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Activism among exceptional patients with cancer

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Abstract

Background The “exceptional patients” with cancer are survivors who had advanced cancer considered incurable by medical report and who subsequently became disease-free or experienced unexplained survival time given the nature of their disease or treatment. This experience is a puzzling phenomenon that has not been formally investigated in a cancer population. The purpose of this study was to understand exceptional patients’ accounts of their experience.

Materials and methods This study used a narrative approach with a cross-case thematic analysis. Recruitment took place at health care centers in the USA and Israel. Oncologists in both centers were asked to identify patients who had an exceptional disease course. Patients were then contacted and interviewed; an audio recording was made of each narrative account and then transcribed. Interviews and thematic analyses were conducted independently at each site. These thematic findings from each site were discussed with both research teams and a common underlying theme was identified, which is the focus of this report.

Results Twenty-six participants were interviewed: 14 from the USA and 12 from Israel. All the participants have had advanced disease with a range of diagnoses that included breast, colorectal, pancreatic, ovarian cancer, glioblastoma multiforme, and others. The main recurrent theme from both the US and Israeli sites was personal activism. This was manifested in taking charge and getting involved in the process of diagnosis and treatment, as well as becoming more altruistic in their relationships with others. In many cases, this was reflected in a change in a philosophy about life

Conclusions In this study, we found that activism was a major theme that was independently observed in both Israel and the USA. This has implications for health care providers to facilitate patient engagement in the care and treatment of their disease. Further research on this phenomenon is needed.

Keywords Exceptional patient · Spontaneous regression · Remarkable recovery · Spontaneous remission · Cancer care · Hope · Activism · Resilience · Cancer survivorship

Introduction

An individual is considered a cancer survivor from the time of diagnosis through the balance of his or her life [1]. According to recent data released from the National Cancer Institute Office of Cancer Survivorship, it is estimated that there are now over ten million cancer survivors in the USA (approximately 3.7% of the US population). This estimate is for individuals who had a diagnosis of cancer other than non-melanoma skin cancer or in situ disease at some point in their

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lives. An impressive 14% of these individuals were initially diagnosed more than 20 years ago [1]. A subset of these survivors had advanced cancer that was considered incurable at the time of diagnosis, but became free of disease or experienced long-term survival that could not be explained given the nature of their disease or treatment. Such survivors comprise a group that is defined as "exceptional patients."

The experience of the exceptional patient with cancer is a puzzling phenomenon that has not been well researched. The rare occurrence of remarkable recovery against all odds, totally inexplicable but real, is something that most oncologists have seen in their practice. In the past, other terms have been used to describe the phenomenon: "spontaneous remission," "spontaneous healing," "spontaneous regression," "miracle cures," "remarkable recovery," "resilient cancer survivor," and "exceptional disease course" [2-5]. For the purpose of this paper, we will use the term "exceptional patient(s)."

There is a lack of congruence in the literature about identifying and studying exceptional patients, possibly related to the lack of consensus on the definition. Most previous studies mentioned the phenomenon of the exceptional patient as a rare occurrence [2, 6]. Challis and Stam [7] reviewed reported cases from 1900 to 1987 and estimated that approximately 20 cases a year are reported of exceptional patients. Jerry and Callis [6] estimated that exceptional patients occur no more than once in 60,000–100,000 patients with cancer, but the true incidence is unknown. Some argue that exceptional patients are reported only in the rare case when regression is both dramatic and durable and that less dramatic, yet real cases of exceptional patients are almost never reported [8]. A recent report suggested that exceptional patients may occur much more often than was previously estimated [9].

There is no clear explanation for the phenomenon of the exceptional patient. Certain mechanisms have been suggested, including apoptosis, telomerase inhibition, angiogenesis inhibition, elimination of a carcinogen or antigen, immunological response, effects related to psychosocial factors, nutritional factors, complementary medicine, and others [2, 4, 5, 10-12]. Others have noted that some exceptional patients experienced a spiritual awakening before the remission took place, suggesting that the patients themselves had an important role in the healing process [13, 14].

