How Dangerous can be the Venom of Some Snakes from the Oncological Point of View?

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Introduction

According to the available experimental and epidemiological data, some toxins can trigger a malignant transformation of a normal cell [1]. For example, the carcinogenic action of the mycotoxin-aflatoxin has been established [2]. Recently, a definite correlation between bacterial toxins (especially of membranotoxins with hemolytic action) and the possible development of cancer has also been found [3-5].

In order to prove the possible carcinogenic potential of membranotoxins of cytolytic effect and to demonstrate the presumptive mechanism of effect of these toxins on target cells, we think it possible to cite as an example the acquired hemolytic anemia of different origin. As is well known, the induction of such a situation (or hemolytic anemia) occurs due to some exogenic hemolytic agents: organic (some snakes and mushroom venoms, bacterial toxins) and inorganic hemolytic toxins (phenylhydrazin, arsenic, lead), as well as infections, different drugs, radiation, burns, etc. In some cases, hemolytic anemia can be induced by antibodies and T-killers targetes at own tissues (autoimmune hemolytic anemia). At the same time a strong interrelationship exists between autoimmunity and B-cell oncogenesis. According to clinical studies malignant tumors in autoimmune hemolytic anemias appear in 45-47% [6].

It needs to be noted here that the cellular, subcellular or molecular mechanisms of normal cell conversion into tumorous one in case of hemolytic anemia are still unknown. Therefore, many questions of this sphere remain.

According to the scientific opinion, some toxins, even different infectious viruses and carcinogenic agents may induce both fusion process and cytolytic (destructive) effects in somatic cells [7,8]. Such different effects of these agents on somatic cells possibly depend on the size and number of plasma membranes' pores (holes) induced by them. In the case of large pores, irreversible changes and cytolysis take place. For instance, high doses of carcinogenic agents lead to considerable increasing of quantity of giant polynuclear cells, but further increase of this dose induces massive cellular lysis. In low doses of carcinogenic agents, dikaryons with high oncogenic potential are observed most frequently.

Based on the karyogamic theory of carcinogenesis, tumorous cell represent the hybrid, the so-called tumorous synkaryon, emerging as a result of the fusion of two normal somatic cells [9]. Stem cells, fibroblasts, macrophages, lymphoid cells, undifferentiated cells of various tissues and others show an increased capability to create viable hybrids. The initial target for any carcinogens is receptors of cellular plasma membranes. Any agent or factor inducing fusogenicity shall be regarded as a potential carcinogen, as fusogenicity of somatic cells might lead to the formation of first a precancerous and then a true tumor cell [10]. Antibodies, like cytotoxic cells are known to induce damages (perforations) of different degrees of the plasma membrane of somatic cells [11]. Membranotoxins also affect primarily determinants of plasma membranes of somatic cells: they link to specific receptors of plasma membranes, provoke their lysis and, correspondingly, the development of perforations of different size and number in these organeloids which can, in some cases, become a precondition for fusogenicity. In result of this, may form dikaryons with high oncological potency, and then, in case of synchronous mitosis or mechanical reunification of nuclei, they may form mononuclear hybrid cell – precancerous cell, with tetraploid or hypotetraploid sets of chromosomes on initial stage of hybridization. On the promotion stage, after the influence of perfect (full) carcinogens or promoters on tissue, where precancerous synkaryons pre-exist, in these cells, the chromosomal aberrations of different types and genes amplification may arise. After above-marked conversion on subcellular and molecular levels, there may arise true cancerous synkaryon with the ability of uncontrolled proliferation.

As rigidity of leucocytes' plasma membranes is higher, it is possible that during destruction of erythrocytes by some agents (chemical carcinogens, some membranotoxins, infectious viruses, T-cytotoxic cells, antibodies, etc.), in leucocytes damages (perforations) of plasma membranes and pores of definite size, which may promote process of fusion of somatic cells, may be formed. Larger perforations induce considerable destruction of cell membranes and following cytolysis together with the perishing of these cells [12].

Thus, in hemolytic anemia of different genesis side by side with hemolysis, process of somatic cells fusion may take place. All the more that, there are our own suspicions and observations about the association of Vipera lebetina bites (hemolytic action of venom) with the development of cancer of different localization and histogenesis. For instance, after a bite of snake with hemolytic action of venom (for example, Vipera lebetina, Vipera russelli, etc.) together with massive destruction of erythrocytes (hemolysis), there may be induced a fusion process of other cellular types with more rigid plasma membranes (for instance, leucocytes of different maturity, and probably of cells of other type), with possible development of precancerous, and then true cancer cell. Approximately similar action one may expect from bacterial and fungus hemolytic toxins. Taking into consideration the fact that lymphocytes and macrophages are dominant cells with respect to activity in immunologic reactions and phenotypic properties, in most cases of tumors, malignant cells may have lymphoid (T- or B-cell), macrophagal or the so-called “intermediate” morphology.

It would be desirable, if the humans being in contact with the snakes (the venom of which is of hemolytic action), be monitored for the presence of malignant tumors.
References