Biological Features of Tumors Results of Experimental Studies

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Tumor anaplasia can be of varying degrees, being especially marked in fast-growing malignant tumors. Blastomatose tissue is characterized by morphological, chemical, physico-chemical and energetic anaplasia. Structural changes of the tissue specific to blastomatose growth often provide the opportunity to differentiate this tissue from a normal or any other growing tissue. Out of various factors that may influence the external environment of tumors, we should mention food, profession, living and working conditions. Tumors and especially malignant tumors are accompanied by changes in the entire body. These are not just a consequence of the blastomatose growth but also play a role in its subsequent development. Experimental tumors are one of the methods of studying the issue of blastomatose growth. The tumor transplantation method is widespread and extensively applied in laboratory practice. It uses standard strains of tumors (rats, mice, etc.). The simplicity of the tumor transplantation method, which consists of the inoculation under the skin of animals of tumor fragments using a trocar or of the injection of a tumor emulsion under aseptic conditions, enables researchers to maintain the purity of the strain for a long time. Various views have been formulated at different times on the origin of tumor growth in accordance with the level of knowledge on this issue.

Keywords: tumors, biological changes, biological features, transplantation, etiology, pathology

The statistics of malignant tumor diseases shows that these appear more and more often. It may be explained by better cancer diagnosis; in accordance with available data, the number of cases of internal organs undiagnosed in the past has increased, while the number of skin cancer cases has been stationary.

Experimental part

Tissue anaplasia

One of the peculiarities of tumors is their atypical character, namely, all biological properties that distinguish tumor tissue from all other tissues. The atypical nature of tumors is based on tissue anaplasia which is characterized by weaker differentiation or a rejuvenating tissue, specific features of functional and morphological behavior compared to the tissue in which the tumor originated.

Morphological features of cells defining the immaturity of tumor tissue and its weak differentiation are not always strictly specific to the growing tissue. Tumors are composed of two tissues: the parenchyma and the stroma; the latter is not the bearer of features typical to blastomatose tissue; due to its growth, the stroma is the result of unformed connective tissue of the tumor.

Chemical anaplasia consists of the modification of the chemical composition of tumor cells, a higher concentration of water in cells. More intense is the tissue growth, more quantity of water and less mineral substances it contains. The concentration of water in any young tissue decreases with the reduction of growth energy. The blastomatose tissue contains large amounts of potassium, which conditions the imbibing of colloids, and relatively small amounts of calcium salts. The K/Ca coefficient changes are dependent on the blastomatose growth speed. In tumor cells, we may often note the infiltration of fat and the increase of the concentration of unsaturated fatty acids and an increased quantity of lipoids, especially cholesterol.

The glycogen content of tumors also increases in relation to the disorder of carbohydrate metabolism in tumors, which also explains the accumulation of lactic acid.

The tumor tissue is characterized by protein metabolism disorder. There appear cells with protein structure different from the normal structure. The modification in the composition of the amino acids of tumor proteins is a proof in this sense. Tumors have low concentrations of cystine, methionine and tyrosine; since the concentration of ribonucleic acid is higher, it can be transformed into deoxyribonucleic acid; proteolytic processes increase in tumors. More intense is the tumor growth, more malignant it is and more pronounced are the chemical changes in the tumor. Since the protein, lipid and carbohydrate metabolism processes are modified, insufficiently oxidized metabolism products accumulate in the tumors.

Physicochemical *anaplasia* is accentuated especially in intense blastomatose growth. Physicochemical deviations include the change of colloidal properties of the protoplasm. The degree of dispersion of colloids grows and their superficial tension is low; the osmotic concentration of the tissue environment increases due to metabolic disorders and the accumulation of insufficiently oxidized metabolic products.

The electric charge in tumors is higher than in the corresponding normal tissue. The electrical conductivity of the blastomatose tissue is disturbed. The more malignant the tumor, the lower the tissue resistance to electric current.

All physicochemical modifications may be explained by a change in the balance of the electrolyte and with the increase of electric conductivity; they condition the increase of permeability regulating the metabolism between tumor cells and the environment.

Anaplastic energy is related to the protein, nucleic, lipid, lipoid and carbohydrate metabolism disorder. Metabolic disorders are caused by the chemical and enzymatic composition of tumors. Significant modifications show that carbohydrate metabolism is the main source of energy for blastomatose tissue growth.

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The ability to live in anaerobic conditions, the growth and multiplication of tumor cells due to anaerobic glycolysis is specific to blastomatose tissue.

