Why do some cancers suddenly disappear without treatment?

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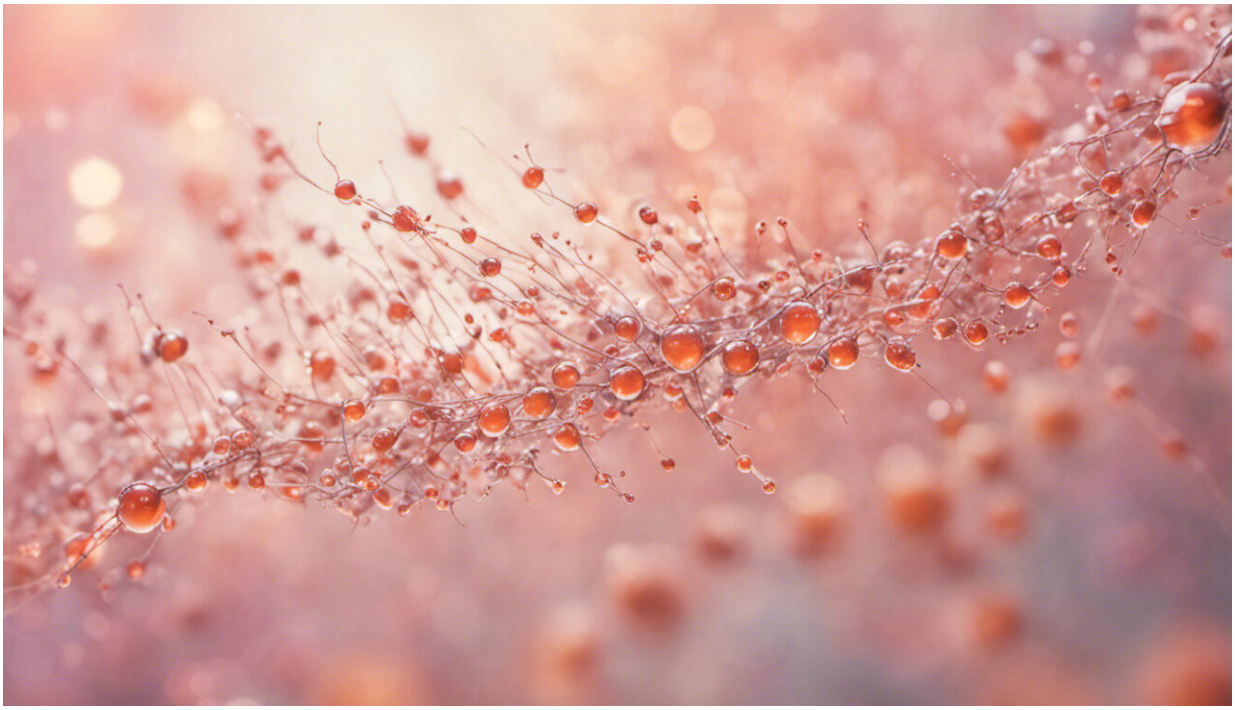

Credit: AI-generated image (disclaimer)

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 tumour. 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 tumour regression. He developed a bacterial vaccine ("Coley's vaccine") that was successful in reducing tumours in many of his patients.

Tumours 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 tumour 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 tumour cells. Support for this idea comes from the observation that some skin tumours (malignant melanoma) show excessively high numbers of the body's immune cells inside the tumour.

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

But tumours are notoriously varied, both in their genetics and their behaviour, which can result in relentless disease progression in some people, but cause spontaneous regression in others. Tumours of the same type (such as breast cancer) can mutate in many different ways. This can influence the rate of tumour 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. Tumours 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% survival rate (type 2).

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

Another possible explanation is that type 1 neuroblastomas show very low levels of activity of an enzyme, telomerase, compared with type 2 tumours. Telomerase controls the length of specialised 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 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 tumours destroying themselves. Recent studies showed significant differences in tagged genes in type 1 neuroblastomas compared to type 2, although these are preliminary findings.

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 tumours 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 tumours based on their genetic makeup. Developing animal models that mimic human spontaneous regression would be an invaluable tool towards this.

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