Rabson–Mendenhall Syndrome (RMS): a rare cause of severe insulin resistance

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Rabson-Mendenhall syndrome (RMS) is a rare autosomal recessive disorder marked by severe insulin resistance, associated with various phenotypic manifestations.

We report the case of a 15 year old female with poorly-controlled diabetes who was referred to our paediatric diabetes clinic. She was diagnosed with RMS at the age of 50 days; genetic study showed homozygous mutation for R141W in INSR gene known to cause RMS. A strong family history of Rabson-Mandhall syndrome in her mother's cousins (one affected and two carriers) was noted.

She was born full- term through normal vaginal delivery; birth weight was 2.19 kg. She required admission to the neonatal unit for 1 week. She was re-admitted on day 50 with diabetic ketoacidosis (DKA); insulin level was high at 737 μIU/mL, IA2 and GAD antibodies negative and C-peptide > 18 ng/ml. After recovery, patient's blood glucose level was stabilized on high concentrated insulin dose 600-800 IU/day through continuous subcutaneous insulin infusion (CSII); Oral rosiglitazone was added after 2 months. At the age of 6 years, she was continued on CSII, with Rosiglitazone replaced by oral Mecasermin.

At age 12, she had three further episodes of DKA, associated with acute infections- right lobar pneumonia, cellulitis of the abdominal wall, and acute gastroenteritis respectively. In each episode, she required even higher doses of intravenous insulin infusion (up to 2 IU/kg/hour). CSII treatment led to development of severe lipodystrophy at the cannula insertion sites. Therefore, on two occasions her treatment was temporarily changed to multiple daily injection therapy (MDI); Glargine 300 IU daily, Lispro 20 IU TID along with Mecasermin and SGLT2 inhibitor. Her fifth and latest episode of DKA in 2020 was precipitated by severe MRSA septicaemia, was managed with very high doses of intravenous insulin infusion and resolved within a few hours.

Currently, the patient is on combined therapy with Mecasermin 25 units subcutaneously twice daily, oral Dapagliflozin 10 mg once daily along with CSII (Medtronic 640G) with insulin lispro (total daily dose is 261 units /day (4.6U/kg/day) with an insulin to carbohydrate ratio of 1:3 gm, and insulin sensitivity factor of 20 mg/dL. Despite patient compliance, family support and the intensified therapy, her glycaemic control remains poor with an average blood glucose of 304 ± 86 mg/dL and HbA1c of 10.8 ± 1.2 %. She has recently started a trial of recombinant human leptin and shifted to CSII closed loop system (Medtronic 780G), with the aim of improving her insulin resistance, glycaemic control, and quality of life.

In conclusion, we have presented the challenges in management of RMS. RMS is very rare, but life expectancy is short with early mortality related to diabetes-related complications, resulting from severe insulin resistance and poor glycaemic control. Using a closed loop insulin pump together with recombinant human leptin therapy to improve insulin sensitivity and reduce hyperinsulinemia, may offer new potentially useful lines of management.