

# Surviving COVID-19 and multiple complications post total laryngectomy

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Accepted 13 July 2021

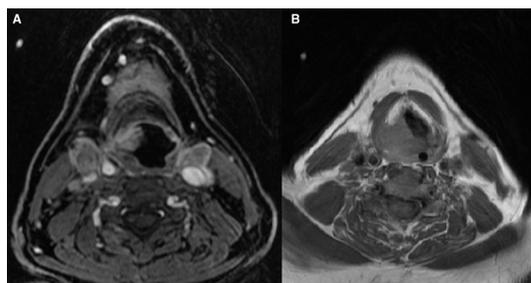
## SUMMARY

The clinical manifestation of novel COVID-19 is variable. Pre-existing carcinoma and other comorbidities have been associated with increased COVID-19-related morbidity and mortality. Surgical intervention for advanced laryngeal carcinoma in old age during the COVID-19 pandemic may pose multiple challenges to the patient and the treatment team. We report a case of a 67-year-old elderly man who developed SARS-CoV-2 infection on the 21st day following total laryngectomy and neck dissection. The postoperative period was complicated by sequential development of pulmonary embolism, neck infection, pharyngeal leak and COVID-19 which were managed successfully. No close contacts were positive on the reverse transcription-PCR test for SARS-CoV-2. The patient is in follow-up for the past 7 months without any recurrence or COVID-19-related morbidity. The successful recovery and no cross-infection may be attributed to early diagnosis, immediate intervention and properly implemented institutional infection control policy.

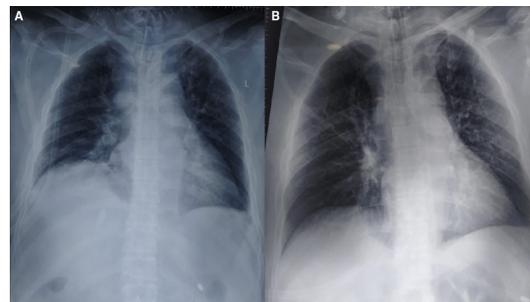
## BACKGROUND

COVID-19, first recognised in Wuhan, China, in December 2019, was determined by the WHO as a global pandemic.<sup>1</sup> It is associated with rapid progression to severe acute respiratory distress, leading to intensive care.<sup>2</sup> There are various risk factors like advanced age, comorbid conditions (heart, renal, liver and respiratory diseases), carcinoma, immune compression, smoking and pregnancy for acquiring severe COVID-19.<sup>3</sup>

Patients with carcinoma are in a state of immunosuppression, making them more susceptible to COVID-19-related complications and mortality.<sup>4</sup> Moreover, most of the patients with laryngeal carcinoma have a chronic obstructive pulmonary disease component, which probably may accelerate the impact of COVID-19 infection on the airway.



**Figure 1** Axial T1-weighted contrast images showing (A) bilateral cervical lymph nodes at level 2 and (B) right supraglottic growth invading thyroid cartilage.



**Figure 2** Chest X-ray images on (A) day 6 showing blunting of bilateral costophrenic angle suggestive of pleural effusion and (B) day 20 showing resolution of earlier findings.

In post total laryngectomy (TL), the alteration of airway physiology happens with the loss of nasal humidification and warming and mucociliary clearance, increasing the risk of severe respiratory disease.<sup>5</sup> Also, as patients with laryngeal carcinoma are primarily elderly, the risk of acquiring a severe form of COVID-19 increases because comorbidities and ACE2 expression (increased expression associated with worse prognosis) increase with age.<sup>6</sup> As per evidence, the risk of developing severe clinical events was higher in patients with cancer who concomitantly contracted COVID-19 after surgery.<sup>7</sup>

We report a successful recovery from COVID-19 in a case of a 67-year-old man who developed the infection, pulmonary embolism (PE), neck infection, and pharyngeal leak after undergoing TL and bilateral modified radical neck dissection (MRND) for stage IV supraglottic carcinoma.

## CASE PRESENTATION

### Preoperative

A 67-year-old male patient with difficulty swallowing for 1 month was diagnosed with moderately differentiated squamous cell carcinoma of the supraglottis, staged T4aN2cM0 based on radiology (figure 1).

The patient had no history of substance abuse, contact with SARS-CoV-2-positive patient or any chronic illness. At admission, examination revealed body temperature of 98.6°F, blood pressure of 124/86 mm Hg, heart rate of 82 beats/min and respiratory rate of 16/min. The patient was anaemic with a haemoglobin of 11.2g/dL. Other haematological parameters, chest X-ray findings and ECG findings were within normal limits. As per our institutional protocol to rule out false negativity for elective surgeries, the patient underwent testing of reverse transcription (RT)-PCR for SARS-CoV-2 twice before



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**To cite:** Singh A, Bhardwaj A, Ravichandran N, *et al.* *BMJ Case Rep* 2021;**14**:e244277. doi:10.1136/bcr-2021-244277

surgery: the first 72 hours before surgery and the second 24 hours before surgery. Both test results were negative.

