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Confronting the therapeutic misconception

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CLINICAL CASE

A 40-year-old woman with metastatic, estrogen receptor–positive breast cancer is referred by her medical oncologist to an experienced gynecologic surgeon for consideration of bilateral oophorectomy. The patient’s disease has progressed despite treatment with several standard endocrine therapies, including tamoxifen, and even after subsequent addition of targeted therapies. She has been on pharmacologic ovarian suppression with luteinizing hormone-releasing hormone agonists to allow aromatase inhibitor treatment, which she has tolerated well so far. The oncologist feels treatment options are now limited to clinical trial enrollment, standard-of-care cytotoxic chemotherapy, or best supportive care. The patient has been reluctant previously to consider chemotherapy due to concerns over potential effects on her quality of life.

Of the clinical trials available at the nearest tertiary care center, only one for which the patient meets eligibility criteria is currently recruiting. This trial, however, has an additional requirement that patients must be definitively postmenopausal. Hormonal studies indicate the patient is premenopausal and, therefore, bilateral oophorectomy would be required. In talking with the patient, the surgeon learns that the patient believes that there is a high likelihood of cure from the clinical trial. She states that her goals are “to beat the cancer and get on with my life.” Physical exam and basic laboratory studies are unremarkable, with the exception of a palpable mass in the left chest wall. Despite the advanced state of her disease, she has an Eastern Cooperative Oncology Group performance status of 0 and is an acceptable candidate for this operative procedure.

The surgeon’s choices are (1) perform bilateral oophorectomy, (2) refuse to perform the operation, (3) discuss the patient’s expectations of the clinical trial again and proceed only when satisfied that the patient has an accurate understanding of the situation, or (4) contact the referring physician to discuss the patient’s expectations of the study.

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THE ETHICAL DILEMMA

Informed consent is ethically and legally required for any operation and must satisfy a number of requirements.¹ First, the physician is required to discuss the nature of the disease with the patient and to disclose the proposed treatment, the possible benefits and risks of the treatment, and any alternative treatments. The patient must understand the information presented and have the capacity to weigh the information in order to decide whether to proceed with the treatment. Finally, the patient's decision must be voluntary and free from coercion or undue influence.

In the research setting, US federal law requires disclosure of additional information about participation in clinical studies, such as the study purpose and design.^{2,3} This responsibility adds a substantial layer of complexity to the routine consent process because the treatment is not the standard of care, and there is typically no, or limited, evidence available to guide an estimate of the likelihood of the patient's response to the trial treatment. In this case, the ethical dilemma is obtaining consent for an operation when the patient has a therapeutic misconception of the intended goals and outcome of the study.

BACKGROUND

Although they may seem similar to patients, there are fundamental differences between ordinary clinical care and the care provided in the clinical research setting. In standard approved treatment, the physician acts to provide a benefit and avoid causing harm to an individual patient. In contrast, the primary purpose of a research study is to generate data for the collective benefit to biomedical science and society, not necessarily for the benefit of any one individual.⁴ Certainly, many individuals have had medical conditions treated successfully while participating in clinical studies, particularly in situations where therapies are either nonexistent or inadequate; however, the efficacy of study drugs or procedures is uncertain and may even be inferior to the standard treatment. In some studies, such as phase 1 trials, the goals of the study may not even include efficacy or may include efficacy only as a secondary end point.

Therapeutic misconception occurs when research participants mistakenly attribute therapeutic intent to study drugs or procedures.⁵ In 1982, Appelbaum et al⁶ first described therapeutic misconceptions in psychiatric patients participating in drug trials. Since then, it has been recognized in a variety of study settings,⁷ including intensive care units⁸ and phase 1 drug studies.⁹ Patients may continue to confuse clinical care and research even when the researcher has disclosed information properly about the study during the informed consent process. They may understand the study design and procedures and yet still believe that the primary purpose of the study is to treat their own disease.

Some authors have distinguished a related situation called therapeutic optimism, in which patients may realize intellectually that research participation may not help them but strongly hope that it will.^{10,11} The patient's estimation of the chances of successful treatment is often substantially greater than those of the physician or research personnel. In a mild form,

therapeutic optimism is not incompatible with informed consent.¹⁰ It likely reflects a strong American cultural tradition that encourages hope, positive thinking, and faith.

