Two Siblings with Mutation in the Leptin Receptor Gene

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Monogenic obesity is a rare cause of obesity. Mutations in the orectic or anorectic pathways are the important reasons of monogenic obesity. We present here two siblings with mutation in the leptin receptor gene (*LEPR*). A male patient was evaluated with the cause of obesity. On admission, he was 1.9 decimal age and his anthropometric measures were as follows: weight 28.2 kg [+6.49 standard deviation score (SDS)], height 81.9 cm (-1.01 SDS), and body mass index (BMI) 42.04 kg/m^2 (+8.1 SDS). His birth weight was 3700 g. The parents were healthy and non-consanguineous. The patient had a history of rapid weight gain and over-nutrition after birth. There were anxiety attacks when access to food was restricted. He had a sister with similar symptoms. On physical examination, the patient had significant obesity and o-bain deformity; the rest of the systemic examination was normal. His external genitalia were at Tanner stage I with no axillary hair. His sister was evaluated with similar complaints. On admission, she was 6.5 decimal age and her anthropometric measures were as follows: 58.7 kg (+5.13 SDS), height 125 cm (+1.43 SDS), and BMI was 35.57 kg/m^2 (+3.93 SDS). Her birth weight was 4050 g. There was a history of gestational diabetes mellitus during pregnancy. The patient had a history of rapid weight gain and over-nutrition after birth similar to her brother. She was in primary school at the admission, and her school performance history was normal. Her physical examination was normal, except obesity, and she was pre-pubertal. Both siblings had normal mental-motor development according to their age. We suspected secondary or pathological obesity because of the severe infantile-onset obesity in both cases. Patients' serum leptin levels were significantly higher. Genetic investigation revealed that both patients had a mutation in the *LEPR* gene. LEPR mutation is a rare disorder and was described in small number of families in the literature. Monogenic obesity should be kept in mind in patients with severe infantile-onset obesity. LEPR mutations can be detected only by molecular genetic analysis in suspected patients.

Key words: Obesity, monogenic obesity, children, *LEPR* mutation, leptin resistance

Investigation of BRAF Hotspot Mutations in Papillary Thyroid Tumor Samples

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Objectives: Papillary thyroid carcinoma is the most common type of thyroid cancer and is associated with BRAF (MIM 164757) mutations. Here, we report our 3 years of experience of pyrosequencing of BRAF hotspot regions in papillary thyroid carcinoma.

Methods: Genomic DNA was isolated according to the manufacturer's protocol (QIAamp DNA FFPE Tissue Kit) from formalin-fixed paraffin-embedded tumor samples of 181 female and 81 male patients pre-diagnosed with papillary thyroid carcinoma. Pyrosequencing of BRAF mutation regions (codon 600 and codon 464-469) was performed as indicated in the protocol of the kit used (therascreen BRAF Pyro Kit, Qiagen).

Results: BRAF mutations were defined in 33.3% of samples tested. V600E mutation was the most frequent mutation (31.98%). V600K mutation was present in only two of the samples (0.9%), whereas G466E mutation was defined only in one sample (0.45%). Percentages of the mutations between male and female patients were not significantly different.

Conclusion: Presence of a BRAF mutation is commonly accepted as an additional prognostic feature of papillary thyroid carcinoma following tumor histology, primary tumor size, and invasion. Our results confirm the high frequency of BRAF mutations in papillary thyroid carcinoma. As a second point, we suggest that pyrosequencing is a practical method to study targeted mutations in the tumor samples.

Keywords: Papillary thyroid carcinoma, BRAF, pyrosequencing, V600E, V600K, G466E