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P108 - HEREDITARY COLORECTAL CANCER - FIRST REPORT ON MUTATIONAL PROFILE IN SERBIA

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Background

Hereditary colorectal cancer (CRC) accounts for approximately 5-10% of all newly diagnosed cases. It is characterized by the presence of a germline mutation in one of the high-risk genes. Lynch syndrome (hereditary non-polyposis colorectal cancer-HNPCC) and Familiar adenomatous polyposis (FAP) account for 3-5% and 1% of all newly diagnosed CRC cases, respectively.

Method

In Serbia, genetic counseling and testing for hereditary CRC have been available since 2018 at the Institute for Oncology and Radiology of Serbia (IORS), specifically at the Department of Genetic Counseling for hereditary cancers. So far, 111 families suspected of having hereditary CRC have undergone testing. Patients eligible for genetic testing were selected according to the Amsterdam criteria and/or the Bethesda guidelines. A certain number of patients who have not been previously diagnosed with malignant disease were referred to genetic counseling because of a diagnosed colon polyposis or because of a positive family history of CRC.

Results

Genetic testing was conducted on 93 families until now, and pathogenic or likely pathogenic variants were identified in 26 of them (*MLH1*-8, *MSH2*-4, *MSH6*-1, *APC*-6, *CHEK2*-4, *MUTYH*-3).Three of the detected variants were found for the first time in *MLH1*-2 and *APC*-1 genes. To our knowledge, these variants have not been reported in the literature and/or genetic databases so far. The same *MLH1* gene mutation c.392C>G (p.Ser131Ter) was detected in three young non-related CRC patients. Additionally, all four patients with detected *CHEK2* mutation had the same c.470T>C (p.Ile157Thr) variant, while two from three patients with detected mutation in *MUTYH* gene had c.1103G>A (p.Gly368Asp) heterozygous (monoallelic) variant. Variants of unknown significance (VUS) were found in *MLH1, MSH2, MSH6, PMS2, APC, CHEK2*, and *MUTYH* genes in 15 patients.

Conclusions

The analyzed group of patients indicates that Lynch syndrome is present in 14% of the tested families, while FAP is present in 6.5% of them. Based on the current hereditary CRC mutational profile in Serbia, further population screening is crucial as a promising approach for disease prevention and identification of founder mutations.

Keywords

Genetic counseling,Lynch syndrome, FAP.

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