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Role of estrogen in the etiology of peliosis hepatis

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Summary

The aim of the study was to determine the relationship between estrogen and the development of peliosis hepatis. The experiment was conducted on female Wistar rats. Oestradiolum benzoicum was administered i.m. for 8 weeks in different doses. On the basis of the obtained data the authors claim that estrogen can be responsible for the development of vascular disorders described as peliosis hepatis. Furthermore, there is a relationship between the intensification of observed changes and the dose of the injected estrogen. An increased awareness of peliosis hepatis may become an important symptom for a pathologist, especially in patients at risk.

Keywords: liver, estrogens, peliosis, vascular disorders

There is evidence that drugs, primarily anabolic steroids, may be associated with hepatic lesion (2, 5). Hepatic peliosis was first recognized in the German literature in 1861 by Wagner and named by Schoenlank in 1916 (10). This a rare condition is characterized by the presence of blood-filled lacunar spaces and by areas ecstatic sinusoids (7). The exact pathogenesis of peliosis is unknown. This damage of the liver is most often asymptomatic and an incidental finding at autopsy. However, other experimental and epidemiological studies are needed to explained the etiology of this condition. The aim of our study was to determine relationship between estrogen and the development of peliosis hepatis.

Material and methods

The whole experiment was based an animal experimental model. The studies were designed according to the guidelines Bioethical Committee University School of Medicine of Lublin. Experiment was conducted on female rats of Wistar bleed with initial body weight of 180-300 g. The animals we subjected to reverse light cycling for 2 to 3 weeks before use. The middle dark point was set at 10 a.m. Rats were housed in standard laboratory cages (max. 6 pieces per cage). After acclimation period, animals were gathered in 5 experimental groups of minimum 10 in a group. *Oestradiolum benzoicum* (Jelfa, Jelenia Góra, Poland) was used for the purpose of this study. *Oestradiolum benzoicum* was given i.m. once time per week for 8 weeks in three different doses: E1 – 0,00075 g/kg of the body weight (n = 15 number of rats); E2 – 0,0015 g/kg b.w. (n = 15); E3 – 0,03 g/kg b.w. (n = 15). Two control groups were designed: K0 – the untreated animals (n = 15); K1 – the animals received the adequate quantity of *oleum pro injectione* (n = 15). All the animals were killed by decapitation after 9 weeks of experiment and the liver were delivered by laparotomy. Fragments of organ assigned for histological examination were fixed in 10% buffered formaldehyde solution and transformed into paraffin sections, routinely. Histological preparations were evaluated in light microscope (Axioscop of Zaiss make). The histological asses were determined using: hematoxylin-eosin, azan, and histochemical paS (periodic acid-Schiff) stains.

Results and discussion

There were more dead rats in the groups of treated animals (32,3%) than in the both control groups (19%). Histological evaluation revealed the presence of not regular staining of cells and the circular nuclear showed different stainability (K0, K1, E1, E2). The hepatic triad was clear visible. Stainability of nuclears were the same in all cells. Similar, the cytoplasm stained using the hematoxilin-eosin method did not show any significant changes (K0, K1, E1, E2). In all groups of animals, the places of regular lobulated structure were visible. The liver's cells were organized into clusters with not clear visible borders. The lumen of vessel was dilated and the clusters of erythrocytes inside the vessel and blood extravasation within the triads were noticed (E1, E2). In cases of animals treated by higher doses of estrogens, the large inflammatory infiltrations and vasculitis involving small

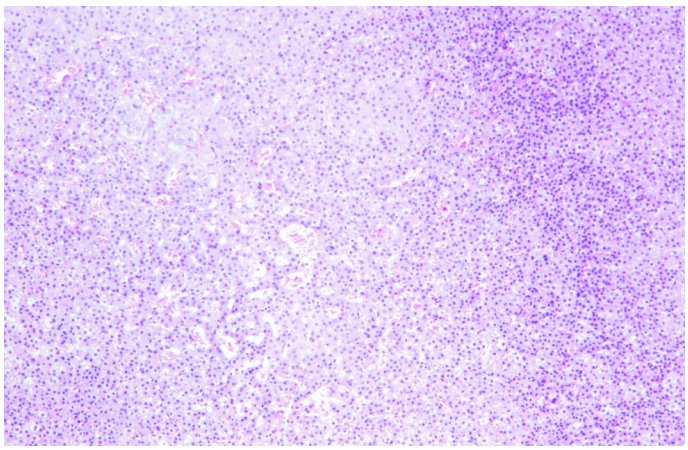

Fig. 1. Peliosis hepatis. The inflammatory infiltrate remains within the portal tract

caliber vascular channels were observed (E2, E3). The inflammatory infiltrate consisted of eosinophils and mononuclear cells (E2, E3, E1). We observed numerous, diffusely distributed rounded spaces with bloody fluid inside, which was occasionally clotted. In single cases the foci of parenchymal hemorrhage of some spaces were revealed (Fig. 1). Neighboring hepatocytes were swollen and microvesicular fatty changes were clear visible.

The results show that long-term estrogen administration initiates changes which are described as peliosis hepatis. Yanoff and Rawson (9) described two morphologic patterns of hepatic peliosis. The parenchymal type is characterized by irregular blood-filled spaces, not lined by endothelium or fibrous tissue. They are associated with areas of focal necrosis in the surrounding hepatic tissue. The phlebectatic pattern shows minimal hepatocyte necrosis. The regularly spherical, centrilobular blood-filled spaces are lined by endothelial cells and fibrotic tissue and freely communicate with the hepatic sinusoids (8). Microscopically, rounded blood filled spaces were seen to be involved in different areas of liver. These areas were occasionally adjacent to areas ectatic sinusoids. The spaces contained erythrocytes were founded (E2, E3). In 3 cases there were changes identified as a vascular hamartoma. These changes were compared with results obtained by Molleken. This author, occasionally observed areas of organizing hemorrhage with parenchymal necrosis which we also noted, in single cases in light microscopy. These findings could explained the pathogenesis of liver lesions. The progressive numbers of erythrocytes accumulated within hepatocytes hepatocellular necrosis are responsible for the formation of blood space (4). In available literature, association of peliosis hepatis with hepatic tumors was described (1). It is difficult to refers the results of experimental studies to human peliosis hepatis. On the base of our study, we can say that this is possible, but the higher doses of estrogens and long-term treatment are required to the development of hepatic-tumors. Peliosis hepatis can be the important symptom of carcinogenesis (3). The higher doses of sex steroids have given through the long time led to the peliosis hepatis. Early development these changes has allowed to avoid the tumors, especially in patients of risk groups.

Conclusions

1. Estrogen can be responsible for the development of peliosis hepatis.
2. There is the relationship between the intensification of observed changes and the dose of injected estrogens.
3. An increased awareness of pelosis hepatis may become an important symptom for pathologist, especially in patients at risk.

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