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REVIEW PAPER

Covid-19 and Cancer

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ABSTRACT

Coronavirus disease (COVID-19) has affected healthcare delivery all across the globe, particularly for chronic diseases like cancer. Everyday new literature and guidelines are emerging. In this review article, we aimed to discuss the essential insights of cancer care during COVID-19 pandemic. Cancer patients are at higher risk of morbidity and mortality from COVID-19. Yet they should not be deprived of necessary treatment while minimizing the risks of the spread of COVID-19 at the same time. Different recommendations about surgery, chemotherapy, radiotherapy and general cancer care have been proposed by different leading groups on how to deal with cancer during Coronavirus pandemic. Although these are troubled times with limitations in resources and challenges in providing healthcare, yet there is a need to evaluate cancer patients on case to case basis and deliver optimum care to all.

Keywords: SARS-CoV-2; cancer care; pandemic.

INTRODUCTION

The Coronavirus disease (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has emerged as the largest global public health issue of our era.[1] It originated from seafood and wet animal market in Wuhan, China in late December 2019 as a zoonotic virus transmitted to human by Chinese horseshoe bats.[2] However, within 3 months it spread all across the globe via rapid human to human transmission causing a large number of deaths.[3] Subsequently, the World Health Organization on 11th March 2020 declared COVID-19 disease as a global pandemic.[4] As of now, over 10 million cases and 500,000 deaths from COVID-19 have been confirmed worldwide with the highest incidence and fatality reported from the United States of America.[5] India ranks 4th in the list with total 548,318 confirmed cases and over 16,000 reported deaths due to COVID-19till 29th June, 2020.5 In Assam, the largest north-eastern state of India from where we are writing this report, there have been 7,493 reported cases of COVID-19 with 11 deaths till now.[5]

The pandemic has severely affected the healthcare resources of the most developed nations. Medical facilities in Europe and America were so overburdened with Coronavirus cases that recommendations had to be formulated to ethically consider triage protocols by caregivers.[6] In the absence of any definite vaccine or curative therapy for SARS-COV-2, the only effective means to combat the disease spread was by isolating the diseased persons by performing extensive testing and quarantine of suspects and contacts besides restricting travel, maintaining the norms of physical distancing and adopting proper hygiene and sanitization. The preferred first step to implement these measures for controlling COVID-19 by most countries was a Lockdown. India went into lockdown from 24th March 2020 as per government directive, which has subsequently been extended

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in multiple phases and has crossed Day 96 at the time of writing this report.[7]

Initial reports from China by Liang et al.[8] suggested that patients with cancer were more susceptible to COVID-19 infection because of their immunosuppressed state. Additionally, they showed that patients with cancer had poorer outcomes from COVID-19 and hence called for more intensive handling of cancer patients during this pandemic. This drew the attention of oncologists all over the world to modify their practices and formulate specific guidelines to deal with the diagnosis, treatment and follow up of cancer patients, minimizing the associated risk of infection while providing optimum cancer care. This review article will provide insights on cancer care during COVID-19 pandemic.

EFFECTIVE CANCER CARE DURING COVID-19

Cancer patients are often immune-compromised and cancer treatment causes myelosuppression that leads to lowering of innate immunity. Other factors like advanced age, presence of comorbidities, malnutrition, debilitating surgeries and supportive medications like steroids also affect the immune response, putting patients at increased risk of COVID-19 related morbidity and mortality. Researchers from the COVID-19 and Cancer Consortium (CCC19) published data on 928 cancer patients with confirmed coronavirus infection from US, Canada and Spain and found 13% incidence of all-cause mortality within 30 days of diagnosis. Risk of death was higher among elderly, males, smokers, those with multiple co-morbidities and in patients on active cancer treatment with Eastern Cooperative Oncology Group (ECOG) performance status 2 or higher. They also found that treatment with hydroxychloroquine and azithromycin for COVID-19 had an increased risk of causing mortality in cancer patients.[9] The other group from the University of Birmingham and the University of Oxford, UK, observed 800 patients enrolled in the UK Coronavirus Cancer Monitoring Project.[10] Risk of death was significantly associated with patient's age, male sex and presence of co-morbidities like hypertension and cardiovascular disease. However, unlike the CCC19 study, they observed that COVID-19 positive cancer patients on active treatment with chemotherapy, immunotherapy, hormonal therapy, targeted therapies or radiotherapy did not have the additional risk of death compared with those who did not receive those therapies. The investigators of this study from the UK concluded that withholding effective cancer treatments from many cancer patients during the pandemic ran a very real risk of increasing cancer morbidity and mortality, perhaps much more than COVID-19 itself.