### Operative details

The patient underwent TL with partial pharyngectomy, bilateral MRND type V and pharyngeal reconstruction. The intraoperative period was uneventful. Postoperatively, the patient was kept on Ryle's tube feed and started on broad-spectrum antibiotics, anti-inflammatory drugs, oral calcium and thyroxine supplementation. For a description of events, the day of surgery has been considered as day 1.

### Development of PE

On day 6, the patient's oxygen saturation ( $SpO_2$ ) at room air dipped below 90%, and he was started on supplemental oxygen of 6 L/min. Chest X-ray (figure 2) revealed the possibility of pleural effusion, which was confirmed on ultrasound, revealing less than 10 mL collection on both sides; diagnostic pleural tap did neither reveal any malignant cell nor any microbe. As pleural effusion persisted until day 9, CT angiography was done, revealing embolus in the right main and left inferior pulmonary artery. Echocardiography was normal. The patient was started on injectable low-molecular-weight heparin (LMWH) 60 mg per day and oral ecosprin 75 mg per day on day 9. Oral ecosprin is continuing; LMWH continued until the day of discharge and was replaced with oral rivaroxaban 5 mg, which continued for 1 month.

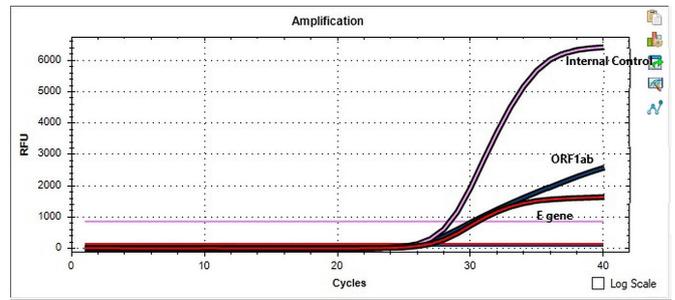
### Development of neck infection and pharyngeal leak

The patient developed gaping with slight blackening of neck incision wound on day 6, with the progression of neck flap necrosis consecutively and development of pharyngeal leak on day 10. Aseptic dressing of neck wound was done two times per day by residents in partial personal protective equipment (N95 mask, surgical gown and eye-protective goggles); healthy granulations developed on day 19 (figure 3).

### Intensive care unit stay and the first episode of fever

As  $SpO_2$  dipped to 80% with 8 L/min of oxygen on day 12, the patient was shifted to the intensive care ward. He was kept on synchronised intermittent mandatory ventilation for 36 hours, after which he was shifted back to the ward as his  $SpO_2$  improved to 95% at room air.

On day 13, he developed fever that persisted for 2 days with a temperature ranging between 99°F and 101°F. Nasal, oropharyngeal and tracheal swabs were sent for SARS-CoV-2 testing, and reported as negative on day 15.



**Figure 4** RT-PCR graph showing amplification in the target genes (E/ORF1ab) with Ct values 27/28. Ct, cycle threshold; RFU, relative fluorescence unit; RT-PCR, reverse transcription-PCR.

### Diagnosed positive for SARS-CoV-2 infection

On day 20, the patient was stable with  $SpO_2$  more than 96% on room air and healthy granulation in the neck wound bed. He was planned for flap reconstruction of the neck wound; hence as per the institutional protocol of a requirement of a negative report for SARS-CoV-2 infection before elective surgery, nasal, oropharyngeal and tracheal swabs were sent for RT-PCR. He was reported positive for the infection on day 21 with cycle threshold values 27/28 (targets—E/ORF1ab), suggesting a high viral load (figure 4). Blood examination showed monocytosis with neutrophilia and lymphopenia. Direct bilirubin and liver enzymes (serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and alkaline phosphatase) were increased. The patient was shifted to the COVID-19 isolation ward. During the period of isolation, there was no episode of fever, respiratory difficulty or oxygen desaturation below 90%. He was started on budesonide (1 mg) nebulisation 12 hourly. His oxygen saturation at room air fluctuated between 91% and 94%, and he was kept on high-flow oxygen (8–10 L/min), which maintained  $SpO_2$  more than 96%. No anti-viral drug or systemic steroid was given to the patient.

All close contacts were screened for SARS-CoV-2 infection by RT-PCR and were negative. On day 26, a repeat nasopharyngeal swab of the patient was sent, which was reported as negative. Blood reports were normal (table 1).

