Anticancer Res. 2001 Jan-Feb;21(1A):253-9.

Bax protein expression in colorectal cancer: association with p53, bcl-2 and patterns of relapse.

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Source

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Abstract

This study evaluated the frequency and the prognostic significance of bax, bcl-2 and p53 proteins in stage B and C adenocarcinomas of the colon and rectum. Paraffin-embedded specimens from 268 patients with colorectal adenocarcinomas, treated with surgery, were assessed; of these 160 cases were Duke's stage B and 108 cases were Duke's stage C disease. Adjuvant chemotherapy was given to all stage C and to 108 out of 160 stage B cancer patients, while those having rectal malignancy also received pelvic radiotherapy. Duke's stage B patients were treated either with surgery alone or with surgery and radiotherapy. The follow-up period at the time of analysis ranged from 12-72 months (median 32 months). Immunohistochemical expression of bax, bcl-2 and mutant p53 proteins was detected with a frequency of 42%, 37% and 48%, respectively. However, the expression was strong only in 17% of tumours, on average. A strong bcl-2 expression was significantly associated with a strong bax expression ($p < 0.0001$) and with absence of p53 nuclear accumulation ($p < 0.005$). There was, however, no correlation between bax and p53 proteins. Furthermore, bcl-2 expression was significantly more frequent in grade I and 2 adenocarcinomas compared to grade 3 disease ($p = 0.01$). In stage B (but not C) adenocarcinomas, bax expression was directly associated with higher risk of local relapse ($p = 0.04$). By contrast, cases with p53 nuclear accumulation, when they had received adjuvant radiotherapy, were significantly associated with a lower incidence of local relapse ($p = 0.01$), but a higher rate of distant metastasis ($p = 0.06$). Multivariate analysis for disease free and overall survival showed that bax expression and high Duke's stage were independent prognostic parameters associated with an unfavourable outcome ($p = 0.009$ and $p = 0.0001$, respectively). It was concluded that the immunohistochemical expression of bax is a marker of poor prognosis and of a higher risk of local relapse in patients with colorectal adenocarcinomas. p53 nuclear accumulation is associated with a better local control, following radiotherapy and with a metastatic phenotype. The development of novel monoclonal antibodies recognising specifically the mutated versus the wild type form of proteins would apparently improve the prognostic and predictive value of the immunohistochemically detected apoptotic proteins.