Case Report

A case of spontaneous hypoglycemia

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ABSTRACT

We describe a case of systemic lupus erythematosus with POEMS syndrome presenting as spontaneous hypoglycemia. A 58-year-old female suffered repeated episodes of hypoglycemia. During thesehypoglycemic episodes, her postprandial insulin level was inappropriately high. Further blood tests revealed the presence of antinuclear antibodies, anti-double-stranded DNA antibodies,low C4level.Altered albumin-globulin ratio,monoclonal gammopathy (IgG LAMBDA), polyneuropathy and organomegaly lead to suspicion of concurrent presence of POEMS syndrome.Bone marrow examination revealed plasma cell dyscrasia and plasmacytoma in trephine biopsy confirmed the diagnosis.Here, we emphasize on autoimmune cause of hypoglycemia.

***Key words**: Systemic lupus erythematosus,insulin receptor, type B insulin resistance syndrome, hypoglycemia,POEMS syndrome.*

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INTRODUCTION

Hypoglycemia occurs when blood glucose levels fall below 4 mmol/L (72mg/dL).Hypoglycemia in diabetic patient is a common complication but in non-diabetic individual, hypoglycemia is unusual and need further extensive evaluation. Autoimmune forms of hypoglycemia are the third leading cause of hypoglycemia in Japanese people but this condition is rare among other ethnicities. As a consequence, it is often misdiagnosed or identified late, after numerous expensive and unnecessary biochemical and radiological examinations have proved fruitless. Autoimmune hypoglycemia is generally classified into two types. One is insulin autoimmune syndrome and the other is type B insulin-resistance syndrome, which are characterized by the presence of autoanti-bodies directed to endogenous insulin and to the cell-surface insulin receptor, respectively.[1] Only a small minority of patients with type B insulin-resistance syndrome experience hypoglycemic manifestations; most of them present with severe hyperglycemia asso-ciated with extreme insulin resistance.[2]A common feature of type B insulin-resistance syndrome is the co-occurrence of autoimmune disorders, such as SLE.[2] We report here a very rare case of type B insulin-resistance syndrome, which presented with hypoglycemia and was associ-ated with SLE and POEMS syndrome.

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CASE REPORT

A 58-year-old, non-diabetic, hypertensive Bangladeshi woman suffered from hunger, tremor,palpitation followed by unconsciousness at home. She was brought to emergency where her blood sugar was found 2mmol/l.

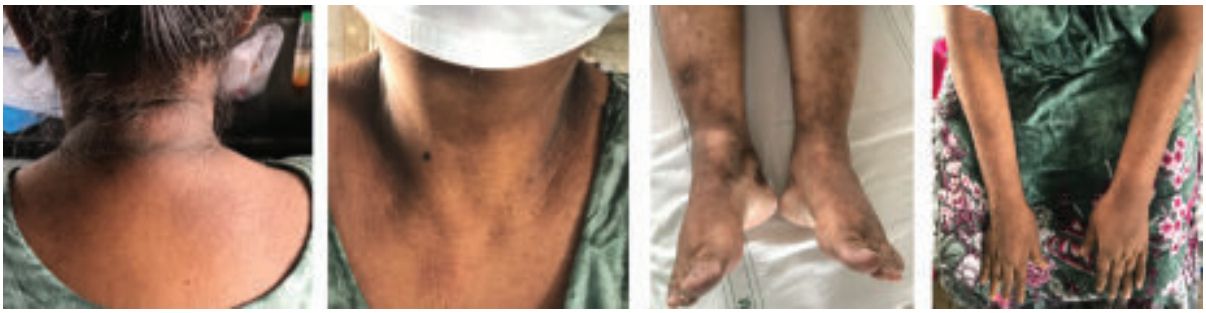

Figure 1 Grade IV acanthosis nigricans (a) and hyperpigmentation in limbs (b)

She recovered her senses after intravenous infusion of 25% dextrose.She had no relevant medical or family history.Patient denied any use of exogenous insulin or oral hypoglycemic agents.

Her physical examination revealed anaemia, kolionychia, angular stomatitis, grade 4 acanthosis nigricans (Figure 1), body mass index was 30.5kg/m^2. There was 8-cm hepatomegaly and just palpable spleen,features of proximal myopathy, deep tendon jerks were diminished with flexor planters bilaterally, muscle power 3/5. During hospital stay patient developed repeated episodes of symptomatic hypoglycemia, both fasting and postprandial. These episodes were happening even when patient was on 10% dextrose. During these episodes serum insulin level was high (32.7 Uiu/ml, normal range 3-27Uiu/ml), C-peptide 0.42ng/ml(normal range 1.1-4.5ng/ml). Electromyography with nerve conduction study of cross limbs revealed acute severe predominately distal sensory motor polyradiculopathy(axonal type)with featuresof active denervation suggestive of underlying immune pathology suggestive of acute motor sensory axonal neuropathy (AMSAN).With presence of acanthosis nigricans, hyperinsulinemia, polyneuropathy our differential diagnosis were insulinoma, autoimmune hypoglycemia and paraneoplastic syndrome .Further investigations revealed anaemia, blood films showed increased rouleaux formation. LDH was 1321U/L(230-460), CPK 1760U/L(24-170).MRI of abdomen showed hepatosplenomegaly and thickened pancreatic tail (Figure 2). Urine RME albumin 2+. UTP-0.7g/day, skin biopsy –acanthosis nigricans,positive ANA and anti-Ds DNA, C4-low, C3-normal. Serum proteine-lectrophoresis-monoclonal gammopathy, immuno-electrophoresis-IgG Lambda,Bone marrow examination showed plasma cell dyscrasia (40% plasma cell), trephine biopsy with imprint revealed plasmacytoma. Other tests

