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Histological and Ultrastructural Study on the Effect

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Abstract : Tamoxifen (TM) is a synthetic non-steroidal antiestrogen. It is one of the most effective drugs for treatment of estrogen-dependent cancer by binding to estrogen receptors, suppressing of epithelial proliferation and as a chemotherapeutic agent. Recently, more attention has been paid to the protective effects of natural antioxidants against toxicities induced by anti-cancer drugs involving free radical-mediated oxidative stress and tissue injury. Vitamin C is a potent antioxidant that has the ability to scavenge factors causing free radical formation in animals receiving tamoxifen. The present study aims at pinpointing the TM-induced histopathological and ultrastructural changes in the kidneys and to assess the possible chemoprotective role of vitamin C against such TM-induced microscopic changes. Thirty adult male CD-1 mice, 25-30 g in weight and 3 months old, were divided into three groups. The first group served as control. The second group received the therapeutic dose of TM at daily oral dose of 40 mg/kg body weight for 28 days. The third group received the therapeutic dose of vitamin C at a daily dose of 500 mg/kg body weight simultaneously with the therapeutic dose of TM used in group two for 28 days. Animals were sacrificed and kidney samples were obtained and processed for histological and ultrastructural examination. Histological changes induced by TM included damage of the renal corpuscles including obliteration of the subcapsular space, congestion of the glomerular blood capillaries, segmental mesangial cell proliferation with matrix expansion, capsular adhesions with the glomerular tuft especially at the urinary pole of the corpuscles. Moreover, some proximal and distal tubules suffered various degrees of degeneration in some lining cells. Haemorrhage and inflammatory cell infiltration were also observed in the intertubular spaces. Ultrastructural observations revealed damage of the parietal epithelium of Bowman’s capsule, fusion and destruction of the foot processes of podocytes and great increase of mesangial cells and mesangial matrix. The cells of the proximal convoluted tubules displayed marked destruction of the microvilli constituting the brush borders and degeneration of the mitochondria; besides, abundant lysosomes, numerous vacuoles and pyknotic nuclei were observed. The distal convoluted tubules displayed marked distruction of both the basal infolding and the mitochondria in some areas. Histological and ultrastructural results revealed that treatment of male mice with TM simultaneously with vitamin C led to apparent repair of the injured renal tissue. This might suggest that vitamin C (an antioxidant agent) can minimize the toxic effects of TM (an antiestrogen).

Keywords : tamoxifen, vitamin c, mammalian kidney, histology, ultrastructure
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