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Identification of oncogenic mutations in a pedigree affected by inherited cancers: A case report.

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Aim. The aim of this study was to identify genetic causes of a hereditary cancer in Ukrainian pedigree. **Background.** Currently, the most commonly prescribed screening for suspected hereditary cancer in Ukraine is PCR for the seven most common mutations in the *BRCA1* gene. We have explored a more efficient strategy based on the multiplexing capabilities of AmpliSeq™ and the Ion Torrent™ platform for targeted next-generation sequencing (NGS) of 60 genes of interest. **Methods.** A pedigree comprising 10 members was studied, with 5 of these exhibiting different types of oncological conditions. Ethics approval and informed consent were obtained. Four members of the aforementioned pedigree have undergone DNA sequencing. Genomic DNA was amplified using the custom Ion AmpliSeq™ panel. The DNA Libraries were pooled, barcoded and sequenced using an Ion S5 sequencer. **Results.** Prior to this study, a heterozygous mutation c.5266dup (rs80357906) in the *BRCA1* gene was identified by PCR in a Proband with endometrial adenocarcinoma and her mother. The mother had been diagnosed with breast cancer at 45 years of age, colon cancer at 60 years of age, endometrial cancer at 62 years of age, and lung cancer at 65 years of age. However, Proband's maternal aunt with colorectal cancer at the age of 57 had no mutation c.5266dup detected. The results of our sequencing revealed that the Proband carries not only a *BRCA1* c.5266dup mutation, but also a mutation c.2150_2153del (rs267608058) in the *MSH6* gene. The Proband's aunt and son carry only a mutation c.2150_2153del in the *MSH6* gene. The Proband's daughter does not carry these oncogenic mutations. It can be concluded that Proband, her son, mother and aunt are afflicted with Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer (HNPCC) syndrome, as a result of a *MSH6* c.2150_2153del mutation. It can be postulated that the Proband's mother and aunt inherited the mutation in the *MSH6* gene from their father, who had colorectal cancer at the age of 55. Additionally, Proband and her mother are afflicted with hereditary breast and ovarian cancer syndrome (HBOC) caused by *BRCA1* c.5266dup mutation. It can be reasonably presumed that Proband inherited the *BRCA1* mutation from her grandmother, who was diagnosed with ovarian cancer at the age of 47. In accordance with the findings of the study, all participants were furnished with the requisite medical and genetic counselling. **Conclusions.** The efficacy of next-generation sequencing for the diagnosis of hereditary cancers was exemplified using a familial case with a dual genetic predisposition for cancer. It was determined that the P's son, who is 25 years of age, is a carrier of the *MSH6* c.2150_2153del mutation. With the implementation of proper monitoring planning and a responsible attitude on the part of the patient, an early diagnosis strategy can be implemented, which will result in the potential cancer being diagnosed at an early stage.

Keywords. NGS, clinically significant gene variants, hereditary cancer, pedigree.