



## Sampling site matters when testing for COVID-19 after total laryngectomy: a case report

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Patients after total laryngectomy are special in many respects, including the management in the current pandemic of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Here, we report the case of a patient who had undergone total laryngectomy due to laryngeal carcinoma with discordant SARS-CoV-2 test results performed in nasopharyngeal and tracheal samples.

A 63-year-old male patient presented at the emergency department with loss of appetite for 1 week, progressive unproductive cough as well as abdominal discomfort and myalgia. He had undergone total laryngectomy with bilateral neck dissection 2.5 years before due to laryngeal squamous cell carcinoma, currently in complete remission. At presentation, the patient had normal body temperature, oxygen saturation was 92% while breathing ambient air and heart rate was 118 bpm. Laboratory work-up revealed mild lymphocytopenia ( $0.8 \times 10^9/l$ ), D-dimer elevation (0.92 mg/l) and increased inflammatory parameters of C-reactive protein (34.1 mg/l), ferritin (749 ng/ml) and interleukin-6 (23.7 pg/ml). At the time of presentation, in the local district the 7-day incidence of SARS-CoV-2 infection was 169/100,000.

The initial routine screening for SARS-CoV-2 by using an antigen test from a nasopharyngeal swab yielded a negative result. Due to symptoms suggestive of COVID-19, nasopharyngeal sampling was repeated and polymerase chain reaction (PCR) for SARS-CoV-2 by using the Xpert Xpress SARS-CoV-2 test (Cepheid, Sunnyvale, CA, USA) was performed, which also turned out negative. In computed tomography (CT) pulmonary angiography pulmonary embolism was excluded but features suggestive of COVID-19 pneumonia were found ([1]; Fig. 1a, b). This prompted repeated sampling, approximately 4h after the initial nasopharyngeal swab, now obtaining tracheal secretions via the tracheostomy tube. This time the SARS-CoV-2 PCR turned out positive (cycle threshold values of the E and N2 gene targets: Ct-E: 25, Ct-N2: 27). The patient was admitted to the designated COVID-19 ward and was discharged home after 4 days.

The case illustrates the unique situation of patients who had undergone total laryngectomy in cases of viral respiratory tract infections. After total laryngectomy, in the absence of a tracheopharyngeal fistula, the upper and lower respiratory tract are anatomically separated (Fig. 1c). While the lungs are directly exposed to airborne pathogens, the upper respiratory tract is practically excluded from airflow and hardly comes into contact with aerosols; however, it may be contaminated via smear infection. Therefore, it has been recommended to obtain both nasopharyngeal and tracheal samples for the diagnostic work-up of suspected COVID-19 in these patients [2].

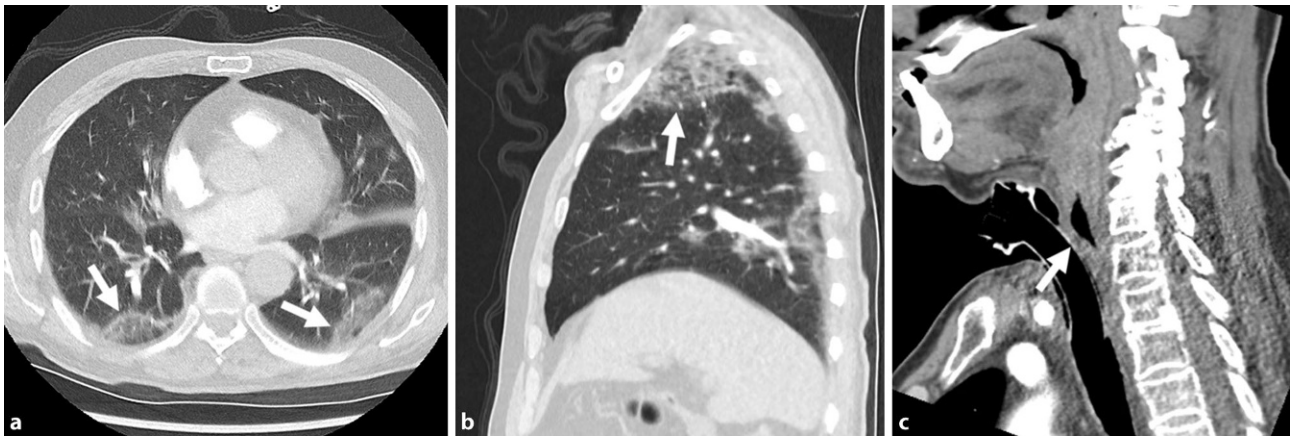
In our case SARS-CoV-2 RNA was detected only in tracheal secretions, a hint that the primary site of infection likely was the lower respiratory tract after a transmission via aerosols/droplets. This may potentially be followed by later infection of the upper respiratory tract via autoinoculation or systemic infec-

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**Fig. 1** Chest computed tomography, axial (a) and sagittal (b) reconstructions: subpleural ground glass opacifications in both lower lobes (arrows in a), reticular pattern ground glass opacification in the apical segment of the right upper lobe (ar-

row in b). Neck computed tomography (c) 2 years earlier: the complete anatomical separation of the trachea (with tracheostomy tube) and pharynx after total laryngectomy can be appreciated (arrow)

tion. In contrast to our case, the few previous reports of simultaneous nasopharyngeal and tracheal sampling in total laryngectomy presented cases with either positive results at both sites [3], or negative result of the tracheal and positive result of the nasopharyngeal swab [4]. The latter finding may indicate a path of infection other than via aerosols, potentially contact infection.

When interpreting SARS-CoV-2 test results, the possibility of a false negative result must be considered. Among other factors, this is critically dependent on the sampling procedure [5]. Yet, our swabs were obtained technically correct by a well-trained nurse.

Importantly, the specific anatomy and resulting differences in the transmission and course of infection in patients with total laryngectomy are often not readily appreciated by treating physicians who are not routinely involved in the care of otolaryngology patients. Thus, a COVID-19 diagnosis may have been missed or delayed by following standard procedures, i.e. upper respiratory tract swabs. Such deferral in diagnosis and inappropriate precautions (masking only the patient's mouth and nose), pose a substantial risk of further spread of the disease by these patients in healthcare facilities.

In conclusion, the presented case of an isolated primary infection of the lower respiratory tract in a patient with total laryngectomy indicates the differential distribution patterns of airway infections in these patients and highlights the importance of both upper and lower respiratory tract sampling to detect a SARS-CoV-2 infection.

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#### Compliance with ethical guidelines

**Conflict of interest** J. Schmid, J. Prattes, A.-K. Kaufmann-Bühler and J.M. Riedl declare that they have no competing interests.

**Ethical standards** This report was approved by the ethics committee of the Medical University of Graz (Nr. 33-162ex20/21). Informed consent was obtained from the patient.

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