ONCOTROPISM OF VIRUSES AND THE PROBLEM OF VIROTHERAPY OF MALIGNANT TUMORS

Summary

Numerous experiments on tumors of various origin and histological structure prove that viruses belonging to different groups are tropic to tumor cells.

Oncotropism of viruses has nothing in common with the malignancy of the cell. In relation between viruses and tumor tissues the same particularities have been observed which have been stated in relations between viruses and different tissues in general. A virus may reproduce in a tumor, may be found in a tumor cell in a latent state, hold on with the tumor, and cause the development of interferon; it may as well cause the destruction of tumor cells, the so-called oncolysis. The latter phenomenon has attracted the attention of many scientists, who hoped to avail themselves of it in their attempts to abolish malignant tumors.

Recently some scientists have dedicated themselves to the study of other properties of oncotropic viruses, for instance, the property of viruses to induce new antigens. Mixoviruses, when reproducing in tumor cells, may acquire tumor-specific antigens. In cancer hospital viruses have been applied in the treatment of advanced cancer. Almost all of the applied viruses affected the tumor process to a certain extent: they caused transitory break in the growth of the tumor, a transient regress of the tumor or metastases, destruction of the tumor, more or less durable remissions in leucosis. Often a subjective improvement of the condition of the patients has been observed. Consequently, the virus infection can influence a tumor process. That is why a search for viruses available for virotherapeutics of malignant processes in man and a study of their effect on tumors is most important.

Virus treatment implies viruses classified as follows:
1) oncolytic, i.e. those reproducing in tumor cells and causing their destruction;
2) transforming viruses — those causing transformation of the antigens of tumor cells;
3) viruses acquiring tumor-specific antigens in the process of reproduction;
4) viruses stimulating the mechanisms of immunity acting on the tumor either non-specifically or specifically;
5) viruses — inductors of interferon which could be applied in cases of tumors and leucosis of virus origin.

Of course, in search of all the mentioned viruses special methods must be applied, considering the properties of viruses to the purpose of the experiment.

In the laboratory for cancer virotherapy of the A. Kirchenstein Institute of Microbiology of the Academy of Sciences of the Latvian SSR, it has been stated that human enteroviruses manifested tropism and oncolytic activity in heterotransplanted human angiosarcoma. Furthermore, it has been stated that different human tumors may adsorb enteroviruses, but the spectrum of the adsorbed viruses depends on the type of virus as well as on the individual properties of a certain tumor. The adsorbed viruses often synthesize virus antigens in the tumor cells of the long-termed tissue culture.

The antigen of enteroviruses has been detected after intramuscular introduction in excised tumors in 52% of cases. The cellular response to enterovirus infection is the following: coarsening of the chromatin and decrease of nuclear size; vacuolization of cytoplasm with the following disintegration of the cell. Thus, the human enteroviruses can affect the tumors oncolytically, but the oncolysis may be immediately interrupted by a simultaneously intensified antiviral immunity. The influence of enteroviruses on human tumor may be rather complicated, as well effecting various immunologic phenomena.

Experimental treatment of rat reticulosarcoma-321 with alkylating agents (sarkolysin) combined with enteroviruses (Coxsackie B-5) resulted in absence of relapse of tumor growth. Sarkolysin has been applied in subtherapeutical dose. The regression of tumors in this case is accompanied by intense proliferation of plasma cells in regional lymphatic nodes.

Now it has been stated that oncolytic viruses as well as immunogenic ones cannot be applied as an independent means of treatment of malignant processes; virotherapeutics should be introduced as a most expedient treatment of malignancy. The application of viruses should be combined with surgical treatment — a radical removal of the tumor or a palliavtive surgical operation could be recommended here. Vitrotherapeutics may be supplemented with chemotherapeutics. Yet chemical preparations should be applied in doses which do not induce suppression of immunity of the organism. A theoretical basis seems to become imminent for the application of oncotropic viruses in the treatment of malignant processes.

The problem of treatment by means of viruses may be solved through development of the following items:
I. Selection of viruses acting on human tumor processes.
   2. Studies of relations between oncotropic viruses and various human tumors in vitro and in vivo with the aim of selecting viruses with oncolytic and transformation trends:
      a) determination of the types of viruses in tumors, the cycle of their development etc.;
      b) studies of reactivity of tumor cells on virus infection;
      c) determination of viral and tumoral spectra.
   3. Selection and study of mutual interference among the slightly pathogenic oncolytic viruses and the elaboration of tactics in mastering immune reactivity of the organism.
   4. Elaboration of methods for the determination of individual sensibility of human tumors to the selected viruses.
   5. Selection of virus stimulating the immune mechanisms of the organism as well as antitumor immunity.
   6. Technology of virus preparations.

II. Methods of virus application for immunologic treatment of malignancy.
   1. Studies of the possibility of applying viruses for strengthening antigenity of tumor cells in vitro and in vivo.
   2. The expediency of applying viruses as immune stimulators of antitumor immunity in the course of a complex cancer treatment.
   3. Tracing of viruses which in the process of reproduction in human tumor cells acquire antigenity of the cells.

III. Methods of applying viruses in cancer hospitals.
   1. Deliberations about clinical harmlessness and epidemiological security of selected viruses.
   2. Studies of antiviral, antitumoral and general immunity of the organism against the selected oncolytic and transforming viruses and the complex virus-tumor cell.
   3. Statement of the dose, site, optimal intervals and successiveness of introducing viruses (also autovaccines) regarding their activity on the tumor process.
   4. Ascertainment of the site for virotherapeutics in a complex treatment of a malignant process.
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