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A combination of plasma exchange and steroids in the treatment of α-lipoic acid-induced insulin autoimmune syndrome

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A 53-year-old Chinese woman was referred to Changzhou Second People's Hospital Affiliated to Nanjing Medical University for experiencing hypoglycaemic symptoms including tremors, palpitations, sweating, and fatigue over a 2-week period. She received an intravenous infusion of ALA (600 mg/d) for trigeminal neuralgia one month prior. The patient had no history of previous significant illnesses and denied use of exogenous insulin.

The patient was obese, but otherwise her physical examination showed to be healthy. Laboratory findings revealed hyperlipidaemia. Pituitary, adrenal, thyroid, and gonadal function examinations were all normal. Tests for C-reactive protein, rheumatoid factor, antinuclear antibodies, anti-dsDNA antibodies, and anti-thyroid antibodies were all negative. During the first days of hospitalisation, the patient developed four spontaneous episodes of hypoglycaemia (Tab. 1). Imaging studies did not reveal pancreatic lesions. A genetic analysis revealed the presence of HLA DRB1*04:06, an allele associated with IAS.

The clinical symptoms and laboratory findings were consistent with IAS. The patient was advised to stop ALA and eat low-carbohydrate meals. Administrartion of prednisone (30 mg/d) began on August 20th 2015. Due to hypoglycaemia and positivity of IAA, treatment with prednisone was stopped and an intravenous infusion of methylprednisolone (40 mg/d) was administered after 4 days. Steroids were then administered combined with plasmapheresis (Tab. 2). As a result, hypoglycaemic symptoms gradually improved. Methylprednisolone was reduced to 20 mg/d after 2 weeks. Steroids administration was gradually reduced. Prednisone (15 mg/d) was administered when the patient was discharged from the hospital.

During a subsequent follow-up, prednisone treatment was eventually reduced before being stopped. The degree and frequency of hypoglycaemia significantly reduced. Blood glucose and serum insulin levels were also recorded during follow-up evaluations. A repeated 180-minute oral glucose tolerance test (OGTT) showed that serum insulin levels gradually returned to a normal range, but peak secretion was still delayed. IAA was shown to be negative at month 36 of follow-up.

We described a rare case of ALA-related IAS in a Chinese woman. As far as we know, serum insulin l (62400.7 μU/mL) levels in this patient were the highest and the follow-up time was the longest in all reported cases of IAS. Moreover, this is the first case of combined application of plasma exchange and steroids to treat ALA-induced IAS.

Studies have confirmed that IAS is closely related to HLA-DR4 from genetic inheritance. The HLA test result was positive for DRB1*0406, which may be the main susceptibility gene in Asian populations, while HLA-DRB1*0403 may be involved in genetic susceptibility to IAS in people of non-Asian background [3].

Most patients recovered by stopping drugs related to ALA, changing eating habits or by taking steroids. Immunosuppressive agents may be administered to patients with recurrent hypoglycaemia or

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Table 1. *Blood glucose, serum insulin, and C-peptide levels during the episodes of hypoglycaemia on admission*

Date/h:min	Blood glucose [mmol/L]	C-peptide [ng/mL] [ref. val.: 1.1–4.4]	Insulin [μU/mL] [ref. val.: 2.6–24.9]	IAA	GAD
Aug. 14/16:30	2.61	29.40	62400.7	+	–
Aug. 15/01:40	1.80	27.44	48070	+	–
Aug. 15/04:20	1.60	27.68	56600	+	–
Aug. 15/06:00	1.80	29.30	58630	+	–

IAA — insulin autoantibody; GAD — glutamic acid decarboxylase antibody

Table 2. *Blood glucose, serum insulin, and C-peptide levels after treatment*

Plasmapheresis Treatment date	Blood glucose [mmol/L]	C-peptide [ng/mL] [ref. val.: 1.1–4.4]	Insulin [μU/mL] [ref. val.: 2.6–24.9]	IAA	GAD
Aug. 26.2015	3.2	16.32	36000	+	–
Aug. 28.2015	4.8	93.5	19000	+	–
Aug. 31.2015	5.7	–	16700	+	–
Sep. 1.2015	8.9	92.5	14000.9	+	–
Sep. 2.2015	5.1	76.6	4300.8	+	–
Sep. 7.2015	5.55	47.1	24000	+	–
Sep. 8.2015	9.1	71.5	1967	+	–

IAA — insulin autoantibody; GAD — glutamic acid decarboxylase antibody

other autoimmune diseases [4]. Strategies to reduce insulin release, such as pancreatectomy, diazoxide, and somatostatin analogues, are also useful for the treatment of IAS [5].

A repeated 180-minute oral glucose tolerance test (OGTT) showed that the serum insulin levels in the patient gradually returned to normal but still showed a delayed secretion peak. There is no clear evidence to explain this result. We suspect it may be related to obesity.

Follow-up records for negative IAA negative went up to 15 months in reported ALA-related IAS cases. However, in our report, the IAA of the patient remained positive until follow-up at month [36]. One limitation is that we were unable to detect IAA titre due to limited equipment.

Because IAS is a rare clinical disease, it is easily misdiagnosed. One must pay attention to medical history and examinations when non-diabetic patients suffer from repeated episodes of hypoglycaemia, especially in the presence of very high insulin levels. If necessary, the HLA genotype can be detected, which is helpful for improving the understanding of IAS from the perspective of disease genetics.

Authors' contribution

X.S. and X.Y. contributed equally to this work.

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Conflict of interest

None of the authors have any potential conflicts of interest associated with this report.

Disclosure

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