CÁNCER GASTRO INTESTINAL

Clinically important molecular features of Peruvian colorectal tumours: high prevalence of DNA mismatch repair deficiency and low incidence of KRAS mutations.

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Pathology. 2011 Apr;43(3):228-33.

Abstract

The incidence of colorectal cancer (CRC) in Peru has been increasing, and no data have been published on the molecular features. We explored the most relevant genetic events involved in colorectal carcinogenesis, with clinical implications. Using immunohistochemistry for mismatch-repair (MMR) proteins (MLH1, MSH2, MSH6, and PMS2) and microsatellite instability analysis, we evaluated the status of 90 non-selected CRC Peruvian patients followed in a nationwide reference hospital for cancer (INEN, Lima). Tumours with loss of hMLH1 were evaluated further for hMLH1 promoter hypermethylation and all cases were evaluated for the presence of KRAS and BRAF-V600E mutations. MMR deficiency was found in 35 (38.8%) patients. We identified an unexpected association between MMR deficiency and older age. Among the 14 cases with loss of MLH1, 10 samples exhibited hypermethylation. Of the 90 cases evaluated, 15 (16.7%) carried KRAS mutations; we found one previously unreported mutation (G13R). Peruvian CRC tumours exhibited the highest prevalence of MMR deficiency reported to date. The expected hereditary component was also high. The age of onset of these MMR deficient tumours was greater than that observed for non-MMR deficient cases, suggesting the ineffectiveness of the Bethesda criteria for Lynch syndrome screening in Peru. Prospective studies are warranted to define the molecular characteristics of CRC in this population.