Colorectal neuroendocrine carcinomas and adenocarcinomas share oncogenic pathways. A clinico-pathologic study of 12 cases

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OBJECTIVE:
Neuroendocrine carcinomas (NECs) are rare neoplasms with an increasing incidence. Oncogenetic pathways of colorectal NEC are still poorly understood, and no treatment standards are available for these rare tumors.

METHODS:
We analyzed retrospectively the clinical records and histology of 12 patients with colorectal NEC. KRAS and BRAF mutations were investigated after the dissection of exoendocrine and neuroendocrine components. ALK alterations and EML4-ALK transcripts were detected by in-situ hybridization and determination of fusion transcripts, respectively.

RESULTS:
At the time of diagnosis, the mean age of the patients was 60 years (40-79) and 10 patients had synchronous metastases. A transient response occurred in two patients and one patient treated with cisplatin-etoposide or fluoropyrimidine-oxaliplatin, respectively. Tumor progression-related death occurred in 11 of 12 patients. Ten tumors contained an exocrine component, accounting for 5-70% of the tumor, and the other two contained an amphicrine component. BRAF/KRAS mutations were found in six of 10 tumors, corresponding to BRAF(V600E) (n=2) or KRAS(G12D) (n=2), KRAS(G12V) or KRAS(G13D). DNA was obtained from both exocrine and endocrine components in seven cases, and the BRAF/KRAS status was identical in all cases. Split of the ALK locus was detected in a minority of tumor cells in two of eight cases, but EML4-ALK transcripts were absent.

CONCLUSION:
The association of an exocrine component in all cases and the similar profile of BRAF/KRAS mutations indicate that colorectal NEC may correspond to a high-grade transformation of colorectal carcinoma. New chemotherapy regimens using targeted therapies should be assessed in these tumors.

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