While normal tissue dies quickly in hypoxia, blastomatose tissue can live through the anaerobic splitting of carbohydrates accompanied by the release of an amount of energy required for protein synthesis. Lactic acid accumulation is the cause of increased acidity which explains swollen connective fibers, modification of superficial tension and other chemical and physical-chemical modifications found in tumor tissue.

Results and discussions

Features of tumor growth

The growth of tumors differs from any other tissue growth; tissue grows involving the normal cellular elements arranged in the vicinity.

Growth by apposition is found in the early tumor growth stage; it is not specific to well-developed tumors. Tumor metastasis of tumors occurs solely by movement of the cell elements of the primary tumor. In the process of its growth, the tumor is used by the metabolic products from the surrounding tissues.

The less differentiated the tumor cell elements that have lost their normal morpho-functional features, the faster the tumor growth.

Unlike other forms of tissue growth, tumors are characterized by irregular growth manifested by the adjustment disorders of the entire system.

Blastamatose growth is usually huge and it often leads to the death of the body. This feature should be understood as a potential capacity of tumor tissue for unlimited growth; the more atypical its structure, the quicker its growth. Due to the fact that the most atypical tumors have the most malignant evolution, the body dies before the tumor has reached big dimensions. Feeding on nutrients from the surrounding tissues, tumors are parasitic formations growing at the expense of the body.

Blastomatoase growth can be of two types: *expansive growth*, which defines structurally less atypical tumors with less accentuated anaplasia with a reduced potentiality to grow and multiply; *infiltrative growth*, in which the tumor invades the surrounding tissue, the boundary between the tumor and normal tissue becoming indefinite; it may invade the lumen of the blood or lymphatic vessels, giving rise to a new tumor growth, tumor metastasis.

The importance of the nervous system in the metastasis of tumors is confirmed by changing direction of metastases after traumatic (sectioning the nerves) or chemical injury (formaldehyde or carbolic acid solutions) of the nervous system.

The infiltrative growth that produces recurrences and metastases, and the anaplasia of cell elements are specific to malignant tumors; in contrast, tumors with expansive growth that do not usually produce metastases and relapses are benign.

The influence of various external and internal environment factors on tumor growth

Diet influences tumor growth; the decrease in caloric value of food leads to delay in tumor growth; tumor growth intensifies when food contains abundant quantities of carbohydrates, cholesterol and potassium.

Profession (if we refer to chemical and mechanical excitations) may have an impact on cancer morbidity in specific contexts.

Age may also be important in cancer morbidity. The increase of morbidity due to tumors was noticed with the aging of specific patients.

We should acknowledge the importance of the nervous system activity disorders in the appearance and evolution of tumor growth. The importance of *moral depression* was noted in the predisposition to cancer disease, as well as the psychic trauma in case of tumor appearance and the role of the cerebral cortex in the mechanism of tumor occurrence.

Based on the theory of nervous system trophic function, some researchers view the tumor as a neuro-dystrophic process. The chronic outbreak of the nervous system lies at the basis of dystrophic processes and maintains this process in tissues.

Body modifications during tumor growth

One of the phenomena observed in the body during malignant tumor cachexia is *general achexia*, i.e. body exhaustion with a sharp drop in weight, intoxication and sometimes severe anemia. Cachectic phenomena may be discovered even in the early stages of tumors. The cause is the disrupted body metabolism and tumor tissue, as well as the fact that, by their enzymatic action on the surrounding tissue, malignant tumors give rise to substances intoxicating the body. In fast-growing tumors, cachexia is due to body intoxication by breakdown products that are formed after tumor autolysis.

In cancer cachexia, metabolic changes occur in the entire body:oxidative processes decrease and fermentative processes specific to blastomatose tissue are intensified causing the accumulation of intermediary products of carbohydrate, parotid, lipid and lactic acid metabolism in blood and tissues. These poorly oxidized metabolic products, such as polypeptides, amino acids, lactic acids and ketone bodies, appear in urine.

The altered metabolism of cancer patients also manifests itself in the ability of their blood to stop the mitogenetic radiation of cells. Malignant tumors cause the inevitable death of the body. In such cases, the decrease is usually of 20-30% and never reaches the critical limit of (50%). The body dies not only due to cachexia but also due to bleeding, infections, disorders of the vital organs affected by cancer and due to the low general resistance of the body that often accompanies the development of malignant tumors.

A general action on the body may also be exercised by the so-called benign tumors (uterine myomas, etc.) sometimes accompanied by strong bleeding that exhausts the patients.

