APC:T1556fs and STK11 mutations in duodenal adenomas and adenocarcinomas

Yohei Kojima, author

Abstrak

ABSTRACT
Purpose: Duodenal adenoma and adenocarcinoma (AC) are rare tumors, and few studies have examined their genetic features. We aimed to determine the key genetic changes in duodenal adenoma and AC, and to clarify the possible involvement of the adenoma-carcinoma sequence in duodenal tumor carcinogenesis.
Methods: Nineteen duodenal tumors collected by endoscopic mucosal resection or surgical resection were classified as AC, adenoma with high-grade dysplasia (HGD), or adenoma with low-grade dysplasia (LGD) per the World Health Organization tumor classification. When a tumor contained two or more components with different dysplasia grades, the highest grade was assigned as the tumor grade. Representative areas of these components with different grades were microdissected and evaluated by a genomic analysis. Mutational hotspots involving 50 oncogenes and tumor suppressor genes were analyzed by next-generation sequencing, and their association with the dysplasia grade was investigated.
Results: We analyzed 27 tumor components of AC or adenoma, with 11 normal mucosal samples obtained from 19 patients with duodenal tumors. The most prevalent abnormality among 50 genes tested was the KRAS mutation, which was detected in 12/19 (63.2%) patients, followed by APC and TP53 mutations (47.4 and 36.8%, respectively). According to the tumor dysplasia grading of each component, KRAS mutations were found in 5/8 (62.5%) tumors with AC components, 6/9 (66.7%) tumors with HGD components, and 3/10 (30.0%) tumors with LGD components. TP53 mutations were found in 4/8 (50.0%) tumors with AC components, 3/9 (33.3%) tumors with HGD components, and 1/10 (10.0%) tumors with LGD components. APC mutations were found in 2/8 (25.0%) tumors with AC components, 6/9 (66.7%) tumors with HGD components, and 5/10 (50.0%) tumors with LGD components. Notably, an APC:T1556fs mutation was detected in six cases (31.6%), five of which were adenoma cases. Furthermore, STK11 mutations were confirmed in 2/8 (25.0%) AC cases and in 1/11 (9.1%) adenoma cases.
Conclusion: APC:T1556fs and STK11 mutations found in duodenal adenomas/ACs highlight the importance of proteins encoded by these genes in tumor development. APC mutations were identified in duodenal adenomas more frequently than in duodenal ACs, which differed from the observations of typical adenoma-carcinoma sequences seen in colorectal cancer, suggesting the limited involvement of this mechanism in duodenal cancer development.