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Case report

Diaphragm dysfunction prior to intubation in a patient with Covid-19 pneumonia; assessment by point of care ultrasound and potential implications for patient monitoring

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ABSTRACT

The clinical research described in this case report was initiated because of the recognized need for early identification of Covid-19 patients at risk of respiratory failure. We used point of care ultrasound to identify diaphragm dysfunction in a spontaneously breathing Covid-19 patient. Measurements of diaphragm thickness and thickening fraction indicated diaphragm dysfunction prior to intubation while respiratory failure was not yet evident from arterial blood gas analysis. Recovery of diaphragm contractility was demonstrated within two days of controlled mechanical ventilation when the patient was switched to a pressure support mode. With recovery of the diaphragm very large fractional shortening was seen after discontinuation of rocuronium, which was associated with a reduced dynamic compliance. In conclusion, this case report illustrates the need to be aware of potential diaphragm dysfunction in spontaneously breathing Covid-19 patients. With recovery, point of care ultrasound allows repeated evaluation of diaphragm function which appears to be responsive to changes in pulmonary compliance.

1. Introduction

Many patients hospitalized with severe pneumonia due to Covid-19 show hypoxemia without clinical signs of dyspnea, a condition which has been coined 'happy hypoxