CLINICAL VIGNETTE

SARS-CoV-2 Infection and Challenges of Diffuse Large B-Cell Lymphoma

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An 85-year-old female with a history of diffuse large B-cell lymphoma (DLBCL), hypertension, and coronary artery disease presented to the emergency department (ED) with generalized weakness, fatigue and fever with associated shortness of breath and cough. She had tested positive for COVID-19 infection five weeks prior and developed worsened symptoms the prior week prompting her visit. Her initial oxygen saturation was 72% on room air with a respiratory rate of 50 breaths per minute. She was placed on non-invasive ventilation (CPAP) with some improvement in respiratory distress. In the ED, she stated that she desired to be a full code and wished to be placed on a ventilator life support if necessary. She also had a recent admission for sepsis and pancytopenia due to chemotherapy. ER labs were remarkable for white blood cell count of 1000/uL with a hemoglobin of 9.6 g/dL and a platelet count of 143,000/uL. Her differential showed 4.9% lymphocytes with 61% neutrophils but had immature granulocytes of 13%. Her chest x-ray showed patchy bilateral airspace opacities compatible with multifocal pneumonia consistent with COVID-19 infection. She was admitted to the COVID unit and was placed on standard treatment with discussion of goals of care in consultation with family members and palliative care consultation.

Oncological history included of DLBCL, which had transformed from a marginal zone lymphoma initially diagnosed in 2012. Treatment after transformation included Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R–CHOP) with growth factor support. Unfortunately, withdrawal from the prednisone led to secondary adrenal insufficiency. She had just received a follow up cycle of R - CHOP with excellent response seen on a positron emission tomogram (PET) scan. However, during the current admission when she was seen by the oncologist a decision was made to discontinue aggressive treatment and consider appropriate palliative chemotherapy if the patient recovered from COVID-19 infection.

As a novel viral disease, it was impossible to predict her recovery and her residual symptoms. Despite her desire for continued chemotherapy all eventually agreed upon a watchful approach. The palliative team assisted the patient and her family in a more realistic goals of care plan. Several meetings with the patient considered of her desire to preserve quality of life and keep chemotherapy as an option. Despite her age, she was relatively healthy with independent activities of daily living.

During her hospitalization, the patient was treated with azithromycin and ceftriaxone. She also received completed remdesevir, convalescent plasma and tocilizumab. She received remdesevir therapy despite a shortage of remdesevir. After twenty days of hospitalization her fever resolved, shortness of breath improved and she was weaned off supplemental oxygen. Oncology made plans to follow her post discharge and to continue pegfilgrastim to support her blood counts. Despite the patient's immunocompromised state, age, underlying malignancy and a recent admission for pancytopenia, she made a full recovery. This raised a series of ethical questions by the team regarding the appropriateness of care of patients with limited survival but who require intense, prolonged and costly medical care in the setting of optimization of care at the end of life.

Discussion

Coronavirus exposure and subsequent development of disease are important consequences of human and animal pathogenic infections. At the end of 2019 coronavirus was identified as the cause of pneumonia in China, rapidly spreading throughout the world to become a global pandemic designated by the World Health Organization as COVID-19.[1] Coronavirus-2 causes COVID-19. The rapidly expanding COVID-19 acute respiratory endemic has altered daily life including medical management of diseases including the care of cancer patients. The care of patients with cancer during this crisis is challenging given the competing risks of death from cancer versus death or serious complications from COVID-19.[2] This patient was both advanced in age and immunocompromised.

The COVID-19 pandemic has made it a challenge to deliver appropriate and timely treatments to many patients especially those with life limiting illnesses. There is a competing risk of death from cancer versus death from infection and a high rate of complications due to infection with coronavirus in an immunocompromised host.[3] We need to balance the risk of delaying cancer treatment with the risk of COVID-19 infection to avoid adverse outcome. We also need to follow social distancing as well limited availability of protective equipment.[4]

Although there have been prior pandemics, the current COVID -19 global outbreak has raised public as well as clinician awareness of how to best deliver care. Recommendations about cancer screening should be based on the state of COVID- 19 in an individual community as well as availability of scarce resources. In a community with severe infection, routine clinic

visits may need to be postponed. There is no evidence to suggest that COVID-19 infection interferes with cancer staging but we anticipate that the year of pandemic isolation has impacted rates of early cancer detection. In patients with newly diagnosed cancer, it may be reasonable to limit staging procedures and pretreatment evaluation to develop a treatment plan.

Rationales for delaying elective surgery during the pandemic include conservation of resources, reducing the risk of viral spread, and avoiding postoperative infections. Patients with high risk of progression should be offered surgical treatments. Examples include lung masses over 2 cm in size, colon cancer with obstruction, type II endometrial cancer, ovarian cancer, liver masses, and high-risk muscle tumors.[5]

Some patients receiving curative intent radiation therapy for rapidly progressive tumors may proceed with therapy as risk of delaying treatment outweighs risk of COVID infection. When available, alternative regimens should be offered. However, radiation therapy should be continued or given to patients with lung cancer, rectal cancer as well as head and neck cancer as these cancers carry a high mortality and are rapidly progressing.

Chemotherapy should be continued or initiated for patients with acute leukemia, large cell lymphoma (as in our patient), symptomatic myeloma, metastatic testicular cancer, small cell lung cancer as well as head and neck cancer except thyroid.[6] There is no evidence to support changing or withholding chemotherapy or immunotherapy in patients with cancer and routinely withholding critical anticancer treatments is not recommended for patients who do not have COVID-19 infection. Patients receiving immunotherapy as well as those with pneumonitis, complications may alter treatment with patients exposed to COVID-19.

The COVID-19 pandemic has increased mental health problems including stress, anxiety, insomnia, denial, anger and fear.[7] These may fuel disease progression or recurrence. Patients may feel loneliness and isolation. A comprehensive palliative care team can offer psychosocial and spiritual support. Advance care planning is essential and important for patients given the additional risk of COVID-19.[8]

Finally, the well-being of clinicians is important. Clinicians are also at increased risk of anxiety because of physical isolation from friends and family, concern about their own health and health of their families, and additional workload secondary to COVID-19 response. New research, ongoing evaluation of treatment options, and limited resources are important in any pandemic especially for patients with advanced and life limiting illness. We have learned a great deal from this pandemic and protocols for rationalizing care in the coming year furthering discussion on optimal delivery of healthcare resources.

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