Thus in this backdrop of competing risk of death and complications from untreated cancer versus COVID-19 infection in the immune-compromised host with cancer, delivering cancer care had become a herculean task. Implementation of lockdowns globally has made access to healthcare facilities by cancer patients even more challenging, especially in developing countries like India because of cancellations of outpatient visits, delays in routine cancer screening,[11] surgery postponements or cancellations. However, it is a well-known fact that delaying cancer diagnosis and treatment adversely affects the prognosis and outcome and is not acceptable under any given circumstances.[11]

There is no "one size fits all" approach, conceptual framework for balancing cancer risk versus infection risk and practical approaches for managing cancer patients during the pandemic are presented below.

General care for outpatients

The American Society for Clinical Oncology (ASCO) suggests the following guidelines.[12] All patients with cancer should be informed regarding the symptoms of COVID-19 and trained to maintain proper hygiene and avoid crowds and should be urged to wear a cloth face cover. Clinic visit that can be postponed without risk to the patient should be postponed. Pre-screening via telephone calls or digital platform for COVID-19 symptoms and exposure should be done before in-person clinic visits. Screening clinics should be developed to allow for patients with symptoms to be evaluated and tested.

CANCER SCREENING, DIAGNOSIS AND STAGING

There are concern about a halt in national cancer screening program during the pandemic and the potential long term detrimental impact of delays inpatient,[11,13-15] population and health care system responses to suspected cancer symptoms. ASCO guidelines recommend postponing cancer screening procedures that require clinic/center visits. However, clinicians should follow guidelines specific to their region. It is reasonable to limit the staging procedure and pre-treatment evaluation only to those that are most necessary to inform the development of the initial care plan.

SURGERY

Various agencies have put forward there consensus statement for surgical management of cancer patient during the pandemic. Salient points of these recommendations are; surgery with shorter hospital stay and lower complication rates should be prioritized. Complicated reconstructive surgeries should be avoided. Surgery should be performed in patients who have finished their neo-adjuvant treatment. Surgery should be deferred in certain cases having a low risk of early relapse. Resection of primary tumour should be postponed in metastatic settings. Palliative surgeries should be postponed, except for life-threatening complications such as respiratory difficulty mandating tracheostomy or in cases with severe bleeding, or when delaying treatment will have negative consequences for patient's quality of life.[16,17]

RADIOTHERAPY

Patients receiving radiotherapy with curative intent for rapidly progressive tumour should reasonably proceed with the therapy, as the risk of delaying the treatment may

outweigh the risk of COVID-19 exposure and infection.[18] where available, alternative hypo-fractionated regimens should be offered e.g. short course neoadjuvant radiotherapy for rectal cancer, FAST/FAST forward-protocol for adjuvant radiotherapy in breast cancer. Radiotherapy for symptom control and in patients with low-risk progression or recurrence should be delayed or adjusted.[19] patients actively undergoing radiotherapy with established treatment plans, the decision to continue requires careful consideration of; indications, dose already delivered and risk and benefits. Site-specific guidelines by American Society for Radiation Oncology (ASTRO), European Society for Radiotherapy and Oncology (ESTRO) and other global radiation oncology response groups can be considered with suitable adaptions fulfilling the local/regional guidelines.[20,21]

