Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Corticobulbar tract involvement following COVID-19 infection: Evidence from MRI-tractography and transcranial magnetic stimulation

Recently, several cases of dysphagia as sequelae of coronavirus disease 2019 (COVID-19) have been reported, but the direct mechanisms leading to swallowing impairment have not been elucidated, though possible involvement of cranial nerves (CN) has been proposed (Todisco et al., 2021). Also, appropriate treatment options for post-COVID dysphasia have not been clearly suggested. This case shows direct corticobulbar tract (CBT) involvement in a post-COVID-19 patient with severe sequalae of dysphagia confirmed via electrodiagnostic assessment and diffusion tensor imaging (DTI). In addition, the patient showed a positive response after prednisolone therapy. Written informed consent was obtained for this report.

The subject of this case report is a 52-year-old male who developed acute respiratory failure and dysphagia after the COVID-19 infection. After continuous renal replacement therapy and a tracheotomy tube placement, complete ventilation weaning was reached. The patient showed good medical recovery. However, at five months, severe persistent dysphagia remained despite several months of conservative dysphagia rehabilitation.

Upon admission to our department at five months post-onset, the patient showed a severe degree of dysphagia with dysphonia and was still on a tracheostomy tube with total tube feeding. Physical examination showed impaired tongue protrusion with left side deviation (Fig. 1). Gag reflexes and sense of taste were impaired. A videofluoroscopic swallowing study (VFSS) showed large amount of aspiration during liquid and thickened liquid swallowing, impaired epiglottic closure and incomplete airway closure (Fig. 1). Fiberoptic endoscopic evaluation of swallowing (FEES) test revealed saliva pooling around laryngeal vestibules resulting in secretion aspiration and demonstrated limited bilateral arytenoids and vocal folds motion and decreased velopharyngeal port motion on the left side (Fig. 1).

The patient's prior brain MRI and angiography excluded any structural or vascular etiology. DTI were acquired upon admission, and CBT was visualized following the same techniques reported by a previous report (Im et al., 2020). Probabilistic tractography showed poor visualization of the right CBT and decreased tract volume on the left side (4.02 cm^3) (Fig. 1). Nerve conduction studies including on the tibial, sural, facial nerves, and needle electromyography of the tongue, trapezius, gluteus, iliopsoas muscles did not show any abnormal values or denervation potentials. Transcranial magnetic stimulation-evoked motor responses were recorded in pharynx via a pair of bipolar ring electrodes built in a swallowed intra-lumen catheter (Fig. 1). The TMS coil was then placed 4–6 cm laterally and 3–5 cm anteriorly of the vertex and a hot spot search was performed in this area to get the largest motor evoked potentials (MEPs) from stimulation of the pharyngeal cortical area of either hemisphere. Resting motor threshold (RMT) was defined as the minimum stimulation intensity which resulted in MEPs of at least 20 μV in 50% of the trials (Mistry et al., 2012). RMT of the right cortex was 48% and RMT of the left cortex was 33% of maximum stimulator output, with the right pharyngeal cortex showing poorer cortical excitability than the left side.

Complete blood cell count, sedimentation rate, and C-reactive protein were unremarkable in laboratory tests. Serum tests for autoimmune diseases, vasculopathy and antiganglioside antibodies were all negative. Given the decreased velopharyngeal port motion in left side, impaired gag reflex, limited bilateral vocal folds motion and left tongue deviation, we hypothesized asymmetric bulbar muscle weakness due to bilateral but predominantly right CBT alteration leading to dysfunction of the CN V3, CN X, and CN XII. A tentative diagnosis of CBT involvement related to COVID-19 was made and oral prednisolone therapy of 50 mg/d was administered for two weeks.

Four weeks after steroid therapy, FEES showed improvement in bilateral arytenoids and vocal folds motion with reduced pharyngeal secretions in the hypopharynx (Fig. 1). Improvement of swallowing was further confirmed through VFSS. Oral feeding was slowly commenced, and both nasogastric and tracheostomy tubes were removed successfully. A follow-up of tractography at four weeks showed improvement of both CBT with increased tract volume (5.69/9.28 cm^3), which was in accordance with the improvement in MEP. Pharyngeal cortical representation improved with RMT values of 23% for the right-hemispheric pharyngeal cortex and 13% for the left-hemispheric one.

