

Case Report**Trick or Treat: Curative Management of Esophageal Squamous Cell Carcinoma of a COVID-positive Patient**Saqib Raza Khan^{1*}, Saad Nasir¹, Muhammad Nauman Zahir², Yasmin Abdul Rashid¹¹Aga Khan University Hospital²Dr Ziauddin Hospital

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Treatment**ABSTRACT**

The novel coronavirus pneumonia COVID-19 which is reportedly caused by SARS-CoV-2 infection can potentially lead to a course of clinical symptoms and fatal illnesses. Reported first in 2019, it has now affected more than 596,873,121 people, worldwide. In addition to its clinical manifestation in humans, the COVID-19 virus in cancer patients is significantly declining a positive prognosis. In the time of an ongoing global pandemic, oncologists are struggling to provide appropriate care to cancer patients due to their increased susceptibility to severe complications of COVID-19 which can be attributed to their immunosuppressed status caused by the malignancy and anticancer treatments. Similarly, the lack of literature, evidence, and consensus on whether to give antineoplastic agents to patients with active COVID-19 infection pose a unique challenge for physicians. In this article, we present a case of a 47-year-old female who was diagnosed with squamous cell carcinoma of the esophagus and later tested positive for SARS-CoV-2. Under unanimous decision, oncological treatment for the malignancy was initiated with a combination of chemotherapy and radiation without a consequential delay as per multidisciplinary tumor board (MDT) meeting decision which results in clinical improvement.

INTRODUCTION

Millions of people across the world have been subjected to the severity of the coronavirus disease (COVID-19) that first emerged in Wuhan, China 2019 [1]. Amidst the vast in-flow of people who have been targeted by this virus, one such unguarded population are those under adjuvant cancer treatment. [2, 3] COVID-19 has proven to deteriorate the health condition of immunocompromised people around us, however, it is much worse for the ones suffering from cancer or undergoing treatment, currently. The reason could be two-fold; a significant delay in the administration of cancer treatment regime until the patient recovers from COVID-19 or ongoing management of cancer coupled with COVID-19 treatment resulting in immunosuppression and a far more critical condition. What remains as a challenging entity is the scheduling of two treatment plans, whether the management for each condition should be conducted independently or simultaneously. This confusion is further complicated due to the minimal evidence on whether to deliver antineoplastic agents to cancer patients infected with active COVID-19 virus or to deal with one condition at a time since aggressive malignancies already manifest

as a unique challenge for the physicians [4]. A study from the United States signified a substantial amplification in 30 day-all-cause mortality in patients with uncontrolled malignancy and active COVID-19 [5]. The cohort study included a total of 105 COVID-19 patients with cancer. The mortality rate increased exponentially in patients undergoing immunotherapy while more than half of the patients developed critical illness [3]. Despite available data, a controversial debate persists each time the idea of antineoplastic regime administration is entertained. Hence, individualized patient-centric management seems to be the most viable option, but limited literature is available to strengthen the claim.

Keeping this discourse in mind, our article sheds light on a case of squamous cell carcinoma of esophagus in a 47-year-old woman who acquired SARS-CoV-2. Due to her consequential health condition, it was unanimously decided to treat her malignancy with targeted chemotherapy and radiation while avoiding any delay. This prompt approach resulted in appreciable clinical improvement of the patient, however she remained asymptomatic throughout her treatment period.

CASE PRESENTATION

A 47-year-old female presented to the outpatient department with active complaints of progressive dysphagia for the past four months. She has no significant smoking history, and her family history for her presenting complaint is insignificant. Apart from this, there is significant undocumented weight loss over the past few months. She remained asymptomatic with unremarkable findings on physical examination. Her Eastern Cooperative Oncology Group (ECOG) score was 1.

The patient initially presented to an otolaryngologist, who conducted a barium swallow test against her worsening dysphagia. The test displayed a peculiar segment of persistent mucosal irregularity coupled with deepened ulceration at the C5-C7 vertebral level targeting the proximal one third of the esophagus. For further investigation a computed tomography (CT) scan of the neck was performed exhibiting diffuse circumferential thickening of the post cricoid cervical alongside the upper thoracic esophagus with compromise of the lumen. Following the scrutiny and assessment, the patient underwent an esophagogastroduodenoscopy, revealing abnormal, irregular mucosal thickening integrated by profuse ulceration of the upper cervical esophagus. Subsequently, the biopsy of lesion confirmed moderately differentiated infiltrating keratinizing squamous cell carcinoma.

For further investigation and confirmation, a positron emission tomography-computed tomography (PET-CT) showed localized disease with no metastasis. Presence of hypermetabolic circumferential soft tissue thickening was highlighted which expanded over the cervical esophagus from C5 to T1 level, measuring 30 x 21 x 65mm, with volumetric maximum standardized uptake value (SUVmax) of 15.8 along with fluorodeoxyglucose (FDG) avid left supraclavicular lymph node, measuring 9.5 x 9.7 mm with SUVmax of 3.7 (Figure 1a,b).