### Flap reconstruction and follow-up

The patient underwent primary closure of pharyngeal leak and reconstruction of neck wound using deltopectoral flap on day 28, which were successful.



**Figure 3** Images showing (A) healthy granulation tissue in neck with a pharyngeal leak; (B) deltopectoral flap and split skin graft reconstruction of neck wound; (C) well-healed neck wound and donor left deltopectoral region after 2 months of reconstruction.

**Table 1** Comparison of laboratory parameters of the patient during illness and after recovery from COVID-19

Lab parameters	During COVID-19	After recovery from COVID-19
Total bilirubin (mg/dL)	1.04	0.78
Direct bilirubin (mg/dL)	0.37	0.18
SGPT (U/mL)	126	23
SGOT (U/mL)	61	25
ALP (U/L)	59	43
S. total protein (g/dL)	4.49	4.2
S. albumin (g/dL)	2.04	2.27
S. globulin (g/dL)	2.45	1.93
A:G ratio	0.83	1.18
Monocytes (%)	11.50	3.90
Lymphocytes (%)	19.70	12.30
Neutrophils (%)	65.20	81.30
WBCs (cells/L)	$2.8 \times 10^9$	$5.7 \times 10^9$
CRP (mg/L)	11.50	5.01

A:G ratio, albumin to globulin ratio; ALP, alkaline phosphatase; CRP, C reactive protein; WBCs, white blood cells.

## INVESTIGATIONS

Investigations have been mentioned as part of case presentation to maintain the continuity of case description, which authors felt essential.

## TREATMENT

Treatment has been mentioned as part of case presentation to maintain the continuity of case description, which authors felt essential.

## OUTCOME AND FOLLOW-UP

The patient was stable, recovered well and discharged on day 43. The patient completed 33 cycles (66 Gy) of external beam radiotherapy, with a post-therapy scan showing no residual or recurrent disease. The patient has completed 7 months of follow-up and has no surgery or COVID-19-related complication.

## DISCUSSION

As per the literature search done on PubMed and Google Scholar with keywords “carcinoma larynx,” “laryngectomy,” “SARS-CoV-2,” and “COVID-19”, on 20 April 2021, this is the second case report of a successful recovery in a patient with laryngeal cancer developing SARS-CoV-2 infection in the postoperative period after TL. In the case series by Ricciardiello *et al*, one case of SARS-CoV-2 infection following TL has been mentioned.<sup>8</sup> Our case developed multiple complications, including PE, and is the first report in this regard.

The study by Wu *et al* reveals that 2%–11% of patients with COVID-19 had liver comorbidities, and 14%–53% of cases had abnormal alanine aminotransferase and aspartate aminotransferase levels during the progression of COVID-19 disease.<sup>9</sup> In mild cases of COVID-19, there is liver damage and patients can return to normal without any special treatment.<sup>7</sup> In the study by Mardani *et al*, white blood cell and lymphocyte counts were low, but the neutrophil count was higher in patients with positive RT-PCR for SARS-CoV-2 infection.<sup>10</sup> Laboratory studies showed leucopenia with leucocyte counts of  $2.91 \times 10^9/L$ , 70.0% of neutrophil (NEU).<sup>11</sup> Their result suggested that there may not be an effect on neutrophils by SARS-CoV-2 in the early course of the disease. It also suggests that SARS-CoV-2 might mainly affect lymphocytes, especially T lymphocytes. In our case, similar findings of raised levels of bilirubin, liver enzymes, neutrophil percentage and

leucopenia were seen, which returned to normal levels on recovery (table 1).

Cancer is considered a risk factor for complications related to COVID-19 infection.<sup>7</sup> In these patients, there is a higher risk of contracting the infection. They suffer from more severe disease course and increased risk of death, with a more significant proportion of such patients requiring higher levels of intensive care.<sup>12</sup> In this context, it is essential to understand the factors that influence the outcome in patients with cancer.

Immunosuppression in cancer plays a vital role in the response and clinical outcomes of SARS-CoV-2 infection, although there is an unclear prognostic value. Immunosuppression could be a poor prognostic factor that may allow higher viral loads and increase secondary infection risk.<sup>13</sup> Nutritional deterioration in patients with cancer leads to anaemia and hypoproteinaemia, which increases the susceptibility to respiratory pathogens as immunocompetence is affected.<sup>14</sup> There is a higher risk of developing COVID-19-related severe clinical events in patients with cancer undergoing surgery.<sup>7</sup> In our case, there was a state of prolonged immunosuppression, both cancer related and treatment induced. The patient was anaemic, for which he underwent multiple blood transfusions.

