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Case Report

Retroperitoneal mesenchymal tumour presenting as recurrent hypoglycaemia and seizures – A rare presentation

***Santokh Singh[a] Gianchand[b] Sumeet Singh[c] Gurveenpal Singh[d] Parampreet Singh[e]**

[a]Professor & Head [b]Astt.Professor [c]Junior Resident [d]Clinical associate [e]Intern
Department of Medicine & Gastroenterology, Govt. Medical College, Amritsar, INDIA.

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ABSTRACT

Seizure disorder is a common disease in the world with a prevalence rate of 5-10 persons per thousand persons. The present patient 24 year old unmarried, non diabetic female, presented with recurrent episodes of hypoglycemia and seizures for the last 4 months, which were relieved on intake of dextrose, orange juice and other eatables. On examination and workout of the patient, there was no suggestion of inherited or genetic disorder, ICSOL, infections, vascular cause, toxic cause, drug use, drug abuse and metabolic disorders . The insulin levels and HbA1c levels were normal. She was found to have a retroperitoneal mass, which on further investigation was proved to be retroperitoneal malignant mesenchymal tumour of spindle cell variety, which was responsible for recurrent episodes of hypoglycemia and seizures. The disease entity is very rare and the presentation in this patient is very very rare. Therefore, this case is being reported.

1. Introduction

Seizure disorder is a common clinical presentation in Emergency Room and OPD. The usual causes of seizure disorders vary in different age groups and in geographical locations common causes being inherited & genetic, tumours, infections, vascular diseases, hippocampal sclerosis, toxic disorders like alcohol, drugs abuse, and metabolic disorders like hypoglycaemia [1]. In the present case under discussion patient had recurrent tonic seizures for last 4 months and was being treated with oral dilantin sodium (300 mg/day) without finding a cause. The patient was investigated in our institution, which came out to be hypoglycemia due to retroperitoneal malignant mesenchymal tumour which is a relatively a rare entity.

2.Case History

A 24 year old unmarried non diabetic female was brought to Emergency Room on 7th July 2011 with complaint of tonic seizure which lasted for 4 to 5 minutes followed by loss of consciousness.

* Corresponding Author : Dr Santokh Singh
9-FF HIG Flats A-Block Ranjit Avenue Amritsar -143001,
Punjab,INDIA.
Mobile :9814313689
E.mail: profsantokhsingh@gmail.com
dr_sumeet2005@yahoo.co.in

There was no history of headache, blurring of vision, vomiting, tongue bite, frothing, urinary or fecal incontinence, fever or neurological deficit. There was no history of drug abuse or drug intake except tablet dilantin. No past history of head injury. She used to have symptoms of sweating, tachycardia, sinking sensation, generalized weakness followed by seizures. These symptoms used to get relieved with intake of sugar, orange juice or other eatables. She had many such episodes in the past 4 months and a most of them used to occur in the morning hours. Physical examination revealed a moderately built and nourished female in deranged state of consciousness, but was responding to painful stimuli, having pulse rate 96 per minute and blood pressure of 120/80 mm of mercury and respiratory rate was 16 per minute. Pupils were bilaterally normal in size and normally reacting to light.

Deep tendon reflexes were absent and plantars were mute bilaterally. Meningeal signs were negative and fundus examination was normal. No neurological deficit was present. Per abdomen examination revealed non tender lump in left hypochondrium, epigastrium with smooth surface, hard in consistency measuring 13 X 11 cm, non ballotable and was not moving with respiration. Examination of CVS and respiratory system was normal. Laboratory investigation revealed capillary blood sugar 55 mg%

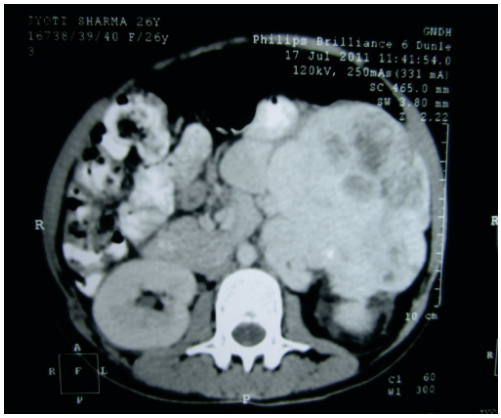
after which immediately I/V dextrose 25% 100 ml was given. The consciousness level of the patient improved with it. Hb 11gm% TLC 5600/ cu mm, DLC- P -65% ,L-33% , E-1% , M-1%. PBF was normal. Malarial parasite was negative. HbA1c was 5.5%. Blood Urea 22.0 mg% , Serum Creatinine 0.8 mg% , Serum bilirubin 1.0mg/Dl , SGOT -22 IU/L, SGPT- 41 IU/L, Total Serum Protein 6.7 g/dL , Serum Albumin 4.1 g/Dl . Serum Na 134.0 meq/l, Serum K 4.0 meq/l and Serum Ca 9.0 gm%.