In 1967, Everson [15] described this phenomenon and reviewed 176 well-documented cases of exceptional patients using stringent criteria, including documented histologic regression of biopsy-proven metastases, radiologic regression of presumptive neoplastic disease, and regression of metastatic tumor after therapy was deemed ineffective. A recent review of exceptional patients noted that the information and reports on these patients are often sketchy descriptions and that many physicians had lost track of their exceptional patients [10].

In this review, it was suggested that there is a need to retrieve these scattered data for a new "Remarkable Recovery Registry" in which new methods of interviewing and reporting will be utilized. The patient's account of his or her experience, often dismissed as merely subjective, should be one of the main sources for this database [10].

By reexamining current therapeutic strategies in the context of exceptional patients, new medical protocols could be developed for the benefit of patients. It gives clinicians a glimpse into the patient experience and sensitizes the clinician to better support the patient through their disease and treatment. Barasch [10] adds that gathering and analyzing solid data on remarkable recovery would give the concerned physician a means of providing "ethical hope" to even terminally ill patients.

To learn more about exceptional patients, a narrative study with cross-case thematic analysis was conducted. Our purpose was to obtain a better understanding about exceptional patients' experiences in two locations, the USA and Israel. Using two sites in different countries allowed for the uncovering of common themes that pervade beyond one medical system. While some cultural differences were apparent, this paper focuses on a common underlying theme from both sites.

Materials and methods

The study used a narrative approach [16] which was deemed most appropriate to capture the perceptions and experiences of exceptional patients. Narrative and other qualitative approaches have been widely used in health care to better understand the patient experience [17, 18]. In many qualitative research approaches utilizing structured interviews, the researcher's interpretive lens is imposed on the actual structure and content of the interview [19]. Therefore, rather than directing the interview participant toward specific issues, we selected an open-ended narrative interview approach as it allowed the participants to frame their experiences and discuss the issues that were significant to them [17, 20]. Additionally, due to the language and cultural differences in the two sites, a narrative approach avoided some of the cultural differences in interpretation encountered in asking more structured questions. The narrative approach allows the informant to tell their experience, with probes only to "tell me more about…."

Setting and participants

Two sites were selected to assure adequate sampling and to explore issues that might extend beyond one institution. Recruitment took place at two locations: The University of Texas M. D. Anderson Cancer Center (M. D. Anderson) in

Houston, Texas in the USA and Tel Aviv Medical Center (TMC), affiliated with Tel Aviv University, in Tel Aviv, Israel. As in the USA, the population of Israel consists of a large number of immigrants from multiple countries and cultures around the world, and there is subsequently sensitivity to multiethnicity in both countries. The practice of medicine is quite similar to the USA. Medical schools and postgraduate programs utilize mainly American textbooks and refer to US peer-reviewed journals. Additionally, Israel has a high percentage of graduates who participate in multiple fellowship opportunities in the USA. The American influence on the medical establishment is quite noticeable. As a result, three of the four medical schools in Israel developed programs of collaboration with US medical schools that attract US students to obtain their MD degree in Israel and return to the USA for postgraduate training and practice. Most academic institutions follow US oncology guidelines in providing cancer care.

The medical environment in both institutions is similar. Both institutions are large academic referral centers and take care of a large number of cancer patients with a great variety of cancer types, utilizing multidisciplinary teams. These commonalities reflected the ability to identify potential participants and to have a large enough pool of exceptional patients.

The study was approved by both institutions' ethics review boards. Oncologists at both sites were asked to identify patients for this study that they had treated and considered to have had an exceptional disease course. Criteria defining the patients' exceptional disease course were based on the four categories suggested by Hirshberg and Barasch [4] (see Table 1). The primary oncologist identified the patient, the chart was reviewed by a member of the research team, and another oncologist independently reviewed the patient's records and concurred that the patient met one of the criteria that established them as an exceptional patient. In this qualitative study, participants were purposively selected based on the above described procedure to assure their "exceptional patient" status [19, 21].

