Why Do Some Cancers Disappear?

By ACSH Staff — June 14, 2016

It is hard to believe that some cancers miraculously disappear, but it does happen. Over 1,000 case studies document cancer sufferers who experienced spontaneous regression of their tumor. So why does this happen, and is it possible to exploit it to benefit cancer patients?

The earliest documented case of spontaneous regression was in the late 13th century. A bone sarcoma in Peregrine Laziosi spontaneously disappeared after a severe bacterial infection. In the late 1800s, William Coley observed that inducing a fever could result in tumor regression. He developed a bacterial vaccine (“Coley’s vaccine”) that was successful in reducing tumors in many of his patients.

Tumors have been known to disappear spontaneously, in the absence of any targeted treatment, usually after an infection (bacterial, viral, fungal or even protozoal). Could this mean that simply stimulating the immune system causes regression?
Not that simple

Over the past 70 years, spontaneous regression has been reported in a variety of cancer types, but particularly in melanomas (skin), renal cell carcinomas (kidney), neuroblastomas (adrenal glands) and some types of blood cancers. However, despite these historical observations of tumor regression, we still do not know the mechanisms that cause this phenomenon. It is also very difficult to quantify, and many cases are probably unreported in research journals.

One likely reason for spontaneous regression is that the body triggers an immune response against specific antigens displayed on the surface of tumor cells. Support for this idea comes from the observation that some skin tumors (malignant melanoma) show excessively high numbers of the body’s immune cells inside the tumor.

In another interesting case report, a patient with kidney cancer had a part of his tumor surgically removed, which resulted in the spontaneous regression of the rest of his tumor. The rationale underlying this phenomenon is that a local immune response following surgery was enough to stop growth of the rest of the tumor.

But tumors are notoriously varied, both in their genetics and their behavior, which can result in relentless disease progression in some people, but cause spontaneous regression in others. Tumors of the same type (such as breast cancer) can mutate in many different ways. This can influence the rate of tumor growth, or the likelihood of spread to different locations, or how responsive they are to treatment. It is highly probable that genetic mutations are also responsible for spontaneous regression.

A rare childhood cancer gives some clues

Neuroblastoma is a type of rare childhood cancer that could shed some light on how genetic changes may affect spontaneous regression. About 100 children are diagnosed with the condition every year in the UK, but the disease progresses very differently depending on the child’s age. Tumors in children under 18 months can disappear with or without any treatment (type 1). But children older than 18 months need intensive treatment and have only a 40-50 percent survival rate (type 2).

Research shows that type 1 neuroblastomas have distinctive genetics compared to type 2. For instance, these tumors typically have high numbers of a cell receptor (TrkA) which can trigger tumor cells to kill themselves. In contrast, type 2 neuroblastomas have a higher number of a different receptor (TrKB), which makes these tumors more aggressive.

Another possible explanation is that type 1 neuroblastomas show very low levels of activity of an enzyme, telomerase, compared with type 2 tumors. Telomerase controls the length of specialized pieces of DNA which enables the cell to divide continually. In type 1 neuroblastomas, these are
very short and unstable due to low activity of the enzyme, and this triggers cell death.

Epigenetic [15] changes cannot be excluded either. Epigenetic changes do not affect the DNA sequence of a cell but modify the activity of various proteins by "tagging" different parts of the DNA. So cells with the same DNA sequence, but with different tags may behave completely differently and result in some tumors destroying themselves. Recent studies [16] showed significant differences in tagged genes in type 1 neuroblastomas compared to type 2, although these are preliminary findings [17].

Although the precise mechanisms underlying spontaneous regression are still uncertain, it is very likely that stimulating a strong immune response must play a big part in people with certain genetic profiles. Further research exploring this link between genetics and stimulating an immune response would provide answers to how we can identify tumors that have the capacity to spontaneously regress.

The next step would be to design drugs that can artificially stimulate the immune system to specifically target tumors based on their genetic makeup. Developing animal models that mimic human spontaneous regression would be an invaluable tool towards this.

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