Anticancer Res. 1998 Nov-Dec;18(6B):4685-92.

p53 and bcl-2 expression in locally advanced squamous cell head-neck cancer treated with platinum based chemotherapy and radiotherapy.

Giatromanolaki A, Koukourakis M, Zaramboukas T, Skordalaki A, Arapantoni P, Georgoulias V, Fountzilas G.

Source

Department of Radiation and Medical Oncology, University Hospital of Iraklion, Crete, Greece.

Abstract

BACKGROUND:

The role of apoptosis regulating oncoproteins in defining response to cytotoxic therapy remains poorly understood. Loss of wild type p53 function and bcl-2 protein overexpression are well known to inhibit the apoptotic pathway in in vitro studies.

METHODS:

We immunohistochemically examined the nuclear accumulation of mutant p53 and the cytoplasmic overexpression of bcl-2 proteins in 76 patients with locally advanced inoperable squamous cell cancer of the head and neck area. Patients were treated with platinum based chemotherapy and radiotherapy (37 with induction and 39 with concurrent chemotherapy). The median follow up period was 72 months.

RESULTS:

Thirty five (46%) cases were positive for p53 and 41 (54%) negative, whilst 19 (25%) and 57 (75%) cases were positive and negative for bcl-2 respectively. A high percentage of bcl-2 positive cells was associated with a low incidence of nodal involvement. A statistically significant higher percentage of p53 positive cells was observed in the group of patients with complete disappearance of the disease as compared to the group with residual disease after treatment ($p = 0.01$). High percentage of p53 positive cells and concurrent chemoradiotherapy was associated with better local progression free survival ($p = 0.05$ and 0.02). In multivariate analysis, the type of chemotherapy (concurrent vs. induction) was the only significant prognostic variable for local relapse ($p = 0.02$) and overall survival ($p = 0.03$).

CONCLUSIONS:

The present study provides evidence that p53 nuclear accumulation may be associated with better response to DNA damaging cytotoxic agents. The association of wild type p53 loss with decreased DNA repair enzyme activity is a possible explanation. Induction platinum based chemotherapy may contribute to the selection of clonogenic cells with a radioresistant phenotype.