Table 1 Criteria defining the patients' exceptional disease course [4]

1. *Delayed progression*—Patients identified by their primary oncologist as having experienced a partial regression of cancer or having lived with their disease in reasonably good health for a long period of time, exceeding the expectations of the physician.
2. *Long survival*—Patients identified by their primary oncologist as having gone through conventional treatment with or without complementary or other nonconventional therapies, yet having survived far longer than the statistics for their type of cancer and treatment would suggest is possible.
3. *Inadequate treatment*—Patients identified by their primary oncologist as having received conventional medical treatment considered insufficient to produce a cure or remission, yet having experienced unusual survival that exceeded the physician's expectations for that specific disease process, or having experienced a response that is clearly not related to any known conventional treatments the patient received.
4. *No treatment*—Patients who were properly diagnosed via X-rays, biopsies, and other medical diagnostic procedures or tests who had no medical intervention and had unusual survival that exceeded the physician's expectations for that specific disease process.

Patients meeting any of these criteria were eligible for this study

Interviews

The study was described and participants consented to the interviews. A single researcher conducted the interviews in each site. (NP in the USA, SL in Israel). Information was collected to describe the sample from the medical records and demographics were collected at the beginning of the interview. In keeping with the narrative approach for the interview, the question was open-ended: "You have been identified as having an exceptional disease course, could you tell me about your experience." Additional probes such as "could you elaborate on that," "you mentioned…could you tell me more" were used as needed. This approach allowed for the participants to voluntarily discuss issues without the interviewer directing the content. Interviews lasted 30–90 min, were audio-taped, transcribed, and the transcriptions validated against the audiotape for accuracy. Transcripts were de-identified and kept on secured computers and any identifying material was secured in locked cabinets or secured computers.

Data analysis and interpretation

A narrative cross-case analysis was used in the thematic analysis [16]. The analyses were done in the native language of the participants (Hebrew or English). The data were analyzed separately in each site in the language of the interview participant, and then in the discussion of the findings, it was translated into English. The Israeli team was bilingually fluent in both English and Hebrew. The exemplars selected by the Israeli team were translated into English, and in order to maintain accuracy to the source, there was retranslation back to Hebrew by a third party.

In each location, an experienced qualitative researcher worked with the research team in the analysis. After validating the accuracy of the transcriptions, multiple readings were done and segments highlighted. From this, the researchers developed codes, categories, and a coding schema, which is a conceptual framework linking categories that suggests patterns and themes [19, 22]. These codebooks and schemas were discussed among researchers until consensus on a schema was reached. This schema was then applied to the entire data set to confirm that the schema and themes were consistent throughout the data set.

After an analysis of the data at each site, the schemas and themes of the overall findings along with exemplars were discussed between the two teams from USA and Israel by electronic email, and conference calls were used for further discussion. The theme of personal activism was agreed on by consensus of both teams as an underlying theme across both sites. This report focuses on this common underlying theme from both sites.

The study endpoint in both locations was aimed at reaching saturation in each location which is when the categories and themes are well described and new interview data are primarily redundant. Other researchers have determined through the examination of saturation in qualitative studies that saturation often occurs within the first 12 interviews [23].

Results

Twenty-six patients—14 in the USA and 12 in Israel—were identified by oncologists and all agreed to be interviewed. All the participants had advanced disease. The mean number of years since diagnosis was 11 years for the US patients and 12.6 years for the Israeli patients (range, 2.5–36 years). The demographics of the participants and their cancer diagnoses were varied, with breast cancer being the most common diagnosis in both sites (see Table 2).

