Intermediate DEND Syndrome: Response to Sulfonylurea Treatment in a 17 Year- Old-Girl with Neonatal Diabetes Mellitus

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Background

Activating mutations in the *KCNJ11* gene is the most common cause of permanent neonatal diabetes. In 20-25% of the cases, epilepsy, developmental delay and muscle hypotonia accompany the disease, which is called DEND (*developmental delay, epilepsy, neonatal diabetes*) syndrome. Intermediate DEND syndrome (iDEND) is a rare mild form of DEND syndrome and is characterized by mild motor, speech or cognitive delay and an absence of epilepsy. Sulfonylureas are successfully used in permanent neonatal diabetes cases with *KCNJ11* gene mutations. However, majority of the cases with DEND syndrome do not respond to sulfonylureas. Previously, a few number of patients with iDEND syndrome are reported to have improvement in glycemic control and neurological findings after sulfonylurea treatment.

Aim

To report the response to oral sulfonylurea treatment in a 17-year-old patient with iDEND syndrome.

Case Report

The patient was born at term with a birth weight of 3300 g. She was diagnosed with diabetes mellitus at two months of age when she was investigated for failure to thrive. She had delayed motor development (started walking at the age of 1.5 years, speaking at the age of 6 years but could not learn reading and/or writing) and diagnosed with attention deficit/ hyperactivity disorder. She used insulin at a dose of 1.2 IU/kg/d when she first came to our outpatient clinic at the age of 17 years.

Laboratory evaluation;

- C-peptide:<0.1 ng/mL
- HbA1c: 10.9%
- Anti-GAD and anti-insulin antibodies: negative
- Thyroid function test: normal
- EMG: *sensorimotor polyneuropathy* (more pronounced in the lower extremities)
- EEG: Normal
- IQ score: 49 (Mild mental retardation)
- Brain MRI: Normal

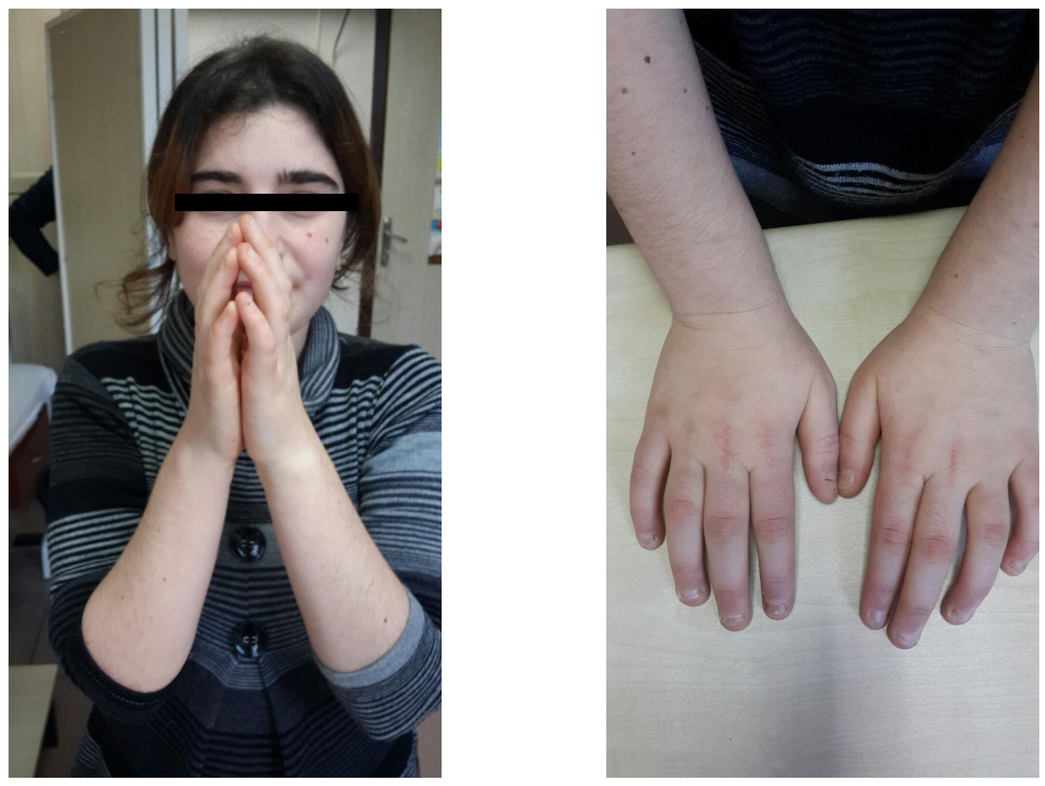

Figure 1. Prayer sign (Limited joint mobility)

Molecular Analysis;

- A heterozygote missense mutation in the *KCJN11 gene*, Exon 1(p.V59M) was identified.

Clinical Observation:

- Glibenclamide (0.1 mg/kg/d) was started and the dose was increased gradually till 1.3 mg/kg/d according to the blood glucose measurements.
- Insulin dose has been decreased concurrently according to blood glucose levels.
- HbA1c level decreased to 8% and daily insulin requirement was reduced to 0.9 U/kg/d. However, insulin could not be weaned off.
- C-peptide level after glibenclamide was increased up to 0.68 ng/mL.
- No significant improvement in cognitive functions was detected.

Conclusion

- The most common cause of iDEND syndrome is p.V59M mutation.
- Previous reports of cases due to V59M mutation indicate that although they had more severe neurological findings, sulfonylurea treatment that is started at younger age, resulted in significant improvement in neurological findings.
- In our patient although insulin requirement was decreased and glycemic control was improved, insulin could not be weaned off and there was no improvement in cognitive functions.
- Early treatment with sulfonylureas can improve developmental delay and neurological findings in patients with iDEND syndrome.

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