PALLIATIVE CARE CASE OF THE MONTH

"Cancer Immunotherapy: New Drugs: Old Lessons"

by

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Case: This month's topic explores the prognostication challenges that the era of Immunotherapy presents to health care providers. We will use two cases to illustrate our points.

Case 1:
JD is a 55 year old Caucasian woman with metastatic Non-Small Cell Lung Cancer (NSCLC) who was initially diagnosed 3 years ago with symptomatic cervical lymphadenopathy. She was initially treated with platinum-based chemotherapy, then PD-1 inhibitor pembrolizumab but developed liver metastases. She was then referred for clinical trial enrollment. She was enrolled into a clinical trial that studied a novel combination of two new immunotherapeutic agents. On the clinical trial, she has had an excellent response with >50% disease reduction, improvement in quality of life and an increased performance status.

Case 2:
SR was a middle-aged man who first underwent a biopsy of a suspicious pigmented cutaneous lesion in 2012 that returned showing malignant melanoma. This was treated definitively and he was lost to follow up. A few years later, he developed 22lb weight loss. Work up revealed widely metastatic melanoma. He was started on ipilimumab and nivolumab without significant clinical improvement over the ensuing weeks. Following a hospitalization for worsening symptoms after 3 cycles of therapy, CT imaging revealed disease progression. At a bedside goals of care discussion, his oncologist recommended hospice. Patient was discharged home with hospice and died a few days later.

To combat threats from infectious agents, the adaptive arm of the human immune system has evolved to be precise, and responsive to change in threat levels. This homeostatic mechanism relies upon an interplay of stimulatory signals and inhibitory signals to fine-tune the adaptive immune response to antigen presentation. Perversely, cancer and chronic infections can hijack these negative signals to evade effective immune responses.

Cancer immunotherapy has overcome this hijacking through antibodies that block the inhibitory signals and allow T cells to suppress or even kill tumors. These immune check points include cytotoxic T lymphocyte antigen 4 (CTLA-4) and programmed death (PD-1). Drugs targeting various components of these pathways including PD-1/programmed death ligand (PD-L1) inhibitors and CTLA-4 inhibitors form the basis of immune-oncology.

Challenges in Prognostication
Immunotherapeutic agents present several prognostic challenges. First, response to immunotherapy agents varies considerably by disease and it is difficult to know who will benefit. For example, the availability of ipilimumab and nivolumab has increased median survival of patients with metastatic melanoma from approximately 6 months to greater than 2 years. In contrast, the rates are lower for Non-Small Cell Lung Cancer (NSCLC) with only 30% patients being eligible for treatment with PDL-1 inhibitors and fewer than half of them responding to first line check point inhibitors.[1] Second, there is the phenomenon of a small minority having a prolonged durable response. For example, of all cancer patients treated with immune checkpoint inhibitors, roughly 20% patients were alive at 18 months, with a smaller minority having no evidence of disease progression at 3 years.[2] Third, the toxicity profile of checkpoint inhibitors is different from conventional chemotherapy with lower rates of nausea, vomiting and hair loss. However, checkpoint inhibitors are associated with autoimmune GI, skin and lung complications, which may prohibit continued treatment with immunotherapy.[3] Finally, it is difficult to decide on the role of performance status in decision making about immunotherapy. Typically, oncologists will modify their treatment of older patients with significant comorbid disease and refrain from administering chemotherapy to a patient who spends more than 50% of the day in bed/chair, indicating a lower likelihood of response to therapy and a shortened life expectancy.[4] While poor performance status is associated with poorer outcomes even in immunotherapy, poor performance status alone is not used to forgo checkpoint inhibitors treatment.

To gain a better understanding of the clinical features that could influence benefit versus risk, various academic groups have studied patients receiving immunotherapy to develop scales to help select patients who are more likely to respond. These scales take into account variety of factors such as age, function, number of metastatic sites, lactate dehydrogenase (LDH) and serum albumin levels, platelet count, absolute neutrophil count, and absolute lymphocyte count (IGR score; MDACC phase I score).[2,5] More recently, overall tumor burden has been proposed as an important prognostic factor.[6] These scales are still under development.

Given that response can be durable for a small group of patients and there is a lower burden of adverse effects, it is hard not to offer immunotherapy to patients.[7] Patients come to oncologists having been inundated with advertisements touting that cancer immunotherapy is curative and non-toxic in patients with metastatic cancer. The hype is clearly not true. In taking care of cancer patients seeking immunotherapy both oncologists and palliative care clinicians will need to communicate hopeful yet realistic expectations and manage the disappointment that patients experience when checkpoint inhibitors are not effective.[3]

Personal details in the case published have been altered to protect patient privacy.
For palliative care consultations please contact the Supportive and Palliative Care ***programs at PUH/MUH, 412-647-7243, pager # 8511, Shadyside, 412-647-7243, pager # 8513, Perioperative/ Trauma Pain, 412-647-7243, pager # 7246, UPCI Cancer Pain Service, pager 412-644-1724, Magee Women's Hospital, pager 412-647-7243 pager # 8510, VA Palliative Care Program, 412-688-6178, pager # 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children's pager 412-456-1518***
With comments about "Case of the Month" call Dr. Robert Arnold at (412) 692-4834.

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