The participants voluntarily described a dominant theme of personal agency or activism. This finding was revealed independently in the analysis in both sites. The theme was initially labeled personal agency in the USA and activism in Israel. After discussions among all the investigators at both sites, we reached consensus that the accounts of the participants were very similar and that this was a major underlying theme in both sites. The fact that similarity in meaning was found between the two cultural groups is an interesting finding and suggests that despite any cultural differences or differences in medical systems, there might be some enduring or innate trait for activism that is not sensitive to culture. This personal agency/activism was reflected in being active and involved throughout the chronology of their disease experience (Table 3). From the time that the participants first encountered the disease, they felt the need to actively face the disease. This activism continued to be expressed in the way they coped with the diagnosis, gathered information, selected the treating team, selected the therapy, and extended into changing a philosophy of life, seeking meaning in the experience, and becoming more altruistic.

Activism in facing cancer

Immediately after their diagnosis, many participants chose to take a very active part in their disease care by not denying it or downplaying their situation. This was notable in their language with the frequent use of active verbs with personal pronouns such as "I did" or "we (referring to the physician) decided." Some examples of this active stance in the early stage of their diagnosis are reflected: "I don't want you to hide anything from me, I want to know the truth… don't hide anything…don't cover up", "I've decided", "I was really scared, but I knew that I had to take the bull by the horns and run with it. I had to do whatever I could to get rid of it or to manage it."

Activism in getting information and fighting the disease

Activism was expressed in obtaining information and educating oneself about the disease process and the possible options for treatment. One participant, who served in the Israeli military extended the military metaphor into actively combating disease by collecting the right information: "…I had just completed military service for 22 years. It was three months after my discharge. I understood that cancer was a kind of war. And in a war, you need intelligence" (Isr Pt 1).

Activism in selecting and interacting with the treatment team

Activism found expression in choosing the physician and treatment team. In many cases, this involved an active process of data collection, examining the various physicians, and seeking a second opinion. This activism carried over into their relationships with their physicians and health care providers. Many referred to making joint decisions: "we (my physician and me) decided…" or "getting a second opinion…and maybe a third before you do something." They were quite clear, however, on their respective roles: "I expected him (the physician) to do everything he could" (Isr Pt 2) and "I would do everything I could to beat the odds" (Isr Pt 3). Another participant stated: "Sometimes the doctors don't always know everything that's out there. It takes a proactive patient to be successful" (US Pt 1). Another patient who switched doctors described her experience: "…the second time when I didn't feel the doctor was listening to me, then I just went ahead and switched doctors" (US Pt 2).

Activism in choosing the therapy

Most of the narratives revealed an active role in decision making concerning their medical treatment. This activism can be separated into two approaches:

(a) *Following the physician's recommendations after building a relationship of trust*

The patients followed their physician's recommendations only after building a relationship of trust. At that

Table 2 Patient demographics (USA, $n = 14$; Israel, $n = 12$)

	Number of patients (USA)	Number of patients (Israel)
Gender		
Male	4	4
Female	10	8
Age		
<44	1	0
44–55	4	3
55–81	8	9
Marital status		
Married	12	6
Divorced	1	4
Single	1	2
Years of education	Average = 16	Average = 15.2
Employment status		
Yes	6	8
No	3	1
Retired	5	3
Longevity—mean number of years since diagnosis	11	12.6
Cancer diagnosis		
Breast	7	3
Colorectal	2	2 (one Patient had colon cancer + melanoma)
Acute myeloid leukemia (AML)	2	
Pancreas	1	2 (one patient had pancreatic + prostate cancer)
Thyroid	1	
Cervical	1	
Ovary		1
Melanoma		2
Glioblastoma Multiforme		1
Mesothelioma		1
Sarcoma		1
Prostate		1
Advanced disease	14	12
Treatment received		
Chemotherapy	14	9
Radiation	9	3
Surgery	9	10
BMT	4	0

point, they acted according to their physicians' recommendations. Although they trusted their physicians, they wanted explanations; it was not a passive surrender as illustrated in the following statement: "Doctor, I'm in your hands, just explain what's going on" (Isr pt 4). In another example, a participant stated: "I was going to do everything, everything in my power to fight against it (cancer)…, I listened to them (physicians) and (I) made the decision" (US Pt 3). It is clear in both these exemplars that while they trusted their physician, the theme of personal activism was present.

