A novel hMSH2 gene mutation in colorectal cancer patients?

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About 20% CRC patients have a genetic component and HNPCC is the most common autosomal dominant hereditary syndrome. Some Chinese HNPCC pedigrees were recently reported in the January 14, 2008 issue of the World Journal of Gastroenterology because of their great significance for hereditary CRC. This article will undoubtedly bring comfort to many families.

The article describes how five independent Chinese kindreds of HNPCC fulfilled the classical Amsterdam Criteria, as collected by Prof. Yulong He and Dr. Changhua Zhang of Sun Yet-san University in China. The research group has constructed a CRC database since 1994 and the follow-up rate has always been above 90%. Eleven independent Chinese kindreds of HNPCC were collected by deep pedigree investigation until January, 2004 and five of them fulfilled the classical Amsterdam Criteria¢ñ. To identify high-risk populations with HNPCC, the group tested hMSH2 and hMLH1 mutation in these classical kindreds.

A novel hMSH2 gene mutation was found in one HNPCC kindred. In the kindred, there were four colorectal carcinoma patients in two successive generations, and three of them were diagnosed before the age of 45. The proband developed endometrial carcinoma at the age of 61, bladder carcinoma at 66 and CRC at 72, while his father got bladder carcinoma at the age of 70. In addition, one proband¡¯s daughter had CRC at the age of 34 and died of synchronous hepatic metastasis. In the kindred, gene testing was performed on ten family members and four of them were found to have a mutation in hMSH2 at position A1808G. The

mutation sequence variant was in exon 12 of hMSH2 gene, which is a missense mutation. It was a single nucleotide substitution of c.1808A¡úG (Figure 2), which resulted in Asp 603 Gly of hMSH2 (NCBI Ref. Seq. NM 000251 and NP 000242 for mRNA and protein, respectively). Three of them with this mutation had developed CRCs and one had no colorectal disease and was still in follow-up.

The results of this study suggest molecular pathological tests should be performed to identify individuals with hereditary non-polyposis CRC and at-risk family members of HNPCC. Although the novel mutation reported by Prof. Yulong He and Dr. Changhua Zhang has not been confirmed as a germline mutation yet, it may be an important factor for CRC development in kindreds. Close follow-up and intensive surveillance should be performed for those high risk family members.

Source: World Journal of Gastroenterology