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CASE REPORT Open Access

Alpha-lipoic acid induced insulin autoimmune antibody syndrome

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Abstract

Background Insulin autoimmune antibody syndrome is an uncommon cause of hypoglycemia in non-diabetic individuals. We report a case of alpha-lipoic acid-induced insulin autoimmune antibody syndrome.

Case report A 40-year-old non-diabetic female presented with unresponsiveness due to severe hypoglycemia. Investigations revealed high fasting insulin levels, elevated C-peptide, and positive anti-insulin antibodies. Further history revealed recent ingestion of alpha-lipoic acid supplements. She was diagnosed with alpha-lipoic acid-induced insulin autoimmune antibody syndrome and managed with symptomatic measures and steroids.

Conclusions This case highlights the importance of recognizing drug-induced insulin autoimmune antibody syndrome as a potential cause of hypoglycemia in non-diabetic individuals, especially in the context of recent supplement or medication use.

Keywords Insulin autoimmune syndrome, Alpha-lipoic acid, Hypoglycemia, Non-diabetic

Learning points

- Insulin autoimmune antibody syndrome is a rare but important cause of hypoglycemia in non-diabetic individuals
- Alpha-lipoic acid, a commonly used supplement, can induce insulin autoimmune antibody formation
- Early recognition and appropriate management can prevent complications of recurrent hypoglycemia

Introduction

Insulin autoimmune antibody syndrome is a rare cause of hypoglycemia in non-diabetic individuals. It can be associated with other autoimmune diseases, chronic conditions, or induced by certain medications and supplements. We present a case of alpha-lipoic acid-induced insulin autoimmune antibody syndrome, a phenomenon increasingly reported with this commonly used health supplement.

Case description

A 40-year-old female with no comorbidities was brought to the hospital after being found unresponsive at home. There was no history of seizures, trauma, or drug overdose. On examination, her vitals were stable, and systemic examination was unremarkable. However, her blood sugar level was very low, necessitating correction with 25% dextrose, which improved her sensorium.

As the patient was non-diabetic, she was admitted to investigate the cause of hypoglycemia. Renal and hepatic parameters were normal, and serum cortisol was within the normal range. An electroencephalogram (EEG) was unremarkable. Notably, her fasting insulin levels were high, and C-peptide was elevated. A computed tomography (CT) scan of the abdomen was within normal limits. Anti-insulin antibodies were positive, leading to a diagnosis of anti-insulin antibody syndrome.

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Further investigations for an autoimmune etiology, including antinuclear antibody (ANA) and rheumatoid factor (RF), were negative. Upon reviewing her history, the patient reported taking nutritional supplements containing alpha-lipoic acid one month prior. Based on these findings, she was diagnosed with alpha-lipoic acid-induced insulin autoimmune antibody syndrome.

The patient was managed with symptomatic measures, including corrections for hypoglycemia. Subsequently, she was started on steroids, which led to symptomatic improvement, and she was discharged. There were no further episodes of hypoglycemia, and steroids were tapered during subsequent follow-up visits.

Discussion

Alpha-lipoic acid, a potent antioxidant and natural dithiol compound, shows significant therapeutic potential in various health conditions [1, 2]. It acts as a chelating agent for metal ions, a quenching agent for reactive oxygen species, and a reducing agent for oxidized glutathione and vitamins C and E [1]. With antioxidant, cognitive [3], cardiovascular [4], detoxifying, anti-aging, dietary supplement, anti-cancer, neuroprotective, antimicrobial, and anti-inflammatory properties [5], alpha-lipoic acid has been studied for its benefits in diabetes, diabetic neuropathy, and other metabolic disorders [1, 2]. Its mechanism of action involves scavenging free radicals, regenerating other antioxidants, and improving insulin sensitivity [1, 2], making it a promising compound for managing a range of diseases.

Insulin autoimmune syndrome is classified into two types: type 1, caused by antibodies against insulin (also known as Hirata's disease), and type 2, caused by antibodies against the insulin receptor. This syndrome can be associated with other autoimmune diseases like systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), or chronic conditions such as multiple myeloma and hepatitis. It can also be drug-induced, with reported associations with carbimazole, methimazole, propylthiouracil, isoniazid, hydralazine, clopidogrel, imipenem, and alpha-lipoic acid [6, 7].

Alpha-lipoic acid (ALA) is a naturally occurring compound with an unusual cyclic disulfide structure. The presence of this disulfide bond and sulfhydryl (-SH) groups may play a role in its potential to induce autoimmunity through mechanisms like hapten formation or altering protein structure/antigenicity [8]. Drugs like methimazole (an antithyroid medication) and alpha-lipoic acid that have been associated with insulin autoimmune syndrome often contain sulfhydryl or disulfide groups in their molecular structure [9]. While the presence of sulfhydryl groups is a common feature, it may not be the sole factor responsible for inducing insulin autoimmune syndrome. Other structural elements, metabolic pathways, and individual genetic/immune factors likely play a role as well [10]. Insulin autoimmune syndrome has been reported more frequently in Japanese and other Asian populations, suggesting a possible racial or genetic predisposition [11]. Some studies have suggested that individuals carrying the HLA-DRB1*0406* allele may have an increased susceptibility to developing insulin autoimmune syndrome, possibly due to the role of HLA molecules in antigen presentation and autoimmune responses [12, 13].

The proposed mechanism involves increased binding of the antibody with insulin following food intake and subsequent physiological insulin secretion. Over time, the insulin is released from the antibody, leading to excess insulin in the serum, disproportionate to the blood sugar levels, and resulting in postprandial hypoglycemia [6].

Treatment for insulin autoimmune syndrome typically involves steroids, with refractory cases potentially requiring immunomodulators like rituximab or azathioprine. Dietary modifications, such as small, frequent meals of complex carbohydrates and avoidance of simple sugars, are also recommended [6].

Our case highlights the importance of considering drug-induced insulin autoimmune antibody syndrome as a potential cause of hypoglycemia in non-diabetic individuals, especially in the context of recent supplement or medication use. Early recognition and appropriate management can prevent potential complications associated with recurrent hypoglycemia.

Abbreviations

ANA	Antinuclear antibody
CT	Computed tomography
EEG	Electroencephalogram
RA	Rheumatoid arthritis
RF	Rheumatoid factor
SLE	Systemic lupus erythematosus

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None.

Patient consent

Written informed consent was obtained from the patient for publication of this case report.

Authors' contributions

Karthik and Jabir contributed to the conception, data collection, and drafting of the manuscript. All authors approved the final version of the manuscript. All the data made into manuscript was edited and modified by Karthik under the guidance of Jabir and Vimal.

Declarations

Competing interests

The authors declare that they have no competing interests.

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