Diaphragmatic paralysis post COVID-19 treated with robot-assisted plication reinforced with acellular dermal matrix: a report of two cases

Patrick Hurley*, Adam Djouani*, Savvas Lampridis, Andrea Billè

Department of Thoracic Surgery, Guy's and St Thomas' NHS Foundation Trust, London, UK
*These authors contributed equally to this work.

Abstract

Coronavirus disease 2019 (COVID-19) continues to be a disease of global importance, with an increasing array of sequelae attributed to infection by the severe acute respiratory syndrome coronavirus-2. One such complication that has been rarely documented thus far is diaphragmatic dysfunction. Here, we report the cases of 2 individuals who developed diaphragmatic paralysis post COVID-19, which failed to respond to conservative management. Both patients proceeded to undergo robot-assisted thoracoscopic plication of the diaphragm reinforced with a bovine acellular dermal matrix. In both cases, there was significant improvement in symptomatology, namely dyspnoea and fatigue. We conclude that robot-assisted diaphragmatic plication should be considered for the treatment of refractory diaphragmatic paralysis post COVID-19.

Correspondence: Patrick Hurley, Department of Thoracic Surgery, Guy's Hospital, Great Maze Pond, London, SE1 9RT, UK.
Tel. +44.20.71887188.
E-mail: patrick.hurley@gstt.nhs.uk

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Introduction

Coronavirus disease 2019 (COVID-19) has been associated with structural and functional alterations of the diaphragm in a small number of cases [1-3]. As the number of critically ill patients who recover from COVID-19 increases, more cases of diaphragmatic pathology are expected to emerge. This long-term sequela of the disease can clinically manifest with dyspnoea and fatiguability, thereby contributing to the substantial burden of chronic disability caused by COVID-19. Due to the scarcity of cases, management strategies for diaphragmatic dysfunction post COVID-19 have not yet been formulated. Herein, we present the cases of 2 patients who developed unilateral diaphragmatic paralysis post COVID-19 and were treated with robotic-assisted diaphragmatic plication reinforced with acellular dermal matrix.

Case Reports

Case #1

A 52-year-old Caucasian man presented with wheeze and breathlessness (grade 4 on the Medical Research Council dyspnoea scale). Fifteen months prior, he had been admitted to the intensive care unit with severe COVID-19 requiring mechanical ventilation via endotracheal intubation and subsequently a tracheostomy. He was an ex-smoker who had stopped smoking 12 years ago, having accumulated a 15-pack-year history. His medical history also included atrial fibrillation and hypertension. Auscultation revealed absent breath sounds on the left lower chest, and peripheral capillary oxygen saturation was measured at 96% on ambient air. Serial thoracic computed tomography (CT) scans demonstrated chronic bilateral fibrotic lung changes, as well as new onset of raised left hemidiaphragm (Figure 1A). He underwent pulmonary function tests the day before his operation, which showed a forced expiratory volume in 1 second (FEV1) of 51% of predicted, forced vital capacity (FVC) of 55% of predicted and diffusing capacity of the lungs for carbon monoxide (DLCO) of 56% of predicted. An echocardiogram showed preserved left ventricular function, with an estimated ejection fraction of 55-60%. Subsequent sniff testing with chest fluoroscopy and phrenic-nerve conduction studies confirmed paralysis of the left hemidiaphragm. Considering the chronicity and severity of symptoms, the patient was offered surgical management, for which he provided informed consent. He underwent robot-assisted thoracoscopic plication of the left hemidiaphragm reinforced with a bovine acellular dermal matrix (SurgiMend, Integra LifeSciences, Princeton, NJ, USA). The chest drain was successfully removed on day 3 and the patient was discharged home on day 7 post surgery. Four weeks after he was discharged, the patient was followed up with a new chest radiograph that showed an improved position of the left hemidiaphragm (Figure 1B). He reported feeling less fatigue and significantly reduced shortness of breath, especially when lying flat. He underwent repeat pulmonary function tests 8 weeks after his operation, which showed an FEV1 of 64% of predicted, FVC of 73% of predicted and TLCO of 66% of predicted

