DONOHUE SYNDROME AND HYPERTROPHIC CARDIOMYOPATHY

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Introductıon

Donohue syndrome, first reported in 1954 by William Donohue, is a rare autosomal recessive disease, caused by mutations in the gene encoding the insulin receptor with prevalence is less than one in a million live births . Its characterized by a severe form of insulin resistance, hyperinsulinemia, loss of glucose homeostasis (fasting hypoglycemia, postprandial hyperglycemia), intrauterine and postnatal growth retardation, absence of subcutaneous fat, coarse facial features, acanthosis nigricans, distended abdomen, hirsutism, enlarged genitalia in males, labial hypertrophy and cystic ovaries in females. We report the clinical, laboratory and molecular characterization Donohue Syndrome with hypertrophic cardiomyopathy.

CASE REPORT

Our patient is the second child of healthy first degree consanguineous parents of Turkısh family.

She was born at 36 weeks of gestation via caesarean section due to severe intrauterine growth retardation (IUGR).

Apgar scores were 9 at 1 minute and 10 at 5 minute, she was admitted to the Neonatal Intensive Care Unit at the age of first day due to severe IUGR.

On clinical examination of the child were ‘elfin faces’ (a depressed nasal bridge, large and prominent ears, antevert nostrils), hypertrichosis, reduced subcutaneous fat, abdominal distention, intercostal retraction, and labial hypertrophy

She had hyperglycemia (328 mg/dl) with hyperinsulinemia (insulin :5253 µIU/ml, C peptide: 76.16 ng/ml) in eighth day of hospitalization.

Urine tests results showed us there was glycosuria but no ketonuria. Full blood count, arterial blood gases, renal function tests, adrenocorticotrophic hormone and cortisol levels were normal.

Because of severe hyperglycemia iv insulin infusion was started at 0.01 U/kg/h and progressively increased to 0.5 U/kg/h.In followed-up clinical time 2 U/kg/day insulin glargine added treatment and potentiated 15 U/kg/day.

Follow up

Molecular study found that the patient was homozygous deletion at exon 3-22 of the INSR gene

At the age of three months she admitted our hospital because of fasting hypoglycemia.

Her insulin glargine dose was decreased 7 U/kg/day because of hypoglycemic episode. On the laboratoty examination: glucose: 52 mg/dl, ALT: 240 U/L, AST: 265 U/L, t.bil: 8.93 g/dl, d.bil: 6.8 g/dl, IGF-1: <15 ng/dl, IGF- BP3: <0.5 µg/dl, HbA1c:%9.8. There was a grade II/VI systolic murmur on cardiac physical examination.

During this admission, echocardiographic examination showed an increase of both inverventriculer septum and left ventricle posterior wall diameter .

Septal thickness increased to 5.4 mm with left ventricular outflow tract obstruction (gradient 62mm Hg) and systolic anterior movement of the mitral valve. Treatment with propranolol was started.

Later echocardiogram (in the 5th month of life) revealed no further significant increase in the thickness of interventriculer septum and ventricular wall (5.5 mm diastolic diameter) and repeat echocardiograms showed the gradual improvement of left ventricular outflow tract obstruction.

At the age of 6 months she was discharged hospital with 5 U/day insulin glargine.

She was died at the age of 7 months because of respiratory insufficiency caused by a fulminant pulmanory infection.

Discussion

Donohue syndrome is diagnosed with clinical characteristics, laboratuary findings and mutation in INSR gene. Hypertrophic cardiomyopathy is frequently observed in Donohue syndrome and has high mortality.

Therefore hypertrophic cardiomyopathy demands extra attention in Donohue syndrome. Treatment is generally hard and unsuccessful. Generally patients die in infantile period of life.

So prenatal diagnosis and genetic counseling are quite important.

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