinical and diagnostic features of 60 consecutive cases. *Mayo Clin Proc.* 51(7):417–429 .

Service FJ, McMohan MM, O'Brien PC, Bellard DJ. 1991. Functioning insulinoma—incidence, recurrence and long term survival of patients:a 60-year study. *Mayo Clin Proc.,* 66:711-719.

Snook JA, Vander Star R, Weller RO. 1986. Insulinoma producing progressive neurological deterioration over 30 years. *Br Med J.*, 293(6541):241–242.

Wang S, Hu HT, Wen SQ, Wang ZJ, Zhang BR, Ding MP. 2008. An insulinoma with clinical and electroencephalographic features resembling complex partial seizures. *J Zhejiang Univ Sci B.* 9:496–9.

Winer JB, Fish DR, Sawyers D, *et al*. 1990. A movement disorder as a presenting feature of recurrent hypoglycaemia. *Mov Disord.* 5(2):176–177.

****