(b) *Seeking to make decisions on the treatment process together with the physician*

The other approach involved active participation with their physicians' decisions regarding their treatment. This was evident by the frequent use of "I" or "we" decided,

Table 3 Increased personal agency—activism

1. Activism in facing cancer
2. Activism in getting information
3. Activism in selecting the treatment team
4. Activism in choosing the therapy
5. Activism in approaching life
6. Activism as "a calling"

indicating that the patient had an active and/or collaborative role in decision making. One participant noted, "I felt like I was in control, like I was making the decisions" (US Pt 4). Another participant illustrates her previous passivity and her transition into a more active position in the following excerpt:

> At first I felt like a chemotherapy tank, a tank for doctors, and a tank for cells. I felt as if there were decayed cancerous cells in my body, and there was a war going on, a war between the oncologists and the tumors. That's what was happening. But I wasn't present, I wasn't there. I let them conduct their war against the cancer, and I went, was taken, at first in a wheelchair, and afterwards, even when I could walk, I was taken all the time, a passive spectator. Until one day I said: "Hey, they're going home, but my medical file stays in the hospital; I'm going home, too, never mind what condition I'm in. In any case, whose cancer is it, whose war is it? Theirs or mine? (Isr Pt 5)

Activism in approaching life

The illness experience forced many to change the way they approached daily life. One participant noted: "it makes life more precious" (US Pt 5). These changes were apparent in both attitude and lifestyle behaviors. One of the participants noted that he needed to take responsibility for his life: "The name of the game is taking responsibility, taking responsibility for your own life. The physician can't take responsibility for your life, nor can your parents or children. Only you can" (US Pt 6).

A woman with young children also noted a change in her priorities by "becoming a little bit more self-centered" and taking care of herself as higher priority (Isr Pt 6).

For some, the experience changed their philosophy of life. One participant noted that the illness experience "completely changed my life…it was probably one of the best things that ever happened to me because it really made me wake up and…put a different perspective on life where I appreciate things more" (Isr Pt 6).

Others described that they were now focused on living in the present which is reflected in the statement "I am doing the things I love" (US Pt 7). In another example, a woman described going from being a high-power professional to being a master gardener, which helped her "feel much better and happier" (US Pt 8).

This change in philosophy became important as people faced the challenges of living with a chronic condition as illustrated in this vignette: "about a month after finishing treatment, I went sailing with friends, and I had a wonderful holiday. I saw that there is life after cancer or even with cancer.…There's something, some inner mechanism, that make me live life to the full, and I don't allow the cancer to rule my life or dictate what I do" (Isr Pt 7).

One woman described her cancer as a turning point contributing to improving the quality of her life:

> I suddenly realized that I had to change my life, that I had to do myself up and do up my house.…I went to a flower shop and told the shop assistant: 'I want a bunch of flowers, that floral arrangement, this vase of flowers, and, oh yes, I must have an orchid. Make them up into a big bunch that will look like cheerful wild flowers'. The shop assistant said: 'Oh, you must have a birthday'. 'No,' I said, 'I have cancer.' And then I began living life differently. I began to understand that I was deserving (Isr Pt 8).

Common to all these narratives was a change in their philosophy. This focused on active participation in everyday life and making themselves a priority in living to the fullest.

Activism as a calling ("I have a mission")

Along with changing their philosophy of life and lifestyles, many patients sought higher levels of meaning in their illness experience as a way to understand and incorporate the illness experience into their personal narrative. Often, this was integrated with a sense of altruism, many times by becoming active with other patients.