Following the rigorous confirmation tests directed to investigate the pathology, radiation-oncology team was taken on board to further discuss the case exclusively in tumor board meetings. Keeping her condition in mind, she was planned for a concurrent chemoradiation therapy (CCRT) as per MDT recommendation.

A routine screening for polymerase chain reaction (PCR) test was carried out as per institutional protocol and she was tested positive for COVID-19 infection. Due to the ongoing debate of whether the administration of antineoplastic treatment was the appropriate approach in patients with COVID-19, her case was further re-discussed in the board now conjoined by the infectious diseases team. Analyzing her deteriorating condition, it was unanimously decided to continue the cancer treatment while the patient tested positive for COVID-19 infection.

A formal consent was drafted after a thorough discussion on risks and benefits associated with the treatment. Following a planned radiation PET-CT scan (Figure 2), patient was initiated on definitive concurrent chemoradiation therapy (CCRT) and received 5400 cGy dose over 27 fractions @ 200 cGy/fraction, five fractions per week on six megavoltages (MV) photon beam on varian (Truebeam) linear along with 5 cycles of concurrent weekly carboplatin AUC 02 and paclitaxel 50 mg/m². She was admitted to the COVID-19 care unit for the first two weekly chemotherapy cycles to ensure close monitoring in isolation during drug infusion and to promptly deal with any immediate adverse effects. She remained positive for COVID-19 by Polymerase Chain Reaction (PCR) for the following weeks after the first initiation of definitive CCRT but exhibited no symptoms and hence her treatment was continued as per protocol with close monitoring.

The patient responded to chemotherapy and radiation therapy with no significant adverse events noted during her therapy regime. Repeat COVID-19 PCR testing turned negative six weeks after her initial positive test result. She

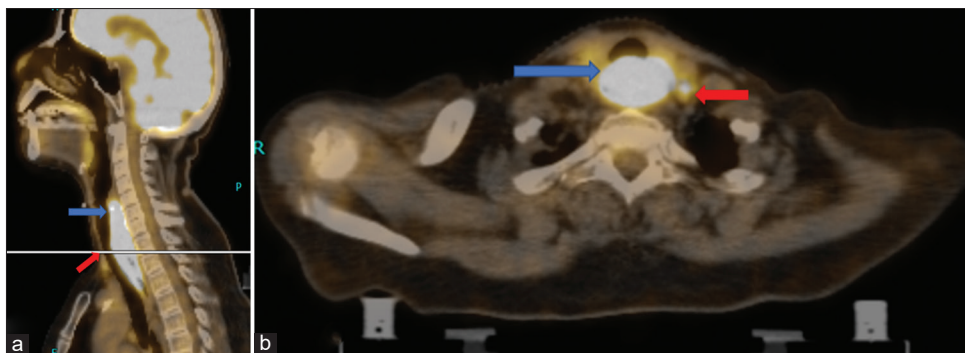


Figure 1. (a) Pre-chemo radiation PET/CT sagittal view showing hypermetabolic circumferential soft tissue thickening, involving the cervical esophagus from C5 to T1 level measuring 30 x 21 x 65mm with volumetric SUVmax of 15.8 (blue arrow) along with FDG avid left supraclavicular lymph node, measuring 9.5 x 9.7 mm with SUVmax of 3.7 (red arrow). (b) Pre-chemoradiation PET/CT axial view showing hypermetabolic circumferential soft tissue thickening, involving the cervical esophagus from C5 to T1 level measuring 30 x 21 x 65mm with volumetric SUVmax of 15.8 (blue arrow) along with FDG avid left supraclavicular lymph node, measuring 9.5 x 9.7 mm with SUVmax of 3.7 (red arrow)

experienced gradual resolution of her presenting symptoms after the completion of CCRT with a subsequent boost in her diet and weight. A follow-up comparative PET-CT scan performed three months after treatment completion, showed interval normalization of the previously seen hypermetabolic soft tissue thickening of the cervical esophagus and the hypermetabolic left supraclavicular lymph node as well (Figure 3a,b).

DISCUSSION

Cancer is one of the leading causes of death worldwide, and data estimates that around 10 million people will succumb to this disease in 2020 [6]. Since the start of the COVID-19 pandemic, there is a sense of ambiguity in the management of patients with cancer and simultaneous SARS-CoV-2 infection [3]. It has been reported that patients with cancer have an increased risk of severe infections, with an ~3.5-fold increase in the risk of needing mechanical ventilation or ICU admission or dying when compared with patients without cancer [7]. Another primary risk for patients during the COVID-19 pandemic is limited access to required health care and inability to receive necessary medical services in a timely fashion due to shortage and high demand of medical staff [8]. Although

the professional societies were quick to form initial guidelines, lack of evidence that supports continuation of these guidelines remains an area of interest. To date, there is a scarcity of a consensus for a strategic approach to treat patients who require aggressive therapy.

