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Suppression of Experimental Liver Tumors by Estradiol-3-Benzoate Treatment or Castration in Male Rats

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Abstract: Epidemiologically the incidence of liver cancer is markedly sex-differentiated, with a much higher frequency in men than in women. In experimental animals, it is also higher in male than in female irrespective of carcinogen-induced or spontaneous tumors. Therefore, we tried to investigate the modulating effects of sex hormones in experimental hepatocarcinogenesis. For induction of liver tumors, mini-osmotic pump containing diethylnitrosamine at a dose level of 47.5mg was implanted into the peritoneal cavity of the rat at 6 weeks old. To remove the effects of male sex hormones, the animals of group 2 were castrated one week prior to DEN treatment. To see the effects of estrogen, pellet containing 1g or 10g of estradiol-3-benzoate was infused subcutaneously to the animals of group 3 and 4 one week prior to DEN treatment. The pellets were exchanged every 4 weeks until sacrifice. All animals were sacrificed at 26 weeks after DEN treatment. The tumor incidences in group 1 (DEN alone), group 2 (DEN +castration), group 3 (DEN +EB 1g) and group 4 (DEN +EB 10g) were 100% (15/15), 93.3% (14/15), 85.7% (12/14) and 66.7% (10/15), respectively, showing that the value of group 4 is significantly different from that of group 1. Tumor multiplicity data of group 1, 2, 3 and 4 were 5.470.73, 2.800.51, 2.070.41 and 1.670.46, respectively, showing castration or EB treatment reduced number of liver tumors significantly ($P<0.001$). With immunohistochemistry and Western blotting of ER the expressions were detected in normal adjacent liver cells but decreased or lost in tumor cells. From these results we conclude that female sex hormone, especially estrogen, may act as a liver tumor suppressor, and it seemed that the down regulation of ER may be associated with liver tumor development.