Results and discussions

The results of the experimental study on the tumor

The first systematic research on the transplantation of tumors was conducted by Novinski in 1875. He managed to transplant dog sarcoma to dogs and dog cancer to horses.

Rats and mice are very suitable for studying experimental blastomatose growth (especially malignant tumors). Most widespread sarcoma in rats and cancers in mice have been transplanted from one another. The tumor transplantation method was used to obtain the material for the study of blastomatose growth.

The simplicity of the tumor transplantation method, consisting of the placing under the skin of animals of tumor fragments by means of a trocar or by injection of a tumor emulsion under aseptic conditions, helps maintaining the purity of the strain for a long time. The percentage of successful transplantations depends both on the properties of the tumor stem and also on the properties of the receiver.

In addition to transplantations, there are other ways of producing experimental tumors by the action of chemical and physical excitation on the body of the animal.

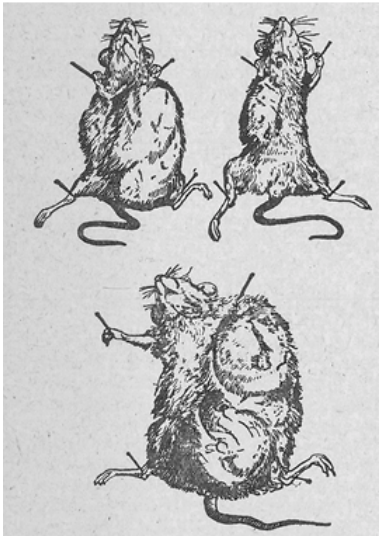

Fig.1. Cancer in mice

Considering the results obtained experimentally, we should mention that animal tumors are not identical to human ones: manifestations of growth, development, evolution and prognosis are different. However, experimental data confronted with clinical observations enabled researchers to study closer the issues of etiology and pathogenesis of tumor growth in humans.

The following conclusions on the occurrence and development of tumors by means of experimental blastomatose growth were drawn:

For a transplant to succeed, it is necessary to transport living tumor tissue from one animal to another. Tumor transplantation is an experimental metastasis in a new animal body. Most transplanted cellular elements are destroyed and those left alive by multiplying give rise to a new mass having all the transplanted properties. In some cases, living cells are not required for a tumor to appear in the recipient.

Tumor transplantation sometimes fails. Resorption of the transplanted fragment often occurs; unsuccessful transplantation has various causes which depend both on the nature of the transplanted material and on the properties of the recipients. In some cases, the transplant does not develop in the new conditions but boosts the development of a tumor that has nothing in common with the transplanted tumor.

Transplantation fails if the tumor is inoculated to animals of the same species (from rats to rats, from mice to mice, etc.); it is rarely successful in different species (from white mice to gray mice).

Successful transplantation, even within the same species, depends mostly on exogenous factors (diet modification, the action of various toxic substances, Rçntgen rays), as well as on the change of the internal environment of the body.

The appearance of experimental tumors can be produced by the action of chemical and physical irritants. Carcinogenic properties, except for polycyclic hydrocarbons, are specific also to other organic compounds: azo compounds, naphthylamine and substances with a simpler structure, such as carbon tetrachloride and chloroform. Arsenic salts, zinc, chromium, beryllium, etc. belong to inorganic carcinogenic substances.

Cancer may occur several months after the animal skin has been sprinkled with these carcinogens; cancer or sarcoma may appear depending on the tissue subjected to the action of these substances, in case of subcutaneous, intramuscular, intraperitoneal or oral, administration. Some of these substances have an intense carcinogenic action.

A common chemical nature has been established between carcinogenic hydrocarbons and sterol (adrenal hormones, bile acids and vitamin D).

Regarding carcinogens, in addition to local tissue changes, these substances also cause general modifications in the body, quantitative and qualitative changes of white blood cells, atrophic and degenerative changes in the spinal cord, lymph nodes, thyroid and especially in the spleen; in these cases, no inhibition of the reticulo-endothelial system was found.

Physical excitants. Prolonged mechanical influences may also cause such tumors; gallbladder cancer occurs in guinea pigs long after the introduction due to stones.

Cancer may be caused in rats and mice under the influence of low doses of Roentgen and radium rays. Depending on their dose, these rays cause the appearance of new masses and accelerate or inhibit their growth. Roentgen and radium rays inhibit the growth of various tissue elements to a different degree: cells that grow and multiply quickly show a great sensitivity to their action; it is on what the treatment of tumors with Roentgen and radium rays is based.

