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Commentary

Cancer as a Disease of the Cell

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Case reports are often ignored or disparaged, but I recently chanced upon one from 1996 that gave me pause. It described a 32-year-old man who underwent resection of a malignant fibrous histiocytoma (MFH) of the abdomen. During the surgery, the 53-year-old surgeon injured his palm. Five months later, he developed a hard mass at the site that proved to be an MFH identical to that of the patient.[1]

This anecdote highlights the fact, not uppermost in our minds, that cancer is unique among all the diseases in medicine as a disease of the cell. Every other disease we deal with in medicine is a disease of an organ or organ system or of the total body, but cancer is uniquely specific to the cell. As illustrated by this case report, cancer can be transferred or transmitted as if it were an infectious disease.

Certainly, we recognize this phenomenon from laboratory and in vitro studies. Malignant cells can be transferred from one Petri dish to another, or from one rodent with a tumor to a healthy rodent, and another tumor will develop. But it is striking to consider that this phenomenon can occur via human-to-human spread as well. Obviously, a cell from a patient with a myocardial infarction will not give another patient a heart attack; a cell from a patient with rheumatoid arthritis will not give another patient joint pain.

There are other circumstances in which human-to-human transfers of cancers have occurred. Donor organs are screened for cancer solely by visual inspection and manual palpation by the surgeon. Recipients of allogeneic organ transplants have been known to develop metastases months or years after the transplant. On work-up, it has been recognized that the donated organ inadvertently contained previously undiagnosed malignant cells from the donor that, in the immunosuppressed environment of the recipient, had the opportunity to proliferate and spread.[2]

Another context in which cancer cells have been transmitted from one human to another and had the opportunity to proliferate and establish tumors is in maternal–fetal transmission. It is not uncommon for mothers to have cancer, known or unknown, during pregnancy. The mother and fetus have independent blood streams. There is a placental barrier between the two blood streams to prevent toxic substances from passing from the mother to the fetus. However, the placenta is leaky. There are multiple published case reports (which suggests that it has occurred significantly more frequently) of tumors passing from the mother to the fetus, generally melanomas, leukemias, or lymphomas.[3] It is estimated that this occurs in 1 in 500 000 births. The transferred tumor cells have been recognized because they have had XX karyotypes in male infants. It has also been observed that twins may share leukemia while in the womb.[4] In these perinatal circumstances, it appears that the primitive neonatal immune system allowed the acquired tumors to be tolerated and not rejected by the recipient's immune system.

The most direct circumstances of human-to-human transmission of cancer have been in the work of Chester Southam. While an ethical cloud hangs over these experiments, they vividly illustrate the principle we are discussing. During the 1950s, while on staff at Memorial Hospital, Southam injected cancer cells into well-demarcated areas of terminal cancer patients. This would usually result in the growth of tumor nodules which would then be excised; the resultant tumors would histologically resemble the tumor cells that had been injected.[5] Another group subsequently transplanted melanoma tissue from a 50-year-old woman to her 80-year-old mother (with informed consent) and a new melanoma as well as metastases developed in the mother.[6]

These scenarios emphasize that cancer is a disease of the cell. But why is that a critical concept? To answer that, we have to consider what exactly allows or permits such transferability to occur. The information to recapitulate the cancer phenotype in a new host and location is clearly centered in the genome, or if not in the genome itself, then in the epigenome or the translation of the genome. The cell nature of cancer makes it clear that, more than any other class of diseases, the genome is at the core of the pathophysiology of cancer.

Organ systems gradually decline as we age and most diseases reflect this phenomenon in one way or another. Addressing and curing these problems is often an elusive problem. But if one cancer cell and its progeny carry the flaw of malignancy, then there is an optimistic message which we have circled for years: eradication and cure are achievable goals.

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Conflict of Interest

Dr. Neugut has consulted for Otsuka, GlaxoSmithKline, Eisai, United Biosource Corp, and Hospira, and sits on the medical advisory board of EHE Intl. He receives grant support from Otsuka.

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