Genomic DNA from the blood of patients was extracted with Qiagen DNeasy blood & tissue kits (Qiagen, Valencia, CA, USA). Whole exome sequencing was performed with an Agilent SureSelect Human All Exon V5 (Agilent, Santa Clara, CA, USA) and the HiSeq2500 Genome Analyzer (Illumina, San Diego, CA, USA) for II-8 in the HSP1 family. Total sequencing yield was 21,524 Mbp. The coverage of the target region (≥20X) was 98.5%.

**Variant analysis**

The raw sequencing data were aligned to the hg19 reference genome with the Burrows-Wheeler Aligner (ver. 0.7.5a) algorithm. Output sequential access method (SAM) files were converted to basic access method (BAM) files and sorted with SAMtools (ver. 0.1.18). Duplicate removal was performed with the Picard tool (ver. 1.95) markduplicates. Realignment around known indel sites and base quality score recalibration were performed with the genome analysis toolkit (GATK) (ver. 2.6-5) to create final BAM files.

Variants were called using the GATK v2.6 Unified Genotyper algorithm for loci with sequencing depth greater than or equal to 20X. Variants were annotated with ANNOVAR (ver. 2013-06-21) using RefGene, dbSNP 138, and the 1,000 Genomes Project SNP (2014 Sep release) of the Asian population and all-population databases. Among called variants, only nonsynonymous single nucleotide variant, frameshift indel, and splicing site variants were chosen. Polymorphisms in the Korean population (n=352) were filtered out. The variants were classified into five categories (pathogenic, likely pathogenic, uncertain significance, likely benign, and benign variants) according to the American College of Medical Genetics and Genomics and the Association for Molecular Pathology (ACMG/AMP) guidelines. Pathogenic variant was validated by Sanger sequencing.