Therapeutic pathomorphism of pancreas cancer under the effect of amitozyn preparation

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Introduction

Pancreas ductal adenocarcinoma is among the first ten most common causes of cancer mortality in Western Europe and the USA (every year 40 000 people die in Europe and 30 000 in the USA). However, in spite of the variety of chemotherapy options, therapeutic pathomorphism has not been addressed in the literature [1].

A great deal of publications on medicinal preparations of Chelidonium majus L alkaloids, amitozyn in particular, indicates that this preparation is accumulated in ontologically transformed tissues [2] which furthered our research on therapeutic pathomorphism after it has been used on patients with pancreas cancer.

Materials and methods. The study of therapeutic pathomorphism of pancreas cancer under the effect of amitozyn was performed in 16 patients who underwent treatment at Kiev centre for liver, bile duct and pancreas surgery on the clinical base of the Department of General Surgery №1, Bohomolets National Medical University [3]. Of all the patients, 12 of which had a second surgery on account of duodenal obstruction in the period of 5±2 months and in 4 more cases a fatal outcome was observed. The patients received 3±1 course of treatment with amitozyn. The preparation was administered daily intravenously at 25 mg, total dosage per a course was ∑=259mg intravenously.

The interval between courses was approximately 1,5 months. The changes observed in the patients were of the same character which gave us grounds to conclude about certain peculiarities of pathomorphism signs.

Therapeutic pathomorphism was studied by comparing the histological material, obtained after the first operation and that after the second operation or at the section. The histological preparations, treated in a standard way, were stained with hematoxylin and eosin, trichrom according to Mason, mucopolysaccharides in sections were revealed by PAS-reaction and mucous substances by mucicarmine.

Results. Therapeutic pathomorphism of pancreas cancer under the effect of amitozyn was observed on both tissue and cellular level.

On the level of tissue the following changes were observed. 1,5±0,5 fold increase was observed in the square of sites of tumor issue necrosis in comparison with spontaneous necroses. Sclerosis signs were found everywhere, including perivascular sites where they were not observed in spontaneous processes in pancreas. More necroses were found at the sites where parenchyma dominated stroma. Stromal elements necrotized far rarely, and in some cases considerable connective tissue strands served as a barrier that separated a vitalized tissue from necrosis sites with the border quite distinct in some cases. PAS-reaction performed on the histological preparation in pancreas cancer enabled us to clearly differentiate a vitalized tissue that produces PAS-positive substances, PAS-slight positive connective tissue fibers and PAS-negative necrosis sites.

Staining with trichrom according to Mason gave much information. This technique proves to be most informative for studying pathomorphism. Due to this technique we were able to follow blood supply disturbance in the form of perivascular and perineural hemorrhages, hemorrhagic invasion of tissue, desegregation of connective tissue fibers, marginal location of blood elements, varicose changes of vessels, and the aneurism of their walls. Fibrinoid invasion of vascular walls and adjacent fascicles of connective tissue was also observed.

We should note that it is fibrinoid extravasation, sometimes observed at spontaneous secondary changes in pancreas cancer, occurred at therapeutic pathomorphism and was detected quite often. We consider it requires our close attention.

When we have the invasion of pancreas tumor to adjacent tissue, particularly to the region where are parapancreatic lymph nodes, however, inside lymph nodes themselves even though they are were lined with pancreas tumor tissue, we found neither metastatic signs, nor pancreas tumor invasion from outside through capsula nodi lymphatici**.** At the same time connective tissue capsula nodi lymphatici bore all the signs of fibrinoid invasion. In our opinion, a fibrinoid transformed connective tissue capsula nodi lymphatici serves as a barrier that inhibits the expansive invasion of pancreas tumor tissue to a lymph node or prevents the metastasis of it through blocking the lymph circulation on the level of a fibrinoid transformed capsule of a lymph node.

The phenomena of an extravascular fibrin formation and the invasion of stromal and parenchymatous componenets of pancreas cancer with fibrin and fibrinoids should be treated as one of universal manifestations of therapeutic pathomorphism. Extravascular fields of fibrin that "get deposited" in the parenchyma of pancreas cancer lead to "immuring" parenchymatous componenets of a tumor at these sites of fibrin. It is clear that the metastasis from the sites captured with fibrin fibers is impossible.

In the course of time (when neocolagenogenesis proceeds on fibrinoid changed sites) separately located cancer cells or even small group of cells lose their inherent in normal conditions ability to synthesize neutral mucopolysaccharides. At the same time, beyond newly formed connective tissue fields the ability for mucin-production in identical preparations retains.

The generation of basophilic structures, which we called " hematoxylin corpuscles" is an interesting, though not frequent but always demonstrative manifestation of pancreas cancer pathomorphism under the influence of Chelidonium majus L. preparations. These structures were found among the centers of necrotizing tumor parenchyma when tumor cells assume a round shape, lose contact between themselves and increase in size. Cytoplasm absorbed acid dyes intensively. Nuclei were in pyknosis and rhexis state, assuming a pronounced likeness to basic dyes and hematoxylin, in particular. With time the lunate structures of cancer components acquired a distinctive appearance: the periphery of every particular lunula was presented with an eosinophilic crown, which arose inside a basic membrane of a lunula from cytoplasmic detritus.

Histochemical peculiarities of "hematoxylin corpuscles" provide reason to state that these corpuscles represent the centers of junction of native DNA of tumor cell nuclei at necrosis that proceeds very fast.

Another important manifestation of the therapeutic pathomorphism of pancreas cancer under the influence of amitozyn is the increase in the differentiation of initially low-differentiated structures. This phenomenon, which can be characterized as prosoplasia was found more frequently in cancers with a dominated parenchymatous component and a high vascularization. On the background of massive necrotic fields and single low-differentiated cancer lunulas among necrotic masses, there can be found bands of epithelial structures along the stromal skeleton. These bands resemble a single-sphere cylindrical epithelium with a clear polarity of nuclei that is located nearer to the stromal skeleton and have the signs of high differentiation.

This epithelium retains (probably acquires) the ability for the secretion of neutral mucopolysaccharides through the apical part of a cell, which becomes apparent at high magnification when stained with mucicarmine.

Conclusion. Therefore, the therapeutic pathomorphism of pancreas cancer under the influence of Chelidonium majus L. alkaloids is a positive and objective phenomenon that has its properties and peculiarities. There is no doubt that like any other pathomorphism, the phenomena, outlined above, have a paraspecific character. At the same time, the recurrence, systematic and cognizable character of the changes that have been morphologically described

and investigated here, allows us to make conclusions about the carcinostatic effect of amitozyn on pancreas cancer.

References.

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