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Case Report

Internal Medicine Section

Recurrent Postprandial Hypoglycaemia in Insulin Autoimmune Syndrome

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ABSTRACT

Insulin autoimmune hypoglycaemia syndrome (IAS) is not a common entity. It is characterised by auto-antibodies to endogenous insulin in persons without previous exposure to exogenous insulin. IAS is relatively common cause of spontaneous hypoglycaemia in Japan (third most common cause of hypoglycaemia). First case in India was reported in 2013. Since then only four cases of IAS have been reported so far.

The present case is about a middle aged Indian male, who presented with spontaneous, recurrent postprandial hypoglycaemia. He had palpitations, sweating, tremor of hands, feeling of hunger 2-5 hours after meal. He got relief by taking sweets, sugar or orange juice. Estimation of anthropological parameters revealed his BMI to be 28.5 kg/m^2. Laboratory findings of serum glucose were 52 mg/dL, serum Insulin >1000 units/mL, Connecting peptide 14.56 ng/mL, Serum Insulin antibody level was >300 units/mL. He was a non-diabetic with HbA1C 5.63%: Rise of serum cortisol was appropriate for hypoglycaemic stress. A diagnosis of IAS was made. He was put on steroid which was tapered in three months. The patient was advised frequent low carbohydrate meals. His symptoms subsided in six moths and after one year all his hormonal parameters returned to normal.

Spontaneous hypoglycaemia with unusually high serum Insulin, high C-Peptide and presence of insulin auto antibodies are strongly suggestive of IAS.

Keywords: Body mass index, Connecting peptide, Serum glucose

CASE REPORT

A 42-year-old Indian male presented to the Accident and Emergency ward with complaints of sweating, palpitation, tremor of hands, feeling of hunger, blurred vision occurring 3 to 5 hours after taking food. The symptoms were alleviated by taking sweets, sugar, orange or mango juice. It was recurrent, occurring almost daily. He reported a weight gain of about 14 kg, during a span of six months, prior to admission. There has been no history of diabetes in the family, nor he was on insulin or oral hypoglycaemic drug intake. His vitals and physical examination were non contributory.

The laboratory investigations revealed normal renal and liver functions, normal TSH, HbA1C was 5.63%. Serum glucose was 52 mg/dL, serum cortisol during hypoglycaemia was 632 nmol/L, Insulin more than 1000 units/mL, C-peptide 14.56 ng/mL and corresponding Insulin to C-peptide ratio was 68.68 [Table/Fig-1,2]. Non-contrast computed tomography of abdomen showed fatty changes in the liver. No discernible mass was found in pancreas.

The recurrent episodes of features was suggestive of hypoglycaemia, relief of symptoms with sugar containing drinks or sweets with significantly elevated Insulin (1000 units/mL), presence of insulin auto-antibodies (300 units/mL) and Insulin to C-peptide ratio more than 1 is diagnostic of Insulin autoimmune syndrome.

Parameters	Result	Reference range
Serum glucose (mg/dL)	52	60-90
Serum insulin (µU/mL)	>1000	2.6-24.9
C-peptide (ng/mL)	14.56	0.81-3.85
Insulin auto-antibodies (U/mL)	>300	12-18
Serum cortisol (nmol/L)	632	171-536

[Table/Fig-1]: Laboratory investigations performed on admission during hypoglycaemia.

Parameters	Result	Reference range
Liver function tests	Normal	-
Renal function tests	Normal	-
HbA1C (%)	5.63%	<5.7%
TSH (µiu/mL)	1.07	0.27-5.92

[Table/Fig-2]: Other laboratory investigations.

In Insulinoma, serum insulin is not found in this range and Insulin to C-peptide ratio in less than 1. Exogenous insulin administration raises insulin level but suppresses C-peptide. Hypocortisolism was ruled out with appropriate rise of cortisol during hypoglycaemia.

Oral hypoglycaemic drugs causes secretion of insulin and C-peptide in equimolar concentration. There was no history of Sulphonylurea intake and the patient was non-diabetic.

Frequent low carbohydrate meals were advised. He was also advised to take 40 mg of prednisolone in divided dosage which was gradually tapered in three months. He continued with frequent low carbohydrate food. After six months of follow-up, suggested lifestyle episodes of hypoglycaemia had subsided as reported by him. After one year, when the patient was reviewed, his C-peptide level came down to 2.41 ng/mL; serum Insulin-216.5 U/mL and serum Insulin auto-antibodies 11.78 U/mL. The patient was completely symptom free.

DISCUSSION

Autoimmune hypoglycaemia due to insulin antibodies to endogenous insulin who are not exposed to prior insulin has rarely been reported from India. Alam S et al., reported a case of 38-year-old Indian female who presented with weight gain of 4 Kg in one month, 5-6 episodes of hypoglycaemia and one episode of unconsciousness. She had no prior history of Insulin or oral hypoglycaemic drug intake. Her laboratory investigations during hypoglycaemia (40 mg/dL) showed serum Insulin 600 IU/mL, C-peptide 5.66 ng/mL and serum Insulin antibodies 47.44 U/mL. A diagnosis of IAS was made by them. The patient improved on dietary modification only [1]. Of over 380 cases reported in medical literature with more than 90% cases reported from Japan [2].

Patients with IAS usually present in adulthood typically after 40 years of age with postprandial hypoglycaemia [3]. A striking feature of IAS is the magnitude of insulin elevation [4]. Insulin level to this

extent is rarely seen in insulinoma. Sahani P et al., studied a case of 65-year-old obese caucasian woman presenting with postprandial hypoglycaemia. During the episode of hypoglycaemia (60 mg/dL), serum Insulin was detected to be 202 IU/mL, C-peptide 8 ng/mL and anti-Insulin antibody 45.4 U/mL. They managed the patient with dietary modification only [5].

C-peptide and insulin are co-secreted from pancreatic beta cells into the portal circulation in equimolar proportions [6]. Despite equimolar secretion, the insulin to C-peptide molar ratio is less than 1. The ratio may be reversed to greater than 1 in two conditions, first being IAS and factitious hypoglycaemia after exogenous insulin, where C-peptide will be suppressed [7,8]. In 80% of patients, IAS is a transient condition with spontaneous resolution within 3-6 months of diagnosis. For those with intractable hypoglycaemia, small frequent meals low in carbohydrate is the first line of treatment which would avoid postprandial hypoglycaemia and act as a stimulus to insulin secretion [9,10]. Short term glucocorticoid therapy may be useful as an adjunctive therapy, as shown in the present case.

CONCLUSION

Most cases of recurrent hypoglycaemia occur in diabetic patients on oral hypoglycaemic agents or in patients on insulin. However, in cases of endogenous hyperinsulinaemic hypoglycaemia, IAS, inspite of rarity should also be taken into account. Symptoms in the index case were suggestive and assessment of serum insulin, C-peptide, as well as insulin auto antibodies clinched the diagnosis of autoimmune hypoglycaemia.

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