The Black Box in Cancer: Dealing With the Unthinkable

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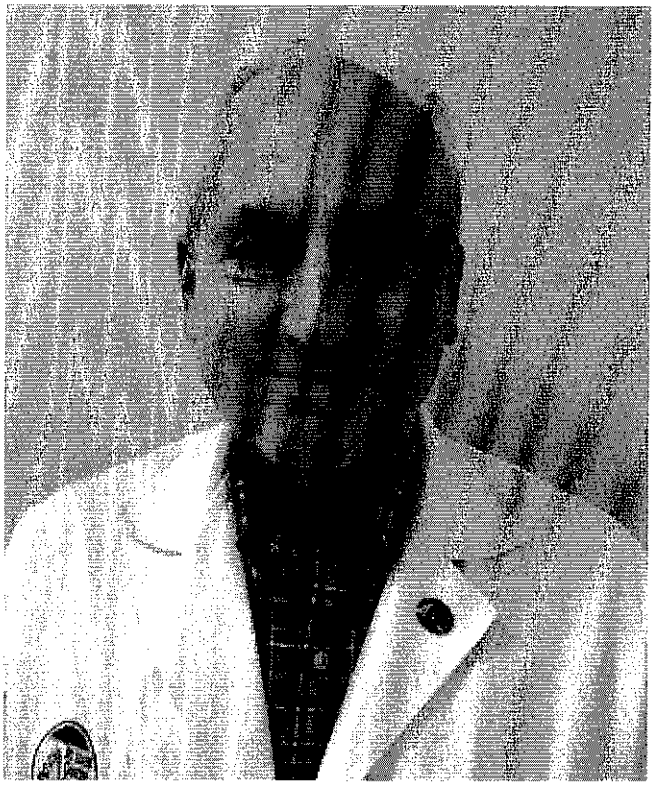
Blogs, Blogs, Cancer Complications



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It is stating the obvious that people living with cancer are at risk for sudden complications, such as pulmonary embolus, which can be terrifying. Here in the clinic we all know to keep an eye on our patients for any signs of distress, but mostly we are confident that all of our visits will be smooth. Terror rarely materializes here, but when it does, no matter how successfully it is met, it can shatter the nerves of the staff. Of all the things that can go wrong, the one emergency I fear the most is the allergic reaction to chemotherapy or immunotherapy.

A few years ago, one of my patients complained of profound itching just a few minutes into her first infusion of a well-known monoclonal antibody. We were well aware of the risk of hypersensitivity with this agent and had given her the recommended premeds to mitigate a reaction. We recognized the symptoms and quickly stopped the infusion. We provided oxygen, intravenous fluids, and antihistamines, and then stood by helplessly as our patient slipped into unconsciousness.

My patient had unwillingly entered the realm of the black box warning.

As new immunotherapy treatments are discovered, tested, and approved for use, tumors that once were hopeless can now be controlled—some say even cured. Melanoma was the first to respond, using the antibody combination of ipilimumab and nivolumab. The Holy Grail of modern treatment—to cheat death—is now possible in many solid tumors. The checkpoint inhibitor pembrolizumab has produced unheard-of results in progression-free and overall survival when added to standard chemotherapy in the treatment of advanced non–small-cell lung cancer. New immuno-oncology agents (I-Os, for short) targeting a variety of antigens, many found on T-lymphocytes that must be recruited and kept active in order to kill cancer cells, are rolling out steadily, to the point where oncologists have to study constantly to keep abreast of developments. They represent a new hope for those with

cancer—and they can be dangerous. Some carry a black box warning and some do not, but all of them advertise a dispiriting list of possible toxicities known as immune-related adverse events. It seems that every organ can be attacked, causing pneumonitis, colitis, hepatitis, dermatitis, or encephalitis, to name a few. Over time oncologists have become familiar with these wonder drugs and have little hesitation in prescribing them. Counseling patients about their risks has become a sobering conversation. Often I feel that I understand these I-Os about as much as my patients do—and I find myself more worried than they are.

The key to overcoming the unique toxicities of the new I-Os is early recognition of symptoms and early intervention. We teach our patients to call us immediately if they notice a rash, or diarrhea, or cough. Communication is critical, as is rapid diagnosis and treatment. I sometimes follow these people on a weekly basis, and have learned to never become complacent.

Imagine the horror, then, if a well-planned and hopeful plan of action comes flying apart due to an immune-related calamity. On the afternoon that my patient went into anaphylactic shock, I reeled with fear and embarrassment. We watched helplessly as EMTs intubated her and performed CPR. No doctor on Earth would ever wish such misfortune on another person, let alone a patient who had entrusted us with helping rid her of cancer.

The black box warning is there for good reason, but does it mean we should avoid using these I-Os? Just because a patient has received informed consent for treatment doesn't guarantee that all will go well. How do we justify the risk, no matter how small? I certainly don't know the answer. We can only weigh the pros and cons, and in the end make a shared decision with our patients to proceed.

Sometimes, as I have mercifully found, outcomes can change. Sometimes luck flies in to rescue our folks from disaster, and in the case of my patient, she had a full recovery from her arrest and is cancer-free 2 years later.

The black box warning is still there, waiting for the next oncologist to contemplate its ramifications.

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