Multiple contributing factors to therapeutic misconceptions have been identified. First, the general public often has a poor understanding of research. Many cannot define basic terminology such as “placebo,” “randomized,” or “double-blind.”¹² The patient’s trust in the physician may produce an assumption that if the physician recommends a clinical study, he or she must believe it will treat their disease.^{13,14} The media often sensationalizes results from “breakthrough” studies while ignoring or minimizing unsuccessful studies, thus reinforcing the assumption by patients that experimental treatments are highly likely to be successful.^{15,16}

In addition, at tertiary care centers, an individual physician may be both clinician and researcher, leading to confusion of the roles by the patient. Institutions may also portray participation in clinical studies as a way to access new treatments before they are widely available to the general public.¹⁷ Finally, physicians and researchers may, consciously or unconsciously, overstate possible benefits and minimize risks, demonstrating a provider bias to support their own beliefs or perceptions about certain treatment methods.^{5,18–20} In these cases, physicians themselves may be operating under a therapeutic misconception, truly believing that a trial represents the best possible treatment option for a particular patient.²⁰

When left uncorrected, therapeutic misconceptions have detrimental consequences both to the patient and to research. Patient autonomy is compromised, because consent decisions based on misunderstandings are not truly informed.^{1–4} Research participants who learn or realize after the fact that therapeutic intent was not part of the study often have feelings of intense anger or betrayal,¹⁶ leading to decreased trust in physicians, researchers, and the sponsoring institutions.²¹ In extreme cases, lawsuits have resulted when participants felt that they were misinformed.^{22–24} For these reasons, physician researchers have an ethical obligation to correct therapeutic misconceptions.

DISCUSSION

Option 1: Perform the bilateral oophorectomy

Can performing an oophorectomy on this patient be justified ethically? The patient seems to be an acceptable operative candidate from a medical perspective, and oophorectomy has a long history as an acceptable endocrine therapy for breast cancer, even when metastatic or highly advanced.²⁵ This patient’s cancer has progressed despite standard-of-care endocrine therapies, but it is possible that the operation itself would provide some additional therapeutic benefit. Furthermore, current National Comprehensive Cancer Network guidelines for breast cancer treatment recommend that premenopausal patients with advanced breast cancer who progress on tamoxifen receive either pharmacologic ovarian suppression or oophorectomy and then be treated as postmenopausal.²⁶

The decision of bilateral oophorectomy versus pharmacologic ovarian suppression is left up to the preferences of the individual patient and clinician because there is no clear evidence that either is superior. From this standpoint, oophorectomy is in line with current medical

practices. Finally, given that this patient has few alternative options, rendering her eligible for a clinical trial that might control her cancer would be in her best interest.

Of course, the surgeon is obligated ethically to perform the usual informed consent process for the operation. That is, he or she would discuss the risks of the procedure, such as infection, bleeding, injury to surrounding structures, and risks of general anesthesia. Although the patient apparently misunderstands the purpose of the clinical study, there is nothing that suggests she lacks capacity to understand the information regarding the operation itself. Strictly speaking, the clinical trial is outside the surgeon's scope of practice. The surgeon is neither involved with nor responsible for informed consent for the trial. Although performing the oophorectomy can be justified and is the most straightforward course, it ignores a larger picture of ethical concerns. The possible ways to deal with these concerns are outlined in the following options.

Option 2: Refuse to perform the operation

Surgeons must determine whether a particular operation is indicated in an individual patient. Given that this patient's disease has progressed despite ovarian suppression, the surgeon may think that operative ablation of ovarian function would be unlikely to provide additional control. With this perspective, the only indication for the operation is to meet enrollment criteria. This patient seems to have a therapeutic misconception regarding the clinical trial. If informed consent for the study is compromised, one could argue that the motive for the operation is also compromised. Without a clear, ethically sound indication, the surgeon could consider the oophorectomy unwarranted and decline to expose the patient to the risks of the operation.

In addition, the principle of autonomy applies to the surgeon as well: The surgeon is not obligated to perform the operation just because the patient was referred for that purpose or because the patient desires the operation. Finally, by refusing to perform the oophorectomy, the surgeon is not depriving the patient of her only treatment option. She could see another surgeon for a second opinion, investigate clinical trials at other institutions that do not require bilateral oophorectomy as a condition of enrollment, or reconsider systemic chemotherapy as a standard-of-care treatment option.

Refusing to perform the operation creates potentially more inconvenience for the surgeon, who risks inducing anger from both the patient and the referring physician and may fear undermining his or her referral base. If he or she is practicing at the same tertiary care center, the surgeon may be perceived as standing against the research goals of the institution. These issues can be mitigated by careful explanation of these concerns to the patient and the oncologist. The surgeon might also leave the door open to performing the operation in the future after the patient has had a chance to speak with the oncologist again. When there are concerns about inadequate informed consent in a nonemergency setting, however, the prudent course is not to do the operation at the present time despite potential drawbacks.

