Phenotype-Genotype Correlations in Bardet-Biedl Syndrome Patients with Molecular Analysis

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Bardet-Biedl syndrome (BBS) is a rare, autosomal-recessive ciliopathy characterized by obesity, rod-cone dystrophy, postaxial polydactyly, renal and genital abnormalities, and learning difficulties. To date, mutations in 18 genes have been described to be responsible for BBS. In this study, we investigated 15 cases clinically diagnosed with BBS and the mutation distribution in 16 *BBS* genes using targeted next-generation sequencing and genotype-phenotype correlation. Mutation analysis of the 16 BBS genes (*BBS1, BBS2, ARL6, BBS4, BBS5, MKKS, BBS7, TTC8, BBS9, BBS10, TRIM32, BBS12, MKS1, NPHP6, WDPCP, SDCCAG8*) was performed with targeted next-generation sequencing in the 15 BBS cases. We discovered the disease-causing mutations in 13 of the 15 patients evaluated in this study. We identified the following mutations: in *BBS1* gene - 1 previously reported (Y284SfsX5) and 2 novel (IVS1-3C>G, Q338X) mutations, in *BBS2* gene - 1 novel mutation (G88AfsX6), in *BBS4* gene - 1 novel mutation (IVS6-2A>G), in *BBS7* gene - 1 previously reported (R238EfsX59) and 1 novel (L317V) mutations, in *BBS9* gene - 1 novel mutation (N35X), in *BBS10* gene - 1 previously reported (S311A) and 3 novel (K619IfsX10, I342NfsX20, T516NfsX8) mutations. The cases were evaluated with clinical findings and molecular genetic characteristics in terms of phenotype-genotype correlation. This is the first study investigating BBS molecular diagnosis and phenotype-genotype correlation in Turkey and one of the few studies in the world. Identification of molecular disorder in patients can help prevent the complications that may develop and contribute to growth of a healthy generation.

Key words: Bardet-Biedl syndrome, next-generation sequencing, mutation, phenotype- genotype correlation

Osteogenesis Imperfecta Presenting with Fractures in Pregnancy or Lactation Period: Report of Three Cases

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Modifications of bone and mineral metabolism in pregnancy and lactation period can worsen the clinically silent osteoporosis and may cause bone fractures. We report three cases of osteogenesis imperfecta (OI) that presented during pregnancy and lactation period.

Case-1: A 32-year-old woman presented with low back and left hip pain in lactation period. She has had blue sclera and multiple recurrent bone fractures. Patient was treated with vitamin D, calcium, and pamidronate 90 mg. On follow-up, she was completely free of fractures during the therapy.

Case-2: A 26-year-old woman presented with gradually increasing low back pain after delivery. Family history revealed that her mother and sister have had multiple recurrent bone fractures and her daughter had blue sclera. Neurological examination revealed moderate hearing loss. Radiologic studies revealed L1 and L2 compression fracture. She was treated with vitamin D, calcium, and parenteral bisphosphonate for a period of 6 years. The patient was completely free of bone fractures.

Case 3: A 29-year-old woman who had a history of OI in her family presented with right first metatarsal fracture at 18th week of her pregnancy. Past medical history revealed that she had recurrent right ankle fractures. After vitamin D was given and calcium replacement was initiated, her lactation was stopped. Bone turnover markers were elevated. L4 Z-score on DXA was -4.3. The patient was treated with pamidronate 90 mg. No bone fractures occurred during follow-up. Although OI is a rare disorder, it might be the reason behind the fractures presenting during pregnancy or lactation period, and gestational and lactation osteoporosis may be concurrent with occult forms of OI.

Key words: Osteogenesis imperfecta, pregnancy, lactation period, osteoporosis, fracture