

Correlation of aberrant expression of p53, Rad50, and cyclin-E proteins with microsatellite instability in gallbladder adenocarcinomas

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ABSTRACT. Gallbladder carcinoma is an uncommon, but highly malignant tumor, with poor prognostic, and diagnostic manifestations in early stages. The Indian Council of Medical Research reported increased incidence of gallbladder carcinoma in the surviving population of the Bhopal gas tragedy that involved exposure of more than 500,000 people to methyl isocyanate gas. The severity of exposure, and increased multi-systemic morbidity in the survivors stimulated us to examine the molecular changes leading to gallbladder carcinoma. Surgically resected samples (N = 40) of gallbladder carcinoma were studied for the p53, Rad50, and cyclin-E expression by immunohistofluorescence bioimaging. Among the 40 samples, 23, 11, and 10 showed p53, Rad50, and cyclin-E expression, respectively, in moderately differentiated adenocarcinomas, demonstrating the prevalence and inva-

siveness of this disease in the methyl isocyanate-exposed population ($P = 0.0009$). Nevertheless, co-expression of Rad50, and cyclin-E with p53 was absent in adenomas with dysplasia, demonstrating their independent roles. We conclude that there was altered expression of p53, Rad50, and cyclin-E in the malignant transformation of gallbladder carcinoma in this methyl isocyanate gas-exposed cohort. Hence, these proteins may be useful as markers to identify premalignant lesions that are likely to progress into malignant adenocarcinoma.

Key words: Gallbladder cancer; Methyl isocyanate; p53; Rad50; Cyclin-E