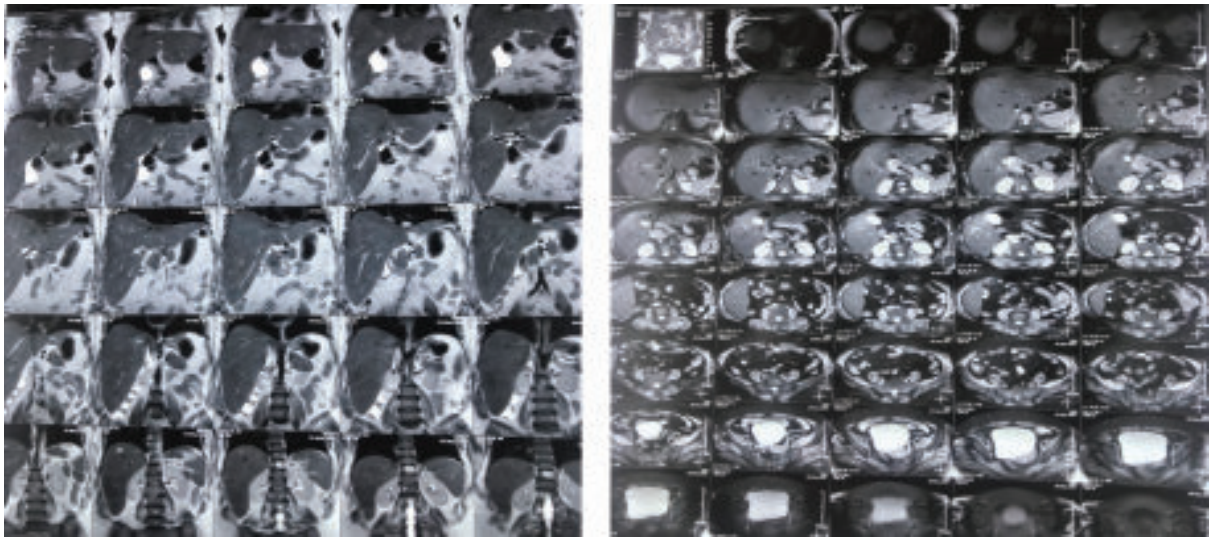

Figure 2 MRI of abdomen showing hepatosplenomegaly, thickened pancreatic tail

including anti-insulin antibody,anti-phospholipid antibody,ASMA,AMA,hormone profile were unremarkable.

Consider-ing all these facts, the presence of type B insulin re-sistance syndrome associated with SLE with POEMS syndrome was diagnosed. After consultation with rheumatologist and hematologist,a combination of pred-nisolone 60 mg/day, hydroxychloroquine 400 mg/day,cyclical course of lenalidomide were initiated.We started diazoxide 150mg/day.She hadno further recurrence of hypoglycemia and the dose of prednisolone has since then been decreased gradu-ally to 5mg/day.

DISCUSSION

Insulin resistance syndromes are classified into two groups.[1] Type A is a group of heterogeneous disorders involving defects in the insulin receptors or in the post receptor metabolic pathways. Type B is characterized by insulin receptor antibodies. It has now been shownthat the insulin receptor antibodies have four in vitro biological effects: they inhibit the binding of insulin to its receptor, they stimulate the effects of insulin on target tissues, they desensitize target tissues to insulin and theydown-regulate insulin receptors.[2]Unlike our patient,the majority of patients with anti-insulin receptor antibodies present with hyperglycemia and extreme insulin resistance.[3] Some patients initially present with hyperglycemia were later reported to develop symptomatic hypoglycemia. However, the pathogenesis of hypoglycemia due to these antibodies appear to be due to either their ability to mimic the action of insulin or hyperinsulinemia by the competitive antagonism of antibodies.[4] The presence of hypoglycemia due to anti-insulin receptor antibodies was first reported by Kahn et al. in1976.[5] Most of the patients with anti-insulin receptor antibodies were reported to have other autoimmune diseases including Hashimoto's thyroiditis, primary biliary cirrhosis, systemic sclerosis, Soegren's syndrome and SLE.[3,4] Although 75 cases of type B insulin resistance syndromes have been reported,there have only been 11 reported cases of hypoglycemia due to anti-insulin receptor antibodies complicated with SLE. The autoantibody interacts with the insulin receptor and appears to act as a partial agonist when at low concentrations, therefore stimulating the receptor and producing hypoglycemia. The presence of antibodies to the anti-insulin receptor should be considered in any SLE patient with hypoglycemia. Glucocorticoid therapy has been reported to improve both hypoglycemia and the activity of SLE.Glucocorticoids may act by inhibiting antibody production or by blocking the cellular responses to the binding ofthe antibody to the receptors, as well as at a post-receptor level by decreasing anti-insulin receptor antibodies.We treated our patient with 60mg prednisolone which was tapered over 3 weeks, immunosupressants, hydroxy-choloroquine, lenalid-omide and low dose diazoxide but many cases reportedly required glucocorticoid, immunosuppressant, steroid pulse therapy or plasmapheresis.

In conclusion, we report this extremely rare case of type B insulin-resistance syndrome presenting with hypoglycemia induced by anti-insulin-receptor antibodies, associ-ated with SLE and complicated with POEMS. While both of these conditions are rare, we should remember that among the myriad diagnostic tests available, a careful physical examination remains a priority.

Authors' contribution: MT was involved in the diagnosis,patient management,manuscript writing.SH involved in literature review.All authors were involved in evaluation and management of the case.

Conflicts of interest:Nothing to declare.

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