Patients with cancer, being common in the older age group, have more adverse outcomes of COVID-19 as ACE2 expression and comorbidities increase with age.<sup>6</sup> SARS-CoV-2 acquired by respiratory aerosols binds to ACE2 receptors in the nasal epithelial

## Patient's perspective

The cancer diagnosis in my voice box was a shock to me as I had never consumed alcohol or tobacco, and there was no family history of the same. It took me almost two weeks to prepare myself for the surgery after doctors counseled me. I was also afraid because of the deaths happening due to COVID-19. It was a difficult decision for me and my family members, who have been supportive throughout. The development of complications after surgery worried my family members and me a lot, and it was a difficult time, but I was happy to get care from the team of doctors. When I was recovering from complications, being diagnosed with COVID-19 came as a shock for me. Remaining in the isolation ward was no less than a trauma as I could not meet my relatives, but daily counseling by my doctors who came dressed in PPE helped me. I was lucky to get out soon of the COVID-19 isolation ward to undergo a second surgery which healed my wound. After discharge, I followed all instructions in a disciplined way and completed my radiotherapy. After more than 7 months of surgery, I feel a bit relieved as I have not been diagnosed with any recurrence whose possibility was told to me initially. I would like to thank my doctors, healthcare staff, relatives, and God for rescuing my life.

## Learning points

- ▶ Development of pulmonary embolism, neck infection, pharyngeal leak followed by COVID-19 after total laryngectomy has not yet been described.
- ▶ Total laryngectomy with complications does not mandate a poor outcome for COVID-19.
- ▶ Anticoagulant therapy, though started for pulmonary embolism, may be the reason for the mild manifestation of COVID-19.

cells in the upper respiratory tract and further invades the type 2 alveolar cells via ACE2 receptors.<sup>15 16</sup> As age increases, ACE2 expression increases and increases the risk of COVID-19 manifestation.<sup>6</sup> In our case, age being 67 years, increased the risk of adverse outcomes. Though the patient did not have preoperative comorbidities other than cancer; but at the time of being detected SARS-CoV-2 infection positive, the patient had already developed PE and neck infection, which again increased the risk of an adverse outcome.

There is an increased risk of lower respiratory tract infection in patients of TL.<sup>17 18</sup> Permanent separation of the upper and lower airway resulting in loss of nasal physiological functions of filtration, humidification and temperature alteration of inhaled air leads to increased risk. Though there are no studies yet on SARS-CoV-2 infection in laryngectomised patients, authors hypothesise an increased risk of the infection due to altered physiology. The study by Paderno *et al* mentions two cases (one survival and one demise) that developed SARS-CoV-2 infection more than 5 years after undergoing TL.<sup>19</sup> High-flow oxygen therapy in such patients increases the risk of airway crusting, which may require repeated tracheal toilets. In our case, high-flow oxygen therapy was required to keep oxygen saturation more than 90%; pre-emptive saline nebulisation and frequent tracheal toilet helped avoid tracheo-bronchial crusting. COVID-19 can lead to coagulopathy, which has a prothrombotic character with a high risk of venous thromboembolism.<sup>20</sup> In our case, LMWH and ecosprin were started for PE 12 days before being diagnosed as positive for SARS-CoV-2 infection; use of anticoagulants may be the reason behind mild COVID-19 in our case and the non-development of COVID-19-induced coagulopathy which could have worsened PE. LMWH has been reported to have beneficial effects (other than anticoagulant effect) in COVID-19, such as reducing inflammation, neutralisation of cytokines and chemokines, and partial attenuation of the cytokine storm. In the study by Shi *et al*, there were significant changes in interleukin 6 level, D-dimer and fibrinogen degradation products in the group of patients who received LMWH as compared with the group who did not receive it.<sup>21 22</sup> In our case, though the patient developed multiple complications other than SARS-CoV-2 infection in the postoperative period, he could be managed successfully because of early recognition and timely intervention. The role of early intervention to reduce COVID-19-related complications has been emphasised in recent studies.<sup>23 24</sup> No close contacts were infected from our case; the reason could be following stringent infection control policies and standard precautions. This case underlines the importance of research to better understand SARS-CoV-2 infection in patients with laryngeal cancer.

**Acknowledgements** We want to thank Dr Amit Kumar Tyagi (Assistant Professor, Department of Otorhinolaryngology, All India Institute of Medical Sciences, Rishikesh, India), Dr Madhubari Vathulya (Associate Professor, Department of Plastic Surgery, All India Institute of Medical Sciences, Rishikesh, India) and Dr Mayank Mishra (Associate Professor, Department of Pulmonary Medicine, All India Institute of Medical Sciences, Rishikesh, India) for their role and support in the clinical management of the patient.

**Contributors** AS and AB have contributed to manuscript writing, conception and idea for the manuscript. NR has contributed to data collection. MM has contributed to critical review and supervision of the manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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