The type B insulin resistance syndrome is an autoimmune disease of low prevalence. It is due to the presence of antibodies against the insulin receptor (1) and its relationship with Lupus Erythematosus is low, having an incidence of 2.6% (2). Although in some cases it manifests with hypoglycemia, it more often presents with severe hyperglycemia with high insulin requirements and exaggerated insulin resistance (3). The immunomodulatory treatment may be the best strategy to achieve metabolic control and can even turn the antibodies negative (3).

Clinical Case

23 year old, thin, female patient, diagnosed with Systemic Lupus Erythematosus since 2010, undergoing therapy with prednisolone 5 mg daily, chloroquine and azathioprine.

In August 2013 she presented diabetic ketocidosis; steroids were suspended and treatment with insulin was begun. During her stay at the hospital she had high insulin requirements (iglarine insulin 90 units every 12 hours and apart insulin 70 preprandial units). Due to poor metabolic control she needed to change from a basal-bolus scheme to an insulin pump plus additional bolus, persisting poor metabolic control with glucometric measurements of 600mg / dl or greater, requiring progressive increases in doses up to 300 units of insulin per day through the infusion pump plus a basal-bolus insulin scheme of glargine and glulisine, with total doses of up to 600 units per day. (Fig.1)

Due to clinical signs of severe insulin resistance in a young woman with high glycemc variability (180 and 480 mg/dl) and HbA1c=14%, diabetes type MODY was suspected; as a result 850 mg of metformin and sulfonylurea every 8 hours were added showing partial improvement of the hyperglycemia. (Fig.2) Subsequent management with a GLP-1 analogue (liraglutide 1.8 mg daily) was required and an evaluation of genetic or immunological origin of the insulin resistance was initiated (anti-insulin antibodies, anti-insulin receptor, anti-GAD, anti B cells, C-peptide, and sequencing of the INS gene). (Table 1)

During monitoring she presented lupus activation with Lupus Nephritis class IV, handled with immunomodulatory therapy, reset of azathioprine and prednisolone, obtaining an adequate response. The results of anti-insulin antibodies were positive, the other antibodies were negative and complete sequencing of the INS gene was inconclusive. A short time after beginning the immunomodulators the patient started to lower her glucose measurements allowing sequential reductions in insulin dosage until the withdrawal of the infusion pump. At the reduction of the basal insulin scheme in March 2015, she received the last dose of insulin; since that time maintaining an adequate glucometric control with liraglutide 1.2mg / day as mono-therapy. In September 2015, mycophenolate was initiated for the management of her renal impairment allowing further withdrawal of liraglutide. Since then, the patient has been without any antidiabetic treatment showing good glycemc control and HbA1c 5.6%. (Fig.3)

Table 1. Laboratory results table

Discussion

Some patients with these antibodies evidence an association with an autoimmune disorder; mainly Systemic Lupus Erythematosus (SLE) and, to a lesser degree, with other undifferentiated autoimmune disorders, although a low incidence of the presence of insulin antibodies in SLE patients has been reported (2).

Often these patients have high insulin requirements associated with signs of insulin resistance as acanthosis nigricans, amenorrhea and hyperandrogenism (4).

Treatment of Type B insulin resistance has been largely empirically based on immunotherapies such as corticosteroids, cyclophosphamide, cyclosporine, azathioprine, mycophenolate rituximab and plasmapheresis, associated with high doses of insulin (1). In this particular case, management with prednisolone, azathioprine and mycophenolate for the lupus activity resulted in a progressive insulin requirement decrease, and eventually in withdrawal of all antidiabetic therapy, achieving a complete resolution of hyperglycemia.

Conclusions

Type B insulin resistance syndrome should be suspected in a patient with autoimmune disease presenting severe hyperglycemia with very high insulin requirements. The study should include anti insulin antibodies and anti insulin receptor; the absence of these antibodies does not rule out disease but allows confirmation with positive reports.

In this patient the positivity for anti-insulin antibodies was confirmed at levels only slightly above the normal upper limit, but with complete resolution of severe hyperglycemia in response to immunomodulators allowed us to confirm the diagnosis and to prevent severe complications of prolonged uncontrolled hyperglycemia.

References