ABSTRACT

Daunorubicin (DAU) was the first anthracycline (ANT) antibiotic with impressive clinical activity in the treatment of acute pediatric leukemias. Later, it has been shown that anthracyclines have broad range of therapeutic activities against both hematological and solid tumors, including breast, ovarian and gastric carcinoma. On the other hand, ANTs are the most dangerous anticancer drugs with respect to cardiovascular toxicity characterized by mostly irreversible morphological changes and cell death. Indeed, ANTs are used also in patients with hypercholesterolemia so the effect on atherogenesis in blood vessels is of interest.

Thus, we hypothesized that DAU treatment and cholesterol diet will aggravate atherosclerosis when compared to rabbits fed by cholesterol diet only. Twelve adult male New Zealand White rabbits were fed with cholesterol diet (0.2% cholesterol). Control group of rabbits (n=7) received saline i.v. once weekly for 10 weeks since the beginning of the 4th week, the second DAU group (n=7) received clinically relevant doses of daunorubicin (3 mg/kg, ≈ 50 mg/m2, i.v.). The systematic uniform random sampling was applied for the quantification of atherosclerotic lesions. The samples from aortic arch were taken for the evaluation. Serial sections of vessel (7 μm) were cut on a cryostat and Hematoxylin – orcein staining was used for the histological and morphometric evaluation.

The results of the morphometric analysis showed that atherosclerotic plaque size was not significantly different between rabbits treated with DAU and cholesterol diet compared to rabbits on cholesterol diet only. The results of this study showed that combination of DAU treatment and cholesterol diet did not aggravate atherosclerosis in aortic arch when compared to rabbits fed with cholesterol diet.

Key words: Cholesterol, endothelial dysfunction, atherosclerotic plaque, anthracyclines, daunorubicin, anthracycline cardiotoxicity