In both sites, many patients attempted to turn their personal experience into a message they wished to promulgate. Even their willingness to be interviewed was part of this sense of mission. Helping others was reinforced by a sense of "calling" and "mission." For one participant, this mission was almost a pledge:

> I feel I have a kind of mission, a calling. It's a bit amorphous, but it's something that's become stronger over time—that I have some kind of mission, or

> calling, and it's also one of the things that I really believe helped me and helps me cope well.…It's awesome, it gives you a sense of tremendous power, will, motivation, and the feeling you can conquer anything" (Isr Pt 1).

Discussion

In this study, we found that there was a recurrent underlying theme of "activism" manifesting in gathering information, making decisions in the treatment team and therapies and in their personal philosophy which often was reflected in altruism and living life to the fullest. The illness experience forced many to change the way they approached daily life. Changes were apparent in both their attitude and their lifestyle behaviors.

The findings from this study are similar to the findings from a recent qualitative study from Sweden where the main themes that participants attribute for the exceptional trajectory were agency and responsibility [12]. In Canada, Cunningham in a qualitative study focused on interviewing patients with medically incurable cancers who had outlived their prognoses by 2.2 to 12.5 years (and have survived further, two more years in most cases, between interview and publication) [24]. They found the following themes common to most or all of their participants:

"Authenticity," or a clear understanding of what was important in one's life; "autonomy," the perceived freedom to shape life around what was valued; and "acceptance," a perceived change in mental state to enhanced self-esteem or greater tolerance for and emotional closeness to others. These results are quite similar to the main findings in our study as both qualities of "authenticity" and "autonomy" can be closely related to our findings of "activism".

Killoran et al. [25], in another qualitative study, interviewed 17 long-term survivors of metastatic cancer and suggested that there are no real lessons to be learned from exceptional patients. Nearly all of the participants framed their unusual recovery as being largely unremarkable, without any major lessons to be learned or any recognition of having a transformational process leading to recovery (e.g., having "a wake up call"). However, in that study, these long-term survivors did report that it was very important to return to daily life and have a sense of normalcy, that they were "cured" through self-control, self-reliance, strong will, managing to maintain a sense of control over their health, and disallowing any further vulnerability to cancer. These findings actually support our main findings that many exceptional patients do have an attitude of "activism," and there are lessons to be learned from these patients.

Limitations

The limitations to this study were that these data were reflective and retrospective and therefore may not necessarily reflect a patient's perspective during their treatment. As true with all qualitative research, findings are by definition not generalizable. However, findings may be applicable to other patients in other settings and add a level of understanding to these situations.

It is important to mention that there is no cause and effect implied in the description of the findings obtained in this study as there may be patients who adopted the attitude of "activism" and did not survive. But one cannot ignore the relevance of this in statements obtained from the few who did. The study suggests that there are commonalities between patients who have experienced exceptional disease course that we can learn from and consider sharing with others. It is also noteworthy that the participants from two countries have described a similar underlying theme of activism or personal agency when asked to discuss their experience as an exceptional patient.

Clinical and research implications

Cancer patients are often characterized as lacking control over their health, subject on the one hand to the whims of the disease and on the other to the latest medical discoveries, over which they have no control. There is a general perception that patients diagnosed with cancer are characterized by powerlessness and a lack of belief in their ability to change their fate [26-32].

The participants' narratives in this study, however, painted a completely different picture. These narratives showed that the participants took responsibility for their health and were extremely active in coping with their disease. This finding suggests that "activism" in its different forms might have a role in survival or more importantly for patient coping. It is important for clinicians to appreciate and possibly encourage this attribute of patient attitude and behavior in their relationships with patients.

Based on this study and other similar findings, an instrument to measure activism could be developed and given to patients throughout the illness process. This would enable a comparison with outcomes and a distribution of these characteristics. This could then be confirmed in future larger studies or through the development of an appropriate registry of these patients. Systematic collection of clinical data and clinical samples for such a registry would provide a base for rigorous analysis and may suggest new and novel ways to approach cancer care.

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