This case is the first to report direct CBT involvement in a patient with COVID-related dysphagia. CBT shows bilateral projections (Rogić Vidaković et al., 2015) and innervates the motor neurons of the cranial nerves. In this case, bilateral but predominantly right-sided CBT alteration may have caused multiple asym-

Abbreviations: COVID-19, coronavirus disease 2019
VFSS, Video Fluoroscopic Swallowing Study
FEES, Fiberoptic Endoscopic Evaluation of Swallowing
DTI, Diffusion Tensor Imaging
CBT, Corticobulbar tract
MEP, Motor-evoked potential
RMT, Resting motor threshold
CN, cranial nerve

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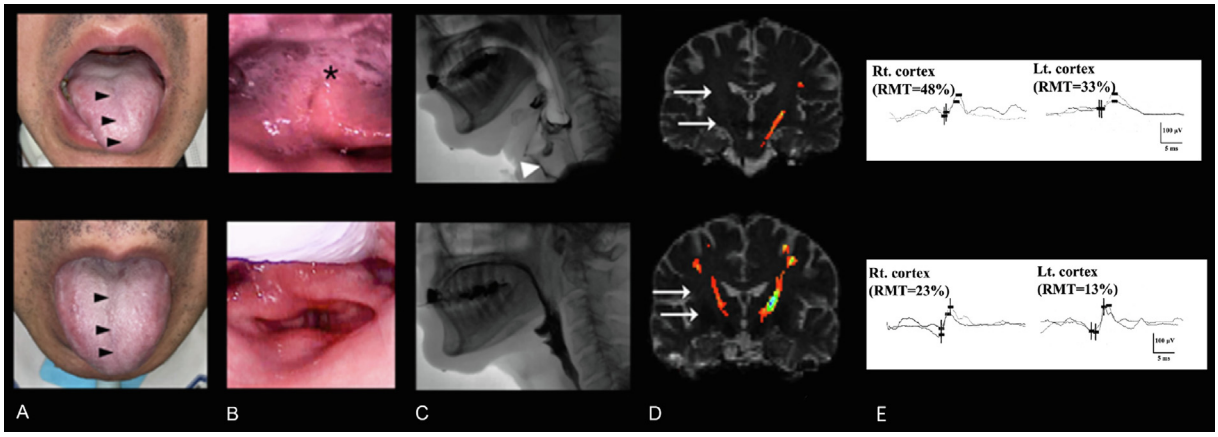

Fig. 1. The upper panels and lower represent the clinical photos taken upon our initial evaluation; post five months after COVID-19 dysphagia onset; and those taken at follow-up after steroid pulse therapy; respectively. **(A)** At initial presentation the patient showed impaired tongue protrusion with deviation to the left side (back arrowhead) and improved tongue protrusion after treatment. **(B)** Initial FEES findings show poor vocal cord mobility with severe saliva pooling around the laryngeal vestibules (asterisks); post-treatment showed improved saliva swallowing and no secretion aspiration. **(C)** VFSS showed large amount of aspiration (white arrowhead) during liquid barium swallowing, post-treatment showed improved airway closure during swallowing. **(D)** Tractography of the corticobulbar tract shows poor visualization of the right-side tract (white arrow) with decreased volume of the left side, but improved visualization and tract volume after therapy. **(E)** Waveforms from motor evoked potentials recorded via swallowed intra-lumen catheter with transcranial magnetic stimulation of the pharyngeal cortices show poor RMT (high values indicating poor pharyngeal representation) at initial presentation with improved RMT post-treatment. COVID-19, coronavirus disease 2019; FEES, fiberoptic endoscopic evaluation of swallowing; VFSS, video fluoroscopic swallowing study; RMT, resting motor threshold.

metric cranial nerve dysfunction. An interesting aspect was that clinical improvement after steroid pulse therapy, which was in line with an increase of bilateral CBT volume and MEP responses.

This report supports the use of corticosteroids in severe dysphagia related to COVID-19. Corticosteroids have been reported to decrease mortality in COVID-19 patients in severe acute respiratory syndrome who were receiving mechanical ventilation or oxygen therapy (Group et al., 2021). Our case supports the use of steroids in COVID-19 patients to improve their swallowing function and quality of life even at the acute disease stage.

Some inherent limitations of tractography should be considered, especially with CBT visualization. However, improvement of tract volume was in accordance with the changes observed in both clinical and electrophysiological parameters. According to our case report, in clinical cases where existing imaging modalities or electrophysiological studies fail to explain unresolved COVID-19 related dysphagia, CBT evaluation via tractography and electrophysiological MEP recording may be useful diagnostic options.

Severe dysphagia and aspiration of secretions can lead to severe respiratory complications. The direct mechanism of how COVID-19 neurological sequelae manifest as dysphagia is a topic that requires more studies but based on our results, probabilistic CBT tractography and MEP recordings may help to determine the extent and etiology of refractory post-COVID-19 dysphagia. In such cases, prednisolone in conjunction with intensive dysphagia therapy can be effective when other, in particular infectious causes are excluded.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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