Journal of the Postgraduate Institute of Medicine 2024; 11(2): E250 1-4

https://doi.org/10.4038/jpgim.8476

Case Report

A case of severe hypoglycaemic coma in a young woman due to insulin autoimmune syndrome

Shahini Winson Gnanathayalan[1], Sharmika Sivageethan[1], Uditha Bulugahapitiya[2]

[1]Postgraduate Institute of Medicine, University of Colombo, [2]Colombo South Teaching Hospital, Sri Lanka

Key words: **Insulin autoimmune syndrome, Insulin autoantibodies, Insulin/C-peptide ratio**

Abstract

Corresponding Author: Shahini Winson Gnanathayalan, E-mail< winsgshahini@gmail.com >

https://orcid.org/0000-0001-6348-6229

Received: 30 Jan 2024, Accepted revised version: 06 Dec 2024, Published: 30 Dec 2024

Oral presentation at the Annual Research Symposium of the Postgraduate Institute of Medicine on 25 Oct 2024

Competing Interests: Authors have declared that no competing interests exist

Introduction

Insulin autoimmune syndrome (IAS) is a rare cause of recurrent hypoglycaemic episodes due to the presence of high titres of insulin autoantibodies. It may be triggered by exposure to some drugs and viruses but may manifest spontaneously as well. Although symptoms are usually transient and mild, severe hypoglycaemia with life threatening outcomes also have been reported [1]. Here we describe a young lady presenting with recurrent major hypoglycaemia due to IAS.

Case presentation

A 25-year-old Sri Lankan woman was evaluated for recurrent episodes of early morning seizures with loss of consciousness associated with severe hypoglycaemia for 1 month. Whipple's triad was fulfilled. When she was admitted once with prolonged loss of consciousness, her blood sugar was 25 mg/dl. She was treated with intravenous dextrose with recovery of consciousness. Vital signs and physical examination were unremarkable. She was previously healthy, denied taking alcohol or any medications and had no access to insulin or oral hypoglycaemic medications. She had increased appetite with weight gain for a similar duration. She had three prior hospital admissions with major hypoglycaemia.

http://doi.org/10.4038/jpgim.8476

During a supervised fast test, her capillary blood glucose dropped to 29 mg/dL at 32 hours with a confirmatory plasma glucose level of 32 mg/dL. Both insulin and C-peptide levels were elevated but the insulin level was disproportionately higher than C-peptide level (See Table 1).

Table 1: Supervised fast test: Investigations done with the critical blood sample with the blood sugar of 32 mg/dL.

Test	Patient value	Normal value
Insulin	15 460 IU/ml	< 3 IU/ml
C-peptide	7.6 ng/ml	< 0.6 ng/ml
Insulin/C-peptide ratio	42.3	< 1

Insulin autoantibodies were detected with the titre of >300 U/ml. Insulin recovery after PEG precipitation was 6%. HbA1C was 7.3% suggesting alternating hypoglycaemia and hyperglycaemia in IAS. Other labs including renal and liver function test, cortisol and TSH were normal. Computed tomography of abdomen was normal. Diagnosis of idiopathic IAS was made and she was started on prednisone 30 mg daily, considering the severity of the disease. She was also advised to have frequent small meals. Symptoms gradually reduced with steroids and further major hypoglycaemic events did not recur. She did not have obvious clinical or biochemical evidence of other autoimmune diseases.

Discussion

IAS is a rare cause of non-diabetic hypoglycaemia due to endogenous hyperinsulinism. It is also known as Hirata disease. It is characterized by frequent episodes of spontaneous hypoglycaemia, presence of insulin autoantibodies and inappropriately elevated insulin and C-peptide levels despite the presence of hypoglycaemia. It can be divided into two categories, drug-induced and idiopathic IAS [1]. Many commonly used drugs are well known triggers of IAS, including carbimazole, proton pump inhibitors, isoniazid, clopidogrel and some antihypertensive medications such as captopril, diltiazem, and hydralazine [1]. A proper drug history is essential to stop the culprit agent. Around 80% of the patients with IAS have other associated autoimmune diseases and the most reported association is Graves' disease [1].

IAS predominantly causes postprandial hypoglycaemia. After food intake, the blood glucose level rises, resulting in an increase in insulin secretion from the pancreatic islets. In patients with IAS, insulin autoantibodies (IAA) bind to insulin and make it ineffective leading to early postprandial hyperglycaemia. This situation prompts large amounts of insulin secretion to tackle this hyperglycaemia. When the binding capacity of IAA is exceeded, insulin-IAA complexes act as a reserve of insulin, leading to late postprandial hypoglycaemia. The half-life of insulin rises from 5 minutes to hours but the half-life of C-peptide

(30-35 minutes) remains the same [2]. In healthy subjects and patients with insulinoma, insulin and C-peptide are secreted in equimolar amounts and as the half-life of insulin is usually lower than that of C-peptide, the insulin/C-peptide ratio is less than one in these individuals. In contrast, due to a significant rise in insulin half-life in IAS, insulin levels during the episode of hypoglycaemia are very high and the insulin:C-peptide ratio is much higher than one [1,2]. Patients with IAS can have high- normal or even higher HbA1C values due to alternative hyperglycaemia and hypoglycaemia [1]. Another important point to highlight is that as described in our case, IAS has also been reported to present with fasting hypoglycaemia. Thus, timing of hypoglycaemia is not a reliable factor to differentiate between the aetiologies in non-diabetic hypoglycaemia [3].

Furthermore, insulin recovery after PEG precipitation is usually 5-10 % in IAS compared to more than 70 % in cases with insulinoma [1]. Both insulinoma and IAS cause endogenous hyperinsulinism and differentiation between them is fundamental to institute appropriate management [3]. Due to the high cost, it is challenging to assess IAA in resource-limited settings. A disproportionately high insulin level with an insulin/C-peptide ratio of more than one and lower percentage of insulin recovery after PEG precipitation might be a cost-effective alternative to diagnose IAS without doing IAA levels [1,2]. Insulin recovery percentage after PEG precipitation can be freely done in the government sector in Sri Lanka.

Although IAS is usually mild and self-limiting, it can also cause severe life-threatening hypoglycaemic events as in this case. [4]. In severe cases, specific treatment is indicated. Short courses of steroids and acarbose are well known treatment options [1,2]. Withholding the culprit medication if there is any and screening for autoimmune diseases clinically and biochemically if indicated are part of the management. Treatment response can be assessed with symptoms and insulin recovery percentage after PEG precipitation during the follow-up. With recovery of IAS, insulin recovery percentage will rise. Monitoring IAA titers would not be a cost-effective way of monitoring, especially in resource poor settings.

References

1. Lin M, Chen Y, Ning J. Insulin Autoimmune Syndrome: A Systematic Review. Int J Endocrinol. 2023;2023:1225676. Published 2023 Feb 15. https://doi.org/10.1155/2023/1225676
2. Censi S, Mian C, Betterle C. Insulin autoimmune syndrome: from diagnosis to clinical management. Ann Transl Med. 2018;6(17):335. https://doi.org/10.21037/atm.2018.07.32

3. Cryer PE, Axelrod L, Grossman AB, et al. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2009;94(3):709-728. https://doi.org/10.1210/jc.2008-1410
4. Boro H, Gupta U, Singh C, Malhotra R, Khadgawat R. Insulin Autoimmune Syndrome - A Case Series. Eur Endocrinol. 2020;16(2):168-171. https://doi.org/10.17925/EE.2020.16.2.168