Case #2

A 39-year-old South-East Asian female presented with a history of severe shortness of breath (grade 3 on the Medical Research Council dyspnoea scale) after a mild infection with COVID-19, for which she did not require hospitalisation. She also reported intermittent episodes of chest pain; however, an invasive coronary angiogram demonstrated no abnormalities. Her medical history also included asthma. She was a social smoker in her teenage years. She stopped smoking 17 years ago, having accumulated a 1.5 pack-year history. Chest radiography following her COVID-19 demonstrated a newly elevated right hemidiaphragm (Figure 2A). The finding was confirmed on a subsequent chest CT, and a diagnosis of diaphragmatic paralysis was made following sniff testing with ultrasonography and electromyography of the diaphragm. Pulmonary function test prior to her operation showed an FEV1 of 96% of predicted, FVC of 93% of predicted, and TLCO of 95% of predicted. An echocardiogram revealed good left ventricular function, with an ejection fraction of 60%, and normal pulmonary arterial pressures. After discussing management options, the patient provided informed consent for surgical management because of the severity and persistence of her respiratory symptoms. She underwent robot-assisted thoracoscopic plication of the right hemidiaphragm reinforced with SurgiMend 7 months after diagnosis. The chest drain was removed on the second postoperative day. By day 5 post-surgery, the patient had developed a small right sided pleural effusion, which was successfully drained under ultrasound guidance. She was discharged 4 days later. Her follow-up review took place in 4 weeks, when the patient reported a

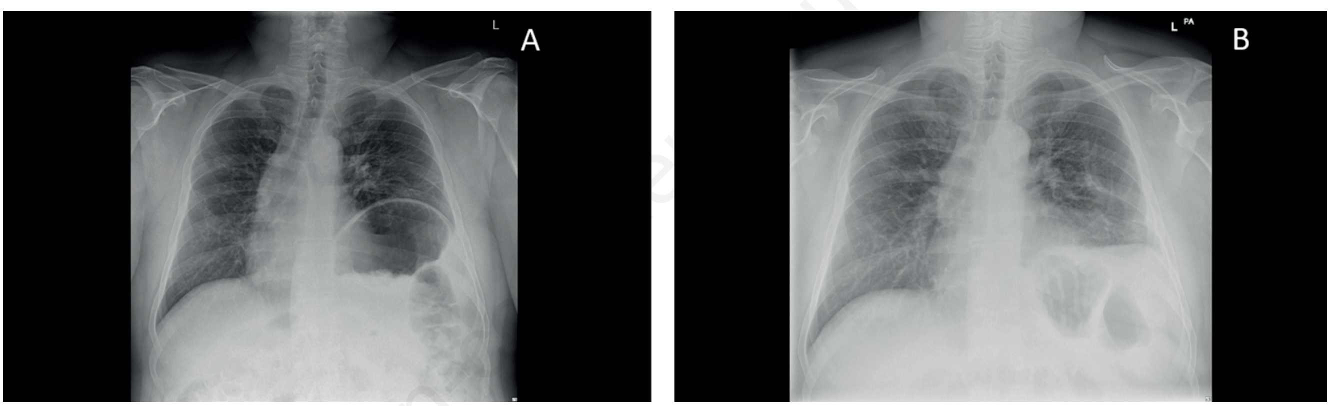

Figure 1. A) Chest radiograph of a 52-year-old man showing elevation of the left hemidiaphragm post COVID-19. B) Chest radiograph of the same patient following robotic-assisted surgical plication showing improved position of the left hemidiaphragm.

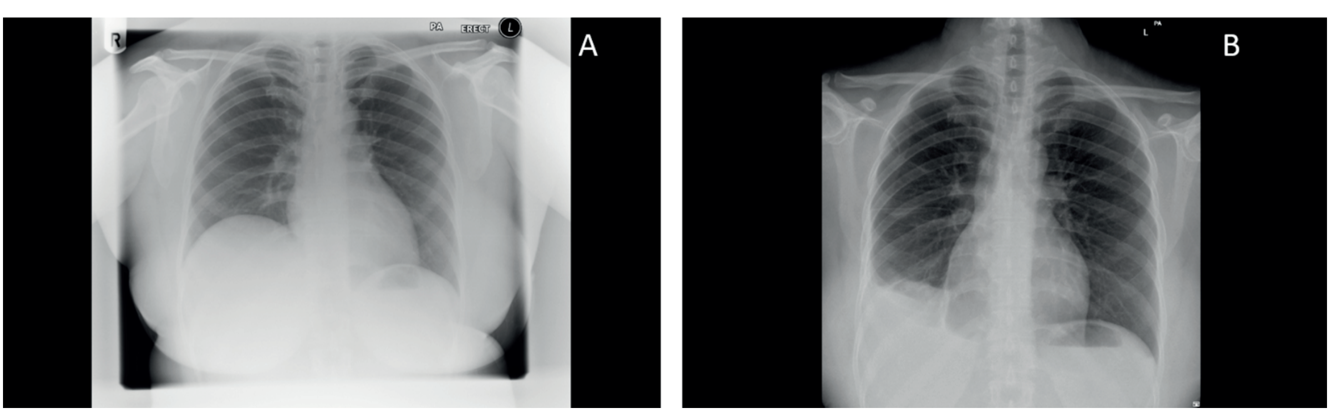

Figure 2. A) Chest radiograph of a 39-year-old woman showing elevation of the right hemidiaphragm post COVID-19. B) Chest radiograph of the same patient following robotic-assisted surgical plication showing improved position of the right hemidiaphragm.

significant reduction in shortness of breath during exertion and when lying flat. A chest radiograph showed improvement in the position of the right hemidiaphragm (Figure 2B). She underwent pulmonary function tests 7 weeks after her operation, but she was unable to comply with the instructions due to chest pain when she attempted maximal inhalation.

