Navigating Cancer Therapy During the COVID-19 Pandemic: A Tightrope Walk

A Levy

The World Health Organization announced the pandemic of coronavirus disease (COVID-19) on March 11, 2020 (1). This disease caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has since globally accounted for 184 974 601 cases and over 3.9 million deaths as of July 7, 2021 (2). In addition to the high mortality rate associated with COVID-19, the oncology community has been faced with unique clinical and technical challenges along the cancer care continuum including navigating diagnostic, therapeutic and supportive care (3). Over the past year, oncology specialists have walked the 'clinical tightrope' of weighing the delay in cancer diagnosis and treatment against the dangers of COVID-19 exposure during clinical decision-making. Alexander Kutikov and colleagues from Fox Chase Cancer Center likened cancer care during the time of COVID-19 to '[a] war on two fronts' and noted how the disruption of the infrastructure for cancer control and prevention presented a challenge in allocating the limited healthcare resources (4). As the scientific community continues to gauge the full extent of the impact of COVID-19 on cancer management, many reports across several countries already show that delays in diagnosis and treatment will eventually result in increases in advanced-stage diagnoses and cancer mortality (5-7).

Patients with cancer are generally more susceptible to infections because of multiple factors including other co-morbidities, declining health status, and systemic immunosuppression caused by both the disease itself and the various pharmacological therapies used. Data from the first few months of the pandemic exposed a pattern of higher utilization of intensive care by cancer patients due to more severe COVID-19 disease presentation (8, 9). This impacted clinical decision-making, and many oncologists and cancer centres were faced with weighing options regarding route of administration of chemotherapy drugs (often avoiding the intravenous route due to the risk of infection), and whether to include radiotherapy and immunotherapy as modalities of treatment as these approaches carry higher risks of further compromising the immune system and increasing vulnerability to COVID-19 (10). The issue of sub-optimal management of cancer patients thus became a growing concern in the scientific community, and the racial disparities and structural barriers to care that already existed for minority patients in the United States of America (USA) especially, further compounded this problem in Black and Hispanic individuals (11).

The response of professional organizations such as the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO) was to develop expert recommendations to support care teams in optimizing cancer care (3, 12). These guidelines were pivotal as they provided the 'first balancing act' in imparting some evidence-based guidance for clinical decision-making. For example, one key consensus statement from ESMO addressed the increased risk of thromboembolic events and associated complications such as lung vessel obstructive thrombo-inflammatory syndrome in patients with cancer and COVID-19 and provided guidelines for prophylaxis using low molecular weight heparin or novel oral anticoagulants (3). This recommendation was impactful as coagulopathies associated with COVID-19 are more likely in cancer patients, and the complications of these coagulopathies often lead to higher mortality rates in hospitalized patients (13). The American Society of Hematology's guidelines for therapeutic anti-coagulation in patients with cancer and COVID-19 also aligned with those from ESMO, and there is now an FDA-approved regimen for thromboprophylaxis after discharge, which includes betrixaban (Bevyxxa) and rivaroxaban (Xarelto).

While these recommendations were helpful, the existing structural barriers (such as inequity in access to technology, testing and health insurance for persons of

Correspondence: A Levy, Dr Kiran C Patel College of Allopathic Medicine, Nova Southeastern University, Fort Lauderdale, FL, United States of America. Email: alevy1@nova.edu

From: Dr Kiran C Patel College of Allopathic Medicine, Nova Southeastern University, Fort Lauderdale, FL, United States of America.

colour) still created a large disparity in health outcomes in patients with cancer and COVID-19. In the USA, racial inequity was a resounding theme in healthcare throughout the COVID-19 pandemic, and especially so, when the 'second balancing act' came with the approval of COVID-19 vaccines. The emergency use approval of these highly efficacious vector, protein subunit and mRNA-based vaccines represented a milestone for cancer patients who were mostly considered as priority groups for initial doses, as they have high mortality rates associated with COVID-19 (14). With over 3 billion COVID-19 vaccine doses now administered worldwide and COVID-19 infection numbers trending downwards, are we beyond the logistical challenges in cancer therapeutics?

American Society of Clinical Oncology endorses COVID-19 vaccination and counselling of cancer patients in the absence of contraindications and severe allergies (15), but one size does not fit all. For example, the National Cancer Institute (NCI) advises that patients with recent stem cell transplant or Chimeric antigen receptor T cells (CAR T) therapy who are typically receiving immunosuppressive therapy delay COVID-19 vaccination until at least three months after treatment completion. The NCI also advises that leukemia patients on intensive treatment regimens delay vaccination until their cell counts recover. Arguably, these are the patients most vulnerable to COVID-19 infections, but the lack of evidence regarding the risk-benefit ratio of the COVID-19 vaccines in these subsets of patients who are also more vulnerable to the potential adverse effects of vaccinations underscores the delay in their administration (15, 16). Two recent studies have so far shown promising results where most cancer patients, including those on chemotherapy, mounted a detectable antibody response to COVID-19 vaccination (15, 16).

Overall, the approach to cancer care remains complex, and for those patients whose care was delayed during the pandemic, completing their course of treatment should be a priority. Acknowledging and addressing the racial and economic disparities that exist regarding access to healthcare and vaccination is key towards accomplishing this for many patients. Finally, oncologists will now be increasingly challenged with keeping abreast of clinical trials and emerging evidence that will guide best practices for cancer care in the post-COVID-19 era.

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