Once again about the carcinogenic potential of venom with hemolytic action.

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Short Commentary

In 2016 the article "How dangerous can be the venom of some snakes from the oncological point of view?" The article concerned the probable oncogenic potential of snake venom with haemolytic action. It is safe to say that we are the first to come up with such an idea. It can also be said that information about snake venom contained in the known to us scientific literature concerns the application of venom only for curative purposes. Therefore, as recommended, we deemed it expedient to comment on the topic in detail.

The idea on the presumably oncogenic potency of the haemolytic venom of some snakes occurred only after) we have tried to explain as far as possible the cellular and subcellular mechanism of malignant tumours' formation in the case of autoimmune haemolytic anaemia [1] we have taken into account the variable rigidity of plasma membranes of cells of different type [2] we have defined presumably the common trigger mechanism of action of diametrically different carcinogens on target cells [3] we have taken into consideration the universally recognized fact about the carcinogenic potency of some toxins [4-7].

Let us discuss these points in more detail

Based on the karyogamic (two-synkaryon) theory of carcinogenesis, the cancerous cell represents a hybrid emerging as a result of fusion of two normal somatic cells [8,9]. The possibility of malignant transformation in autoimmune haemolytic anaemia can be based on the inclusion of immune competent cells of different origin in numerous cellular corporations. The cytotoxic killers perform their functions either from a distance or when in contact with the target cells. The cytotoxic effects of killers is realized in the target cells by special proteins–perforins, granzymes, etc., which can induce perforations of different degree in plasma membranes. The total negative charge of perforated plasma membranes decreases and the cells acquire the capability of being closely approached, which frequently, especially upon coincidence of the perforated parts of these organoids, may serve as a prerequisite to the fusion process and formation of a precancerous, and then a true cancerous cell. Antibodies, like cytotoxic cells, are known to induce damages (perforations) of different degree of the plasma membranes of somatic cells.

Membranotoxins (like snakes venom with haemolytic action) also affect primarily the determinants of plasma membranes of somatic cells; they provoke their lysis and correspondingly the development of perforations of different size (volume) and number of cells with more rigid plasma membranes. Thus, in the initiation stage of carcinogenesis, normal somatic cells form dikaryons-the carriers of high carcinogenic potency, and giant polykaryocytes. The latter are nonviable, non-functional formations. They lose the ability to enter the S-period of cellular cycle and mitosis. The doses of carcinogens are probably of secondary importance in the origin of tumorous cells. Moreover, the high doses of carcinogens of different nature can become the reason of destruction and subsequent elimination of the somatic cells and precancerous (initiated) cells, as well.

More often, an assumptive set of chromosomes must be hypo tetraploid or hyper diploid in precancerous cells. Precancerous cells can remain in the organism in the latent state for the indefinitely long time, probably for decades in certain cases.

As known, plasma lemmas of different types of cells have different rigidity to different actions. The most demonstrative example is the so-called "hypotonic shock", which scientists were and are using for isolation the buffy coat from the whole blood [2]. Together with massive haemolysis, fusion of other cellular types with more rigid plasma membranes can be induced, with the possible development of a precancerous and then a true cancer cell.

Multiplicity of carcinogenic substances and factors of different nature can probably mean that these carcinogens can activate some common mechanism of normal cells transition into transformed states. The influence of physical, chemical and biological carcinogenic agents on cell membranes induces the alteration of summary superficial charge of cells' surface. The perforations of plasma membranes lead to the weakening of the electrostatic forces and enhancement of the Van der Vaals forces. Under these circumstances somatic cells contact with each other.

According to the available experimental and epidemiological data, some toxins (aflatoxin, dioxin, bacterial membranotoxins, etc.) can trigger a malignant transformation of normal cells [4-8]. The mechanism, from which the cancer conversion of normal cells can occur by the influence of the haemolytic venom, has been described above (paragraphs 1 and 3). Based on the above, we have conducted anonymous monitoring of the people being in contact with snakes, particularly of herpetologists, who had at least once suffered from a bite of the snake with haemolytic action (Vipera lebetina), or other snakes possessing the complex venom with a haemolytic component [9]. As a result of the conducted monitoring, most victims bitten by a snake with haemolytic venom were found to be diagnosed with tumours of different histogenesis and localization.

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