Surgical technique

Both patients underwent general anaesthesia with double-lumen tracheal intubation for isolation of the lung on the affected side. Each patient was placed in the lateral decubitus position with the affected side on top, and the operating table was flexed at an angle of 10° and then set to 10° reverse Trendelenburg position to facilitate caudal shift of the diaphragm. Three 8-mm ports and a 15-mm utility port were inserted along a line 3–4 cm cephalad to the upper margin of the diaphragm, with a spacing of 8–10 cm between adjacent ports. The patient cart of the da Vinci Xi surgical system (Intuitive Surgical, Sunnyvale, CA, USA) was docked at the level of the patient's pelvis. The chest cavity was insufflated with CO_2 at a pressure of 6–8 mmHg to increase the workspace and flatten the diaphragm, which was plicated using permanent multifilament polyester sutures (Ethibond, Ethicon, Bridgewater, NJ, USA).

Discussion

Although COVID-19 is primarily a respiratory disease, it has been shown to affect multiple organ systems, including the renal, cardiovascular, and neuromuscular systems. Intact function of the phrenic nerve, and the diaphragm that it supplies, is essential to ensure adequate lung expansion and thus ventilation. Evidence is now emerging that infection with COVID-19 may affect contraction of the diaphragm, with a recent study of 21 patients with severe COVID-19 demonstrating that 76% of patients had radiographic evidence of diaphragmatic dysfunction [2]. As a significant proportion of patients with COVID-19 have lung parenchymal damage, the addition of diaphragmatic dysfunction may significantly increase disease burden and worsen clinical outcomes. In addition, even in patients who have suffered mild to moderate COVID-19 symptoms, diaphragmatic dysfunction alone may lead to significant morbidity.

The exact mechanisms through which COVID-19 causes diaphragmatic paralysis remains to be elucidated; however, several mechanisms have been hypothesised. Firstly, COVID-19 has been shown to cause direct damage to peripheral nerves, as well as to the olfactory and optic nerves [4]. Viral infiltration leads to the release of proinflammatory cytokines, such as IL-6, IL-12 and TNF-alpha, which are directly neurotoxic, leading to a post inflammatory neuropathy [5]. Furthermore, microthrombi and vasculitis of the *vasa nervosum* also compromise nerve function as a result of ischaemia [6]. It is possible that similar mechanisms may result in phrenic nerve damage following infection. Secondly, the cytokine storm generated by COVID-19 can result in immune-complex deposition within muscle cells, leading to an inflammatory myositis [7]. This mechanism may allow COVID-19 to cause direct damage to the diaphragm muscle itself. Finally, a significant proportion of patients with severe COVID-19 require intubation and ventilation. Prolonged ventilation is known to result in atrophy of the diaphragmatic muscle, resulting in what is known as ventilator-induced diaphragmatic dysfunction [8].

The mainstay of treatment of unilateral diaphragmatic paralysis is conservative, with a focus on treating the underlying aetiology in symptomatic patients. If an underlying viral aetiology is suspected, the conservative therapy of choice is specific antivirals, with or without the addition of steroids. Unilateral diaphragmatic paralysis has been described in the course of severe COVID-19 in a 54-year-old man [3]. The patient developed progressive elevation of the right hemidiaphragm from day 7 of the infection, and he was discharged home after 61 days of hospitalisation. At a 9-month follow-up, he reported persistent dyspnoea and orthopnoea and thus, he subsequently underwent surgical plication. In general, asymptomatic patients with well-maintained quality of life may not require intervention [9].

With ever-increasing infection rates and novel therapies leading to improved survival in severe COVID-19 cases, effective management strategies are likely to be required for patients with diaphragmatic paralysis who continue to be symptomatic despite conservative treatment. Surgical correction of unilateral diaphragmatic paralysis was first described by Wright *et al*. [10] in 1985. Since then, surgical plication has been established as a valid option for the treatment of symptoms associated with unilateral diaphragmatic paralysis [11,12]. Minimally invasive diaphragmatic plication has also been shown to be a safe and effective strategy for the management of diaphragmatic paralysis [13,14]. Both of our patients showed subjective improvement in their breathing and quality of life, with an additional improvement in FEV_1 and DLCO.

In conclusion, both severe and non-severe COVID-19 can result in diaphragmatic paralysis with significant morbidity. In refractory cases despite conservative management, robot-assisted diaphragmatic plication reinforced with a biological mesh is a safe procedure that can lead to significant symptom improvement.

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