CT scan of head and CSF examination were normal.

Ultrasonography of abdomen showed a mass of 13.3 cm X 8 cm X 8cm, appeared to be in relation to the body and tail of pancreas with multiple lymph nodes in peripancreatic and paraortic regions. Liver and spleen were normal.

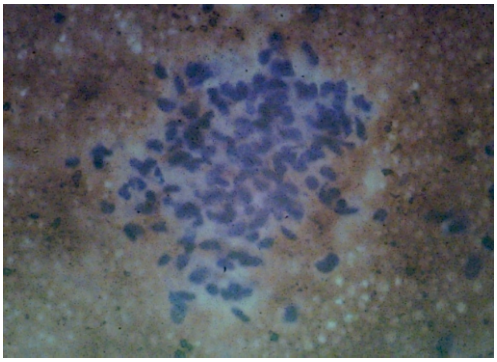
Patient was subjected to Contrast enhanced CT scan of abdomen which revealed a large heterogeneously enhancing mass in retroperitoneum, measuring 12.4 X 10.2 X 9.6 cm in size and showed central area of necrosis with peripheral enhancement. Few small calcified specks were seen in it. The mass was located in the left lumbar and hypochondriac regions with abdominal lymhadenopathy. The possibility of a neoplastic mesenchymal mass was kept. The mass was indenting the greater curvature of the stomach and it also displaced the left kidney inferiorly. Pancreas appeared to be compressed by this mass(Figure 1).

Figure 1



FNAC was done, which showed it to be having ovoid to spindle shaped cells, having hyperchromatic nuclei with contour irregularities thereby suggesting a Cellular Spindle Cell Neoplasm(Figure 2).

Figure 2



In view of her low capillary blood sugar level at the time of presentation and history of attacks more in the morning hours when patient used to be in a fasting state, suspicion of hypoglycemic seizures was thought of and patient underwent prolonged fasting test [2]. At the start of test, blood sugar levels were 186 mg%, after 3hrs 180 mg%, after 6 hrs 160 mg%, after 9 hrs 110 mg%, after 12 hrs 101 mg%, after 15 hrs 105 mg% , after 18 hrs 96 mg%, after 21 hrs 88 mg%, after 24 hrs 78 mg%, after 27 hrs 68 mg%, after 30 hrs 76 mg%, after 32 hrs 64 mg%, after 33 hrs 54 mg%, after 34 hrs 54 mg%, after 35 hrs 44 mg%, and after 36 hours patient started feeling drowsy followed by seizure like activity, at that time blood sample was drawn and sent for blood sugar levels, blood insulin levels and c peptide levels and prolonged fasting test was terminated and patient was given I/V dextrose. The patient improved on administration of dextrose infusion. Blood sugar was found to be 39 mg%, insulin levels came out to be 2.76 µIU/ml (Reference range, fasting: 2-25 µIU/ml) and c peptide levels were found to be <0.10ng/ml (Reference range: 0.9-7.1ng/ml). Ratio of insulin level and blood glucose was found out to be 0.07, suggesting that hypoglycemia is not occurring because of insulin excess (where ratio is more then 0.3) [2].

A PTH level was also ordered initially to rule out the possibility of Multiple Endocrine Neoplasia-I (MEN-I) if lab results came out to be suggestive of Insulinoma. However, the PTH level and Insulin levels were within normal range.

The patient was started on chemotherapy with a combination of inj. Ifsofamide 2g I/V for 3 days, inj Adriamycin I/V 50 mg on day 1 and 20 mg on day 2, along with above two drugs inj Mesna was given. Cycle was repeated after 21 days. After 2 cycles, in the patient there was clinical improvement as well as size of the tumour is regressing significantly.

3.Discussion

Seizure disorder is a common presentation in the hospitals. Prevalence of seizures is 5-10 persons per thousand. The usual causes of seizure disorder vary in different age groups and in geographical locations common causes being inherited & genetic, tumours, infections, vascular disease, hippocampal sclerosis, toxic disorders like alcohol, drugs, metabolic disorders like hypoglycaemia. The most common causes in young adults (18-35 years) are trauma, alcohol withdrawl, drug use, brain tumour and idiopathic. Metabolic disorders commonly cause seizures in the older adults (>35 years). Hypoglycemia being one of those [1].

Hypoglycemia is characterized by Whipple's triad – symptoms consistent with hypoglycemia, low plasma glucose and relief of symptoms after glucose levels are raised. Brain utilizes glucose as obligate fuel. In the absence of enough glucose, there occurs neuroglycopenic symptoms which include – behavioral changes, confusion, fatigue, seizure, loss of consciousness and if prolonged death can occur [3].

