Virtues in Virus

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After the outbreak of coronavirus disease in 2019 (commonly known as COVID-19) about four years back, everyone has been wary of the word virus. However, some viruses are found to be useful in destroying tumour cells and are hence thought to be a potential tool to treat cancer. These viruses, known as oncolytic viruses, are found in nature and could be modified in the laboratory to treat cancer cells without harming the healthy cells. One of the major challenges of cancer treatment is to be able to precisely target the cancerous cells without affecting the healthy normal cells. Usually, conventional chemotherapy or radiotherapy affects all cells without distinguishing between the two and hence produces various side effects.

As early as in the late 1800s, it was observed that some patients with cancer went into remission, albeit temporarily, after a viral infection. This triggered the idea of using viruses in cancer treatment. The idea took several decades to come to fruition, till the advent of genetic engineering. Genetic engineering allowed tweaking the virus to produce more potent, specific and safe oncolytic viruses. Today, several dozen viruses are identified as potential options in cancer treatment. More importantly, some recent clinical trials on patients showed promising results in the application of oncolytic virus in treating cancer.

The viruses—usually benign varieties such as the herpes simplex virus (a common skin-to-skin infection causing painful blisters and ulcers) and adenoviruses (a mild infection causing runny nose, sore throat, fever, etc.)—are often modified to make them safer and more potent. Cancer cells are found to be congenial to viruses and allow them to enter the cells. After entering a cell, the viruses start replicating and finally kill the tumour cells, sparing the normal healthy cells, which is seen as a great advantage. Scientists once considered these viruses as 'magic bullets' that kill the cancer cells only without affecting others. However, although viruses worked very well for animal cells, sometimes achieving 100 per cent cure rate, their applications in human cells were not that wonderful.

Further research and clinical trials showed that viruses kill only a handful of tumour cells in case of humans. But what is important is that in the process of cell death, dying cancer cells send a signal alerting the immune system of an imminent danger somewhere. The immune system immediately sends its anticancer warriors, the T cells, to break down the defence that shields tumours. For this reason, some researchers think that oncolytic viruses are a kind of immunotherapy—a treatment that harnesses the immune system against cancer.

That the oncolytic virus kills the tumour cells and releases antigens (alert signals) to stimulate an immune response for a potential anti-tumour effect led to the

approval of the first oncolytic virus T-VEC, a modified herpes simplex virus type 1, by the US Food and Drug Administration (USFDA) in 2015 to treat advanced cases of melanoma (tumour in the brain). Three other oncolytic viruses got their approval outside the USA soon after.

The success of the application of oncolytic viruses for melanoma raised hope among scientists for further research and its use in other forms of cancers. The success also encouraged several pharmaceutical companies to come forward to produce drugs using oncolytic viruses. At least 90 clinical trials are in progress at this moment.

As published in the 15 December 2023 issue of the *Science*, oncolytic viruses have recently been used with success for the treatment of bladder cancer with an oncolytic virus produced by a California-based pharmaceutical company CG Oncology. According to doctors, if this type of tumour were allowed to grow unchecked, patients would often need to have their bladders removed, but the oncolytic virus treatment could delay or prevent this severe outcome.

The clinical reports of some patients treated with oncolytic virus when evaluated periodically showed that in 76% of the patients, the tumours became undetectable while in 74% of that group, the tumours did not return for at least 6 months. More importantly, this positive outcome for those who have gone through this treatment could not be achieved with the current mainline bladder cancer treatment. However, since the tracking period for these patients has only been six months, it is too early to arrive at a definite conclusion. Doctors will continue to follow up with these patients for 3 years to review the benefits of this treatment.

The development of any new drug, from discovery to market, is a long-drawn journey and takes at least a decade (except in case of emergency circumstances like a pandemic). There are four stages of trial and approval, which are called phases. Phase 3 is the penultimate stage. After a successful phase 3 trial, a drug receives approval for its commercial use and is granted a licence.

This particular oncolytic virus has received a successful phase 3 trial approval for its use in bladder cancer. Scientists were elated with the positive phase 3 result which could be enough to 'shake the world of oncolytic viruses' as remarked by an oncologist. The clinical data obtained so far prompted the scientists to proudly announce that the oncolytic virus would become only the second in the United States to receive regulatory approval. There are several oncolytic viruses currently being tried for other types of cancers such as glioblastoma (brain cancer) which are in different phases of their clinical trials.

This oncolytic virus therapy is expected to usher in a new era in cancer treatment and scientists are optimistic about its use as an effective therapy against cancer. We look forward to the days when this deadly disease can be successfully treated by this therapy, which will undoubtedly bring joy to many who have been looking at a bleak future so far. ■

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