HNPCC-associated small bowel cancer: clinical and molecular characteristics.

Abstract:
BACKGROUND & AIMS: The risk for small bowel cancer (SBC) is significantly increased in hereditary nonpolyposis colorectal cancer (HNPCC). HNPCC-associated SBCs are poorly characterized. METHODS: Thirty-two SBCs were characterized according to clinical, pathologic, and germline mutation data. Histomorphologic characteristics, microsatellite instability (MSI) testing, mismatch repair (MMR) protein expression, and frameshift mutations of 7 coding mononucleotide repeats were investigated in 17 SBCs. RESULTS: Median age at diagnosis was 39 years. Fifty percent of SBCs were located in the duodenum. The Amsterdam criteria were fulfilled in 50% of patients; 45% of patients had no personal history of previous malignancies. Two patients had a positive family history for SBC. Pathogenic germline mutations were identified in 81%; high MSI was detected in 95% and loss of MMR protein expression in 89% of cases. TGFBR2, BAX, MSH3, MSH6, ACVR2, AIM2, and SEC63 frameshift mutations were detected in 69%, 59%, 59%, 35%, 82%, 56%, and 56%, respectively. An expansive growth pattern of the tumor border and an intense intratumoral lymphocytic...
infiltrate were present in 75%, respectively. CONCLUSIONS: HNPCC-associated SBC often manifests at a young age and may be the first disease manifestation. Endoscopy may detect 50% of tumors. Considering recent data on gastric cancer, we propose endoscopic screening of mutation carriers starting at 30 years of age because clinical criteria cannot define a high-risk group. In addition, our study shows that histopathologic criteria, MSI, and MMR immunohistochemistry are often similar to these features in HNPCC.