Hypoglycemia can be caused by various causes, most common among those being drugs used to treat diabetes mellitus for example insulin and sulfonylureas. Other causes are critical illness like hepatic, renal or cardiac failure or sepsis, hormone deficiencies like cortisol, growth hormone, non beta cell tumour, hyperinsulinemia due to insulinoma, ectopic insulin secretion, postgastrectomy, hereditary fructose intolerance [3].

In a patient with no history of diabetes or anti-diabetic treatment, who doesn't appear to be critically ill because of systemic failure or sepsis, which has no evidence suggestive of hormonal deficiency, no history of gastrectomy, we are left with the option of tumour induced hypoglycaemia. There are two major causes of tumor-induced hypoglycemia (a) Insulinoma and (b) Non-beta cell tumors [4,5].

Hypoglycemia associated with insulinomas is due to excess insulin levels produced by the tumour cells. Diagnosed by higher insulin levels (>6 microIU/mL) in the presence of low blood sugar (<40 mg/dL) with insulin to glucose ratio > 0.3 [2]. The incidence of insulinoma is very rare - 1-2 persons per 10 lac population [2].

Data on the exact incidence and prevalence of Non Insulin Cell Tumour associate Hypoglycemia (NICTH) is not available. It has been estimated that NICTH is four times less common than insulinoma (whose incidence is 1-2 cases per 10 lakh populations per year) [2,6]. Therefore, NICTH is one of the rare disease entities . Malignant mesenchymal tumor is listed as a "rare disease" by the Office of Rare Diseases (ORD) of the National Institutes of Health (NIH) [7].

Hypoglycemia associated non-islet cell tumours is caused by mesenchymal or epithelial tumours, including adrenocortical carcinoma, lymphoma, hepatoma, hemangiopericytoma, fibrosarcoma, mesothelioma, malignant pheochromocytoma, leiomyosarcoma etc [6]. Various non-islet cell tumours associated with hypoglycaemia are given in table no.1 [6]

Table 1. Non Iselet Tumours associated with

Type of tumour	Percentage of total
Tumours of mesenchymal origin	**41**
Mesothelioma	8
Haemangiopericytoma	7
Solitary fibrous tumour	7
Leiomyosarcoma/gastrointestinal stromal tumour	6
Fibrosarcoma	5
Others	8
Tumours of epithelial origin	**43**
Hepatocellular	16
Stomach	8
Lung	4
Colon	4
Pancreas (non-islet cell)	3
Prostate	2
Adrenal	2
Undifferentiated	2
Kidney	1
Others	1
Tumours of neuroendocrine origin	**1**
Tumours of haematopoietic origin	**1**
Tumours of unknown origin	**14**

Retroperitoneal mesenchymal tumours are one of these tumours (NICTH) which can cause hypoglycemia. They cause hypoglycemia due to production of incompletely processed insulin like growth factor II (IGF II) called big IGF II. Big IGF II has a higher biological activity to interact with insulin receptors in the liver, adipocytes and muscle, leading to the inhibition of gluconeogenesis and more glucose uptake by skeletal muscle [8]. Big IGF II also has a greater capillary permeability and thus causes a strong insulin-like effect through the insulin receptors, causing profound hypoglycemia [9]. Non islet cell tumours causing hypoglycemia can be diagnosed by presence of low insulin levels (<6 microIU/mL) in the presence of low blood sugar levels (<40 mg/dL) with ratio of insulin to glucose levels < 0.3 [2].

Retroperitoneal mesenchymal tumours present late due to relative paucity of vital structures, and the abundance of loose connective tissue in the retroperitoneum. Symptoms tend to be related to gastrointestinal, urinary or vascular compromise with compression/invasion of adjacent structures. Computerized tomography (CT) scanning and (dynamic) magnetic resonance imaging (MRI) are the radiological procedures of choice in determining the extent of local, regional and distant tumour spread. These procedures are essential for clinical staging, planning an appropriate and optimal biopsy procedure prior to definitive treatment, as well as play an important role in follow-up imaging to assess efficacy of treatment regimens [10].

The main treatment option for the mesenchymal malignant tumours is the surgical resection. The patients in whom surgical resection cannot be undertaken chemotherapy for reducing the size of the tumour and selective emboliztion of the tumour can be undertaken [11-12].

In the present case report, the seizures in the patient were due to retroperitoneal malignant mesenchymal tumours manifesting as recurrent attacks of hypoglycemia and seizures, which is not a common cause of seizure in young adults. Hypoglycemia is very rarely produced by non islet cell tumour and even more rarely by retroperitoneal mesenchymal tumour. In our patient FNAC gave a diagnosis of spindle cell neoplasm, which is itself is a very rare type among the mesenchymal tumours, hence, this case of spindle cell variety of retroperitoneal mesenchymal tumour presenting as recurrent episode of hypoglycemia associated with seizures is rare of the rarest entity, hence, being reported.

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