

# Insulin autoimmune syndrome: A rare cause of hypoglycemia

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### ABSTRACT

Insulin autoimmune syndrome (IAS) is a rare cause of hyperinsulinemic hypoglycemia. It is due to autoantibodies to endogenous insulin in person who has never been sensitized to insulin by injections. IAS is a third leading cause of spontaneous hypoglycemia in Japan and it is increasingly being recognized worldwide in non-Asian population. However, we report a case of IAS in Asian male. A certain class of medication called sulfhydryl compounds have been shown to sometimes cause IAS. Recently a compound called alpha lipoic acid (ALA) has been associated with an increased risk of developing IAS. ALA is sometimes used for dieting purposes. We report a case of 36-year-old Indian male presented with symptoms of dizziness and feeling of hunger with sweating, noted to have low blood sugars on multiple occasions. There is a definite history of ALA compound intake as dietary supplements with multivitamins. Subsequently, he was diagnosed as a case of recurrent hypoglycemia from IAS due to ALA intake and managed accordingly.

**Keywords:** Alpha lipoic acid, Asian male, insulin autoimmune syndrome, recurrent hypoglycemia

### Introduction

Hypoglycemia can have many different causes and can present as a medical emergency. Autoimmune hypoglycemia in patient with very high insulin level should also be considered in the differential diagnosis.<sup>[1,2]</sup> More than half of insulin autoimmune syndrome patients report recent exposure to medication with most of them having consumed offending drug containing sulfhydryl group. Commonly implicated drugs include carbimazole, glutathione, tolbutamide, interferon alfa, procainamide, Isoniazid, diltiazem, and glutathione.<sup>[3,4]</sup> Alpha lipoic acid (ALA) is a commonly used health supplement and has been recently linked to insulin autoimmune syndrome. As per literature from 1970-2017, approx 400 cases were reported, most of them were Japanese.<sup>[5]</sup>

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### Case History

A 36-year-old man from India visited to clinic with repeated hypoglycemia. He has symptoms of dizziness, sweating, feeling of hunger and symptom got relieved by oral carbohydrates. No abdominal pain at presentation. No history of any insulin therapy. Patient had no family history of metabolic, hormonal, or autoimmune disease. Initially, it was worked up with fasting blood sugar, insulin, and C-peptide level.

Fasting sugar was 3.52 mmol/L, insulin was > 6945 pmol/L, and C-peptide level was 7.7 nmol/L.

His HBA1c level was 5.1%.

Initially, it was suspected as insulinoma and further investigation of PET-CT scan was ordered. Fluorodeoxyglucose positron emission tomography (FDG-PET-CT) scan abdomen and pelvis was done in India and it came out to be negative for any mass/insulinoma [Figures 1 and 2], no evidence of metabolically

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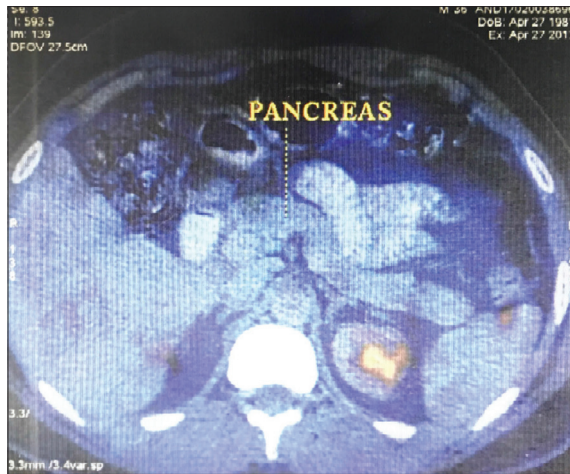
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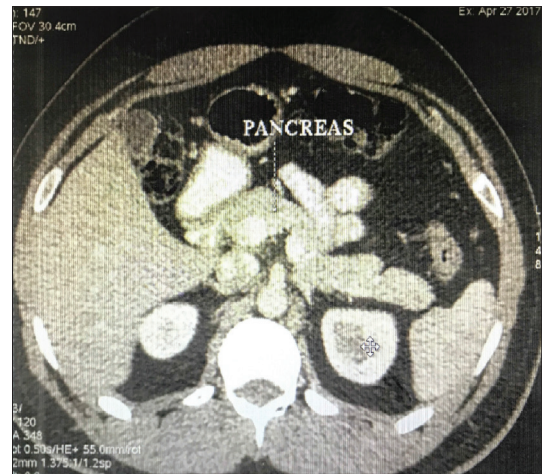


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**Figure 1:** A 36-year-old male 64 slice FDG PET CT abdomen showing no evidence of metabolically active enhancing lesion in the pancreas



**Figure 2:** A 36-year-old male showing normal pancreas on axial CE-CT abdomen

active enhancing lesion in the pancreas, and no evidence of metabolically active disease anywhere in the abdomen. Computed tomography chest screening was also performed and there was no evidence of any pulmonary nodules.

Upon next consultation with further detailed history taking, patient found to take ALA as additional component with vitamin B12 tablet. Hence, a presumptive diagnosis of insulin autoimmune syndrome was done and insulin autoantibodies were ordered to confirm the same and it came out to be very high. Insulin antibodies were  $>625$  uU/mL.

Insulin, C-peptide, and insulin antibodies level were repeated every 2–3 months, but it remained same high level.

Symptoms associated with low glucose levels and high serum insulin and C-peptide levels along with positive antiinsulin antibody had given us the diagnosis of insulin autoimmune syndrome.

Hence, patient was prescribed prednisolone 20 mg per day for 1 week and tapered to 10 mg for 4 weeks then 5 mg for 1 week.

Insulin and C-peptide level came down after steroid therapy dramatically. Insulin was 3905 pmol/L and C-peptide 1.09 nmol/L.

Patient improved symptomatically. Hence, repeat steroid course with the same dosage was advised during next patient visit after 6 months, which led to further decrease in insulin and C-peptide level.

Response to steroid also supported our diagnosis of insulin autoimmune syndrome.

## Discussion

Person affected by IAS has hypoglycemia due to high production of autoantibodies which attack naturally occurring insulin causing

it to work too hard and the level of blood sugar to become too low.<sup>[6]</sup> The number of cases of ALA-induced insulin autoimmune syndrome has been rapidly increasing in recent years especially since ALA supplement for dieting and antiaging have gained popularity. The information we have found suggest that prognosis in general is good. Symptoms typically resolve within a few months of stopping the supplement. Some people do experience recurrent attack of hypoglycemia afterwards. However, with proper hypoglycemia awareness and treatment, recurrent episodes can be controlled. Reportedly immunosuppressant and plasmapheresis have also been used to treat IAS. In our case, dramatic response with sustained euglycemia has been seen with steroid treatment.<sup>[6]</sup> Insulin autoantibody levels in blood reduce gradually after treatment and vary from person to person. Based on certain articles, insulin antibodies remain elevated even after episode of hypoglycemia have stopped. Hence, treatment goal is to treat hypoglycemic episodes, create hypoglycemic awareness, and achieve biochemical cure by normalizing the level of insulin autoantibody in blood.

## Conclusion

Insulin autoimmune syndrome should be considered in differential for adult patient presenting with hypoglycemia and taking dietary supplements.<sup>[7]</sup> High insulin and C-peptide levels with elevated insulin autoantibodies are diagnostic of IAS.<sup>[8]</sup> Once diagnosed, the treatment is with immunosuppressant or steroids and regular follow-up must be assured until antibodies level normalized.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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