CHEMOTHERAPY

There is no direct evidence to support changing or withholding chemotherapy or immunotherapy in patients with cancer who do not have COVID-19.[22] ASCO recommends that clinical decisions should be individualized and consider factors such as the durability of cancer, the risk of cancer recurrence with treatment delay, modification or interruption, the number of chemotherapy cycles already complete and patient's tolerance of treatment. In general, adjuvant chemotherapy with curative intent should likely proceed, but shorter treatment duration should be considered wherever feasible. It is advisable to avoid bone marrow transplant procedures as far as possible. For patients receiving palliative therapy for metastatic disease, the decision to continue requires careful consideration of; indications, response and risk/benefits of continued treatment. Oral chemotherapy drugs or home infusion of chemotherapy drugs may be an option for some, but require coordination from the oncology team to ensure that patient is taking their treatment correctly. Lymphopenia seems to be a specific risk factor for adverse outcomes form COVID-19 and other coronaviruses hence critical re-evaluation of the need for drugs that inhibit B- cells,[23-27] such as anti-CD-20 monoclonal antibodies, during the pandemic.

SUPPORTIVE CARE

ASCO has not recommended prophylactic use on antiviral therapy for COVID-19. Blood transfusion in patients can be given as per usual practice guidelines. For patients who are febrile and likely to be neutropenic based on the timing of their cancer treatment, it is reasonable to start empirical antibiotics if the patient seems stable. Although myeloid growth support is typically administered for those at high risk of febrile neutropenia, it may be reasonable for patients with a lower level of expected risk at the present situation.

RECENT TRENDS AND EMERGING RESEARCH

Remdesivir- a nucleotide analogue prodrug that inhibits viral RNA polymerase, has been found effective in reducing time to recovery in hospitalized patients with COVID-19 in US.[28] similarly, Favipiravir (FabiFlu) is approved to treat mild to moderate COVID symptoms.[29] most recently, RECOVERY trialconducted by NHS in UK, showed that low-cost Dexamethasone reduced death from COVID-19 in one-third of the hospitalized patients,[30] with the highest benefit seen amongst those requiring assisted ventilation at admission. Based on the results, the NIH COVID-19 Treatment Guidelines Panel has recommended using dexamethasone (6 milligrams per day for up to 10 days) in patients of COVID-19 who are mechanically ventilated and/or require supplemental oxygen therapy.[31]

BBCI EXPERIENCE

Our institute is a regional cancer centre catering the cancer patients of the entire North East India. We used telemedicine extensively to reach out to our patients during the lockdown, Patients were educated about COVID 19 preparedness and appropriate advice was given to patients not on active treatment or on follow up and asymptomatic. However, newly registered patients, patients undergoing treatment and those with symptoms were attended and managed as per the protocols designed by COVID Task Force of our hospital. Prepared guidelines by the task force are based on international recommendations with suitable adaptations to meet regional needs. The directive of the Ministry of Health and Family Welfare, India on preventive measures to contain the spread of COVID-19 in hospitals was strictly followed during all stages of patient care in our hospital.[32]

Till now we have encountered 4 positive cases of COVID-19 among our patients and 1 among the health workers, yet our treatment services have continued without interruption as we adopt the norms of Personal Protection and Facility Sanitization strictly which eliminates the risk of spread of Coronavirus in the hospital.

CONCLUSION

Providing timely and optimum cancer-directed treatment during the times of Coronavirus pandemic has been a massive challenge to oncologists and cancer centres worldwide. Cancer patients with COVID-19 infection are at increased risk of morbidity and mortality. Although there are limitations in resources and challenges in delivering optimum healthcare, cancer patients should be evaluated on a case to case basis and treatment should not be delayed or denied. Priority must be given to cancer patients on active curative treatment and those at lower risk of developing morbidity and mortality from COVID-19.

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