Numerous strategies have been suggested till date. According to the Italian Association of Medical Oncology (AIOM) and the French guidelines, an individualized management approach is necessary, based on patient characteristics and after duly assessing the risk versus benefit ratio [9, 10]. A study by Al-Shamsi suggests that in patients with a low risk of disease progression, a delay in adjuvant chemotherapy is likely to be the correct approach [11]. The latest NICE guidelines state better communication with patients, isolation of the hospital staff, modifications to usual guidelines and breaks during treatment as helpful tools in managing cancer patients [12]. Additionally, The European Society of Medical Oncology (ESMO) characterized patients with cancer and COVID-19, in three categories to judge the clinical benefits from the treatment. This includes those with life-threatening disease (high priority), those in which a few weeks' delay may not result in progression (moderate priority), and those in whom chemotherapy can be started once COVID-19 has resolved [9].

In this article, we describe the case of our patient, in whom the investigations revealed squamous cell carcinoma of the esophagus and she simultaneously tested positive for COVID-19. At that time, we faced a challenging situation on how to proceed with her management. In view of her rapidly progressive symptoms and her high priority ranking for treatment as per ESMO guidelines, therapy was initiated without undue delay. Our patient responded well to the given treatment protocol and remained asymptomatic for COVID-19 infection. The favorable outcome of our case further substantiates the ESMO recommendations of proceeding with antineoplastic therapy in high-risk patients with life-threatening malignancy especially if they have asymptomatic co-existent COVID-19 infection [9].

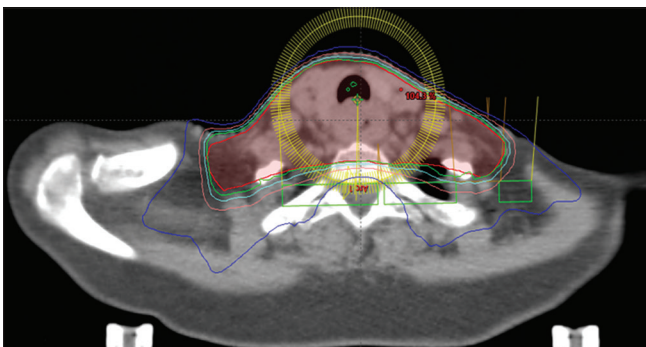


Figure 2. Radiation treatment planning Axial image, green color – 95% coverage of the PTV by 95% of radiation dose

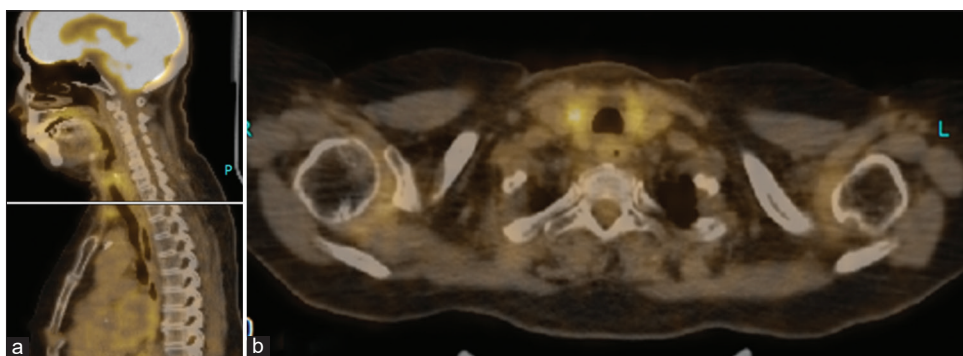


Figure 3. (a) Post-chemoradiation PET/CT Sagittal view interval complete normalization of previously seen hypermetabolic soft tissue thickening involving cervical esophagus. (b) Post-chemoradiation PET/CT Axial view interval complete normalization of previously seen hypermetabolic soft tissue thickening involving cervical esophagus as well as interval complete normalization of the hypermetabolic left supraclavicular lymph node

CONCLUSION

In this study, we have highlighted valuable evidence regarding the ongoing debate of whether the antineoplastic treatment administration is the right approach in a cancer patient with active COVID-19 infection. With our study, we have presented the benefits of immediate oncological treatment in immunocompromised cancer patients that cannot afford a delay in treatment with ongoing infection. A prompt judgment and unanimous planning by various board meetings led to the significantly positive patient outcomes. However, clinical correlation and a case-by-case approach need to be adopted to maximize treatment response and prevent progression to serious COVID-19 disease.

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