There are specific observations that show the occurrence of tumors after an excessive action of ultraviolet rays and even after massive irradiation of the facial skin by sunlight.

Rats subjected to prolonged sunlight action (for one year) developed tumors on the exposed portions of skin uncovered by fur. It is assumed that irradiated areas are rich in ergosterol, turning that into a carcinogenic substance; this hypothesis was not confirmed.

Malignant growth can be achieved by transplanting not only the tumor but also the normal tissue, cultured under specific conditions.

Tissue culture outside the body is very important for the study of blastomatose growth. The tumor transplanted into plasma grows and preserves its metabolic features. Grafted on an animal of the same species, it can give rise to a corresponding tumor. So, for several years, cultivation of murine adenocarcinoma tissue was made by moving it to fresh media; the cancerous tissue preserved all its biological properties. Cell necrosis detected in cancerous tissue cultures leads to the formation of substances that probably stimulate the growth and multiplication of cancer cells remained alive.

The experimental study of blastomatose growth helped to establish the *link between the occurrence of tumors and chronic excitations originated from the action of various biological agents on the body.*

The number of known tumor viruses remains small. Leucosis of mice and some tumors in amphibians and fish belong to the tumor viruses category.

The regeneration or chronic inflammatory proliferation that may trigger a blastomatose growth occurred after the action of various excitants on the tissue. These pathological changes preceding the blastomatose growth are viewed as a fertile ground for the emergence of tumors.

Chronic intoxication of mice and rats with coal tar can cause precancerous states. Malignant transformation is preceded by a precancerous period when tissue trophicity worsens.

The data show the importance played in the appearance of experimental cancer not only of the external excitation factor but also of the response properties of the whole body and its tissue, especially the elements of proliferating and propagating young tissue.

Immunity against tumors is manifested by an acquired resistance to them after spontaneous reabsorption of the

tumor. Artificially acquired resistance is also detected after the reabsorption of a tumor fragment transplanted earlier. Immunity to tumors is explained differently.

Tumor etiology and pathogenesis

Tumor etiology and pathogenesis is one of the most pressing issues in pathology. Various opinions in different times were formulated on the origin of tumor growth consistent with the level of knowledge in this area.

According to Cohnheim's theory of embryonic inclusion, tumors appear from embryonic cells remained in the body after the first stages of its ontogeny due to lack of involution.

The irritation theory considers that the origin of tumors is found in the chronic action of various excitants. This theory appeared after observations stating that tumors often occur after various injuries, tissue damage, chronic inflammation and other prolonged excitations of the tissue; this theory was not considered satisfactory.

The chemical theory (carcinogen) on the tumor origin. In accordance with this theory, the transformation of normal cells into blastomatose cells is caused by carcinogenic substances entered into the body from the outside or formed in the body as a result of changes in metabolism.

Carcinogens act slowly without at first causing obvious changes in tissues. Tumor growth appears only after a long latent period.

The hypothesis concerning the strict specificity of carcinogenic substances and the dependence of carcinogenic action on the chemical structure has not been confirmed. It has been shown that carcinogenic substances may cause the occurrence of various tumors in various tissues, organs or animals.

Moreover, based on the chemical theory, any action on the body able to cause tumors has to lead first to the appearance in the body of carcinogenic substances. There are no convincing data on the role of carcinogens in the development of any malignant tumor. This theory is important only for explaining specific cases of neoplasic transformation.

The hypothesis of the regenerating origin of tumors establishes the dependence of tumor growth on processes of pathological tissue proliferation. Biological phenomena found in blastomatoase cells are close to phenomena of regeneration. Cancer is often preceded by a special precancerous condition of the tissue caused by different excitants and after which cancer occurs.

The infectious theory assigns the occurrence of tumors to the penetration into the body of living pathogens. To prove the infectious origin of tumors, reference is made to cases of their appearance in one family.

Based on the observations of viral agents causing specific tumors in animals, the viral etiology of tumors has been accepted. According to this theory, the action of carcinogens has been viewed only as the factor creating cell proliferation and tissue metaplasia outbreaks in the body; these outbreaks are a necessary condition for the action of viruses entered into the body.

Conclusions

Various harmful actions contribute to the occurrence of tumors.

The occurrence of tumors is not determined only by the properties of excitants but also by the action it exercises on the tissue.

A key role in the mechanism of tumor occurrence is played by the entire condition of the body, disorders in its complex regulation mechanisms and by the nervous system function establishing the unity of the body with the surrounding environment.

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