Option 3: Discuss the patient's expectations of the clinical trial again and proceed only when satisfied that the patient has an accurate understanding of the situation

The decision-making process in this case requires understanding the patient's expectations regarding the clinical trial and deciding whether they constitute therapeutic misconception or therapeutic optimism. Does her comment regarding "beating the cancer" represent a genuine belief that cure is possible or a fear that accepting the truth (that her cancer is incurable) will hasten an inevitable clinical decline? Further discussion with the patient could distinguish between these possibilities.

The surgeon can ask the patient to explain in her own words her understanding of the disease and its prognosis and what participating in the trial would entail. The surgeon's course of action would differ depending on the outcome of the conversation. For example, the surgeon might determine that the patient realizes that her prognosis for long-term survival is poor but feels it is important to have hope that the trial will benefit her, supporting a perspective of clear therapeutic optimism. In this case, she or he may feel that informed consent for the trial has been satisfied and proceed with the operation.

Alternatively, the conversation may reveal that the patient truly believes the clinical trial will cure her disease, a clear therapeutic misconception. Physicians have a duty to speak truthfully with patients. Not correcting a therapeutic misconception makes the surgeon complicit in perpetuating the misconception. The surgeon can discuss the nature of clinical trials and the prognosis of metastatic breast cancer in general terms to help further educate the patient while assessing her insight and her comprehension of the information.

Once satisfied that the patient has a realistic understanding, the surgeon may feel comfortable proceeding with the operation. It is also possible that the patient changes her mind about study participation and the operation after learning there is no certainty of effective treatment. Finally, if the patient persists in the therapeutic misconception, the surgeon may then refuse to perform the operation out of concern that adequate informed consent cannot be obtained. As described above, the surgeon could suggest that the patient discuss the trial with the oncologist again and consider undergoing the oophorectomy at a later time.

These discussions are by nature time consuming. The surgeon might be asked questions by the patient regarding study details or prognosis that he or she feels unqualified to answer. In addition, the surgeon may be seen as overstepping the role of the surgeon by other professionals who feel that consent to the study is their domain. Furthermore, the patient's time concerns should not be understated---the advanced stage of disease drastically decreases her survival outlook and her time to participate in any therapy. Nevertheless, given that the ethical dilemma hinges on what the patient understands, resolution requires a longer conversation with this particular patient than the typical consult.

Option 4: Contact the referring physician to discuss the patient's expectations of the study

Whether the surgeon decides to perform the oophorectomy, refuses to perform the operation, or is still uncertain of the best course of action, there are a number of reasons to contact the patient's oncologist. The surgeon is not a specialist in breast cancer and may have questions

regarding the patient's prognosis or the trial, which would best be answered by the oncologist rather than by the patient. Furthermore, before performing the oophorectomy, the surgeon may want to confirm with the oncologist that postmenopausal status is the only enrollment criteria the patient does not meet.

Performing the operation only to find that the patient is still not eligible for the trial would expose the patient to unnecessary risks with only a small chance of benefit. If the surgeon decides not to proceed with the oophorectomy at this time, professional courtesy should lead the surgeon to explain his/her concerns and reasoning directly to the oncologist. Finally, the referring physician may be unaware of the patient's misconceptions regarding the clinical trial. The oncologist may prefer to correct the therapeutic misconception or to have study personnel talk with the patient rather than leaving this task to a surgeon who is not involved with the research. This strategy avoids inadvertently giving the patient information that conflicts with information already provided by the oncologist.

One difficulty with this approach is that the surgeon must close his or her clinical encounter with the patient without committing definitively to performing or not performing the operation. Depending on how easy it is to reach the oncologist, the patient may have to return to the surgeon's clinic for an additional appointment, thus increasing the patient's cost and potential distress. In addition, the surgeon may discover during the conversation that the oncologist has been perpetuating the therapeutic misconception. This makes any decision very difficult, because the surgeon must then decide how to proceed if convinced the oncologist has misled the patient. Nevertheless, communication between these 2 physicians should avoid ultimately misunderstandings and enhance care of the patient.

ETHICS BOTTOM LINE

Patients confuse frequently the intent of clinical research studies with the intent of routine clinical care and enter into studies with an expectation of personal benefit, a misunderstanding known as a therapeutic misconception. Therapeutic misconceptions fundamentally compromise the process of informed consent. Patients cannot make authentic, autonomous decisions while operating under misconceptions regarding the ultimate goal of treatment and likely outcomes. Therefore, a physician treating a patient who is participating in a clinical trial should assess the patient's understanding of the purpose of the study and take responsibility for the patient's safety.

Physicians and researchers alike have an ethical obligation to consider and correct any therapeutic misconceptions prior to proceeding with study-related medical care. In addition, physicians should examine their own intentions regarding clinical research and consider whether they may be contributing inadvertently to therapeutic misconceptions.

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