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Discussion paper

Spontaneous regression: Surviving cancer against the odds

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Abstract Spontaneous regression, where people survive cancer against expected odds, is an exceptional but well-documented biological event (Abdelcrazeq, 2007). It is not known, however, how often this remarkable phenomenon occurs and studies of spontaneous regression face specific challenges. This article explores these issues and outlines key findings in the literature. Recommendations for future research are also discussed.

Introduction

Instances of spontaneous regression or remission, defined by Bakel (2001) as improvement or recovery without clear medical cause, are often documented in the cancer literature, with approximately 20 cases reported each year (Challis & Stam, 1990). Despite the identification of many individual cases, however, the frequency of this important phenomenon is poorly understood. While it is often quoted that spontaneous regression occurs no more than once in every 60,000 to 100,000 people with cancer, it is not clear from where this figure is derived and the true incidence is unknown (Jerry & Challis, 1984). Research in this area is confounded by numerous challenges, including varied definitions, reporting biases**,** design and ethical considerations. It is essential, however, that research in this field is pursued, as improved awareness of the processes surrounding spontaneous regression will have important preventative and therapeutic implications and bring hope to many who are affected by cancer.

Definitions

Spontaneous regression is said to occur when a malignancy partially or completely disappears without medical treatment or as a result of therapy that is considered inadequate to exert a significant influence on neoplastic disease (Everson & Cole, 1966). The terms ‘spontaneous regression’ and ‘spontaneous remission’ are often used interchangeably, although the Institute of Noetic Sciences (IONS) suggest that spontaneous regression is employed by some to specifically refer to the reduction of solid tumours, while spontaneous remission is used when describing the reversal of a disease process that tends to be more systemic, such as leukaemia or lymphoma (IONS, 2004). For the purposes of this article, which generally refers to all types of cancer, the more commonly used term spontaneous regression (SR) will be used to collectively describe both regression and remission.

Although some cases of SR, appear swift, complete and/or miraculous, it is important to note that the above definitions also include cases in which malignancies are reduced or stabilised and cases where the regression may not be permanent (Abdelrazeq, 2007; IONS, 2004). It should also be noted that the term 'spontaneous' is derived from the Latin word 'sponte' (meaning "of free will") and is defined in Webster's Dictionary as "acting by its own impulse, energy or natural law, without external cause or influence" (Merriam-Webster, 2003). Hence the term SR does not necessarily imply that any changes are sudden or rapid. This definition also acknowledges that although the regression may appear to have no clear external cause, internal resources might be contributing factors and that it is not simply the result of chance or fate.

Reporting biases

Although SR is generally considered to be a rare event, numerous individual case reports and several reviews are documented in the medical literature. In the most comprehensive compilation of SR cases to date, Hirshberg and O'Reagan (1993) reviewed 1,385 articles and identified 874 reports of SR of cancer and 334 cases of SR in other diseases. As noted by Franklin (1982), however, SR tends to be reported only when the regression is dramatic and durable, while less pronounced cases are overlooked, leading to speculation that SR occurs more frequently than is documented.

This point was particularly demonstrated when Hirshberg and Barash (1995) used different definitions in their interviews with physicians. When asked if they had seen cases of spontaneous remission or regression, many doctors indicated they had rarely or never seen such cases. However, when asked about patients that did "exceptionally well" (e.g., a terminal patient who unexpectedly recovered while receiving palliative treatment, or a person whose tumour had reduced or stabilised well beyond expected time frames), many cases were identified. Hence Hirshberg and Barash began to employ the term "remarkable recovery" as it was perceived to be a more inclusive term that more fully embraced the definitions of SR described above.

Experimental design and statistics

In conjunction with the varied definitions and reporting biases described above, Hirshberg and O'Reagan (1993) suggested that research of SR is also complicated because:

- SR is sometimes regarded as an artefact created by the misdiagnosis of the patient's initial conditions.
- SR is difficult to research as it is always identified after the fact, meaning that baseline measures cannot always be established in a systematic way.
- Clinicians have shown an unwillingness to report cases in the literature, possibly because of fear of criticism from their peers.
- The quality or reports vary widely, making the actual occurrence of SR difficult to estimate.
- SR cases reported in the psychological literature do not always contain adequate physical information about the patient, while medical reports might not describe the patient's personal history, making a complete analysis of the case challenging.

SR research is further complicated by issues in experimental and statistical design. Given that majority of reports in the literature regarding SR are individual case studies, they rely on retrospective data and early information (e.g., about diagnosis, prognosis

and treatment) may be obscured. In order to test the occurrence and characteristics of SR, prospective data sets that compare patients undergoing a full treatment regime with others who are receiving no or reduced treatment. Such trials are rarely performed, partly because of the ethics involved in not providing what would be deemed sufficient treatment to one half of the participants in a study, and because very large numbers would be required to reliably detect a SR rate below 1%. In a recent paper by Keilholz (2007), only one prospective, randomised clinical trial investigating the incidence of SR was identified in the literature. In this study, 451 patients with renal cell cancer were assigned to receive the drug Sorafenib, while 452 patients received placebo (Escudier, Szczylik, Eisen et al., 2005). Although no cases of complete regression were observed, 2% of those in the placebo group experienced some reduction.

Survivor characteristics

Kune (1991) noted that those with advanced cancer who survived an unexpectedly long time were likely to have sought wide exposure to both conventional medical and non-conventional opinion and treatment, they made decisions on an intuitive level and were at peace with themselves. More recently, reviews by Schiltz (2004) and IONS (2004) suggest that the following characteristics are associated with unexpected regression and survival:

- A strong sense of self-sufficiency, competency and control.
- Living a fulfilling and enjoyable life, beyond the crisis of cancer.
- Having at least one strong, supportive and trusted relationship.
- Being comfortable with the expression of both positive and negative emotions.
- Finding meaning in the cancer experience and accepting the diagnosis but not the prognosis.
- Working in partnership with health professionals and participating in decisions related to their health and well-being.
- Regular participation in activities and practices that reduce stress.
- Having a sense of spiritual connection or awareness.
- Flexibility and the willingness to try new things and/or to make changes when something is no longer working.

Causative theories

Although each case of SR appears unique and it is unlikely that any single combination of factors is causative, numerous biological and psychological factors may potentially contribute. Abdelrazeq (2007) and IONS (2004) suggest that proposed biological mechanisms include immune mediation; hormonal factors; inhibition of tumour growth by growth factors and/or cytokines; differentiation of the tumour into a more normal type of tissue; elimination of carcinogens; angiogenesis; tumour necrosis; programmed cell death (apoptosis); and genetic factors. Proposed psychological and spiritual factors include the placebo effect; hypnosis; altered states such as meditation and prayer; miraculous healings; and group support.

Hope

Abdelrazeq (2007) emphasised that although cases of SR exist, they are rare and should not be used to deliberately create false hope or to shield the patient from the reality of their diagnosis and prognosis. He also noted however, quoting Osler (1901), that the fortunate people who manifest SR “illustrate the uncertainty of prognosis and the truth of the statement that no condition, however desperate, is quite hopeless.” Similarly, Ali (1995) and others have noted that SR of cancer provides a basis of hope for both

patients and physicians, by demonstrating that even if it has only happened once, recovery is possible. Given the power of the placebo effect (Zajicek, 1995), hope is an important aspect in cancer treatment and management. It is also important to note that life is about more than just surviving; it is important to live fully, to learn from great challenges and to obtain happiness and optimal quality of life (Ventegodt, Morad, Hyam & Merrick, 2004).

Conclusion and recommendations

Although many in the oncology field know of patients who did well "against the odds," reviews of SR in the medical literature have been hindered by challenges in defining and reporting these exceptional cases. This has made it difficult to estimate the prevalence of SR and to understand how and why it occurs. However, given the hope that these cases provide and the potential they have for developing understanding of the aetiology and treatment of cancer, it is important that SR is well documented and studied. It is recommended that future research systematically explores which types of people and in what types of cancer SR most commonly occurs. The author also supports the recommendations of Abdelrazeq (2007) that an international register of SR be created and that a dedicated medical journal be devoted to studies of this remarkable phenomenon.

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