Opinion Induction of Diametrically Opposite Cytopathogenic Effects and Clinical Manifestations By Some Viruses

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Opinion

As known, viruses unlike bacteria, are so called “unequipped” pathogens. They don’t have exo-endotoxins and other pathogenic factors. So, how do this “primitive” pathogens manage to have such variable cytopathogenic effects and pathologies (infections, teratogenies, malignant tumors)?

It had hardly be said that virus cytopathology has been disregarded in the scientific literature. Not only scientific articles but also special monographs have been dedicated to the issue published long ago [1-3].

The viral penetration and budding stages have particularly attracted our attention, since it is obvious that during of these processes the irreversible and reversible structural changes of the plamalemma are being observed. This circumstance in our opinion can acquire a decisive importance in the possible development of some different, often diametrically opposite cytopathogenic effects and pathologies [4].

Are so wide range of pathologies induced thereby (infections, teratogenic effects, tumor growth) dependent on the specificity of the virus penetration to and withdrawal from the target cells? As it is known, the penetration to the target cell or budding of some viruses (retroviruses, toga viruses, paramyxo viruses, orthomyxovuses, arena viruses, poxviruses) results in the plasmalemma disintegration, triggering in the end perforations of different volume and amount in the process of the target cells plasma membranes penetrations or budding process.

The absolute majority of complex viruses leave the cell from the plasma membrane by the so-called budding. An exception are some complex viruses that are being budded from the karyolemma (herpes viruses) and from structures of the endoplasmic reticulum (flavi viruses and corona viruses), which in the case of massive release from the cell, may become a direct cause of disintegration of the target cell plasma membrane too.

As it seems, the intensity of virus infections and virulent properties of the virus itself acquire a decisive importance in the development of all types of pathologies (e.g., infections, tumors, etc.), to be followed by the formation of pores of different volume and amount in the process of the target cells plasma membranes penetrations or budding process.

Here should be mentioned the fact that the plasma membrane perforations can also be induced by the virus-associated immune cytolysis. For example, the humoral immune cytolysis has been described for the cells infected with the rubella, herpes simplex, lymphocytic choriomeningitis, tick-borne encephalitis viruses, ortho and paramyxoviruses, etc.

So, in the interrelation between viruses and target-cells we should take in account 3 different perspectives:

1. In the case of multiple penetration or budding, during formation of relatively large-size pores (approximately 8-10 to 100nm), rapid repair of the plasma membrane by the cell becomes impossible and the cell undergoes irreversible changes – destruction (cytolysis). Such an action, as it seem, should be characteristic of the highly virulent strain of some infectious viruses. In other words, viruses may cause infectious (and teratogenic) processes(a) by means of the sequential penetration and budding processes in the event of massive perforation of the plasma membrane (e.g., highly virulent strains...
The hybrid synkaryon is the precancerous (initiate, immortal) with a tetraploid set of chromosomes in the initial stage of nuclei. Mononuclear hybrid precancerous cells develop mechanical assembly of heterokaryons (or homokaryons) carriers of high carcinogenic potency, are formed [8-10]. As a result of proximity of the perforated parts, the closer they are to each other (adhesion), which frequently, especially upon coincidence of the perforated parts will probably be the prerequisite to fusion process. Thus, at this stage, together with multi-nuclear cellular structures, the binuclear cells- the carriers of high carcinogenic potency, are formed [8-10]. As a result of karyogamy, i.e. after synchronous mitosis or simple mechanical assembly of heterokaryons (or homokaryons) nuclei, mononuclear hybrid precancerous cells develop with a tetraploid set of chromosomes in the initial stage of hybridization. Produced as a result of somatic hybridization, the hybrid synkaryon is the precancerous (initiate, immortal) cell, which exist in a macro organism indefinitely for a long time. From the formation of precancerous cell (synkaryon of stage I) to the manifestation of tumor process, or the formation of proliferated timorous cell (synkaryon of stage II), decades may pass. At the stage of promotion, after the impact of complete (full) carcinogens or promoters on the tissue, where precancerous synkaryons pre-exist, the chromosomal aberrations of all types and genes amplifications may originate in these cells. Out of the chromosomal aberrations, the most dangerous in carcinogenic respect are nonbalanced translocations, also duplications, expressed “complementation” of chromosomes’ identical sites, having the same function. This event usually leads to genes’ amplification, in the consequence of which the expression of genes (oncogenes) responsible or control under the cellular proliferation may ultimately originates. After the above-mentioned conversion on sub-cellular and molecular levels, there may originate a true tumors synkaryon the malignant cell with the ability of uncontrolled proliferaiton. The latter represents a clone, from which formation of malignant tumors substrate at an early stage of carcinogenesis initiates. Such an action can be characteristic of low-virulent infectious viruses (e.g., influenza virus, some paramyxoviruses, retroviruses, etc.). Out of the numerous heterokaryons (or homokaryons) and hybrid cells (synkaryons) formed after the influence of viruses (and other carcinogenic agents), only a few precancerous cells can acquire the potency of unlimited proliferation [11,12]. In the over-whelming majority of cases, precancerous cells seem to die in the phase of transformation into tumors cells due to lethal mitosis. Specifically, because of the imbalance (instability) of karyotypes, they either never reach mitosis or are unable to complete it due to disturbance in the spindle organization or chromosomes motion. Therefore, true tumors synkaryons are probably formed very rarely; their incidence being less than one in 10^6 [13].

Thus, in respect of oncology, dangerous are the low-virulent viruses which (1) penetrate the target cell through membranes, by perforations; (2) are released by budding; and/or (3) lead to cellular-immune or humoral-immune cytolysis.

Of special interest are the diametrically opposite cytopathogenic effects induced by the same virus and the resultant wide range of pathologies [14]. It possible that the same virus could cause both an infectious process and tumor growth, etc.? Or can we suppose that the diametrically opposite cytopathogenic and clinical effects are characteristic of only those viruses, which in the processes of penetration or budding (or during the both processes simultaneously) cause reversible or irreversible perforations of the plasma membrane of the target cell? Such viruses include: herperviruses (infectious mononucleosis and Burkitt’s lymphoma), rubella (infectious process and teratogeny), adenoviruses some serovars (infectious process and experimental cancer), etc. Especially as, according to various scientific data [15-17], some infectious viruses of low virulence or low cytopathogenic action should...
possess fusogenic properties, or the carcinogenic potential. Such are vesicular stomatitis (Rhabdoviridae), parotitis and measles viruses (Paramyxoviridae), some herpesviruses, rubella virus (Togaviridae) and other viruses.

Thus, the infectious and carcinogenic processes, in spite of a principal differences between them (for example, the target cells destruction in one case and cytoproliferation, in the other), in certain cases can be induced by the same virus. The seemingly typical onco-viruses, such as Rous sarcoma and polyoma viruses, can, in some cases, cause various non-tumor pathologies (inflammatory processes, hemorrhages, atrophy of internal organs, etc.), while infectious viruses may, under certain conditions, acquire the oncogenic potential. Therefore, the same viruses in the case of different virulence and dosage can produce two or even three types of diametrically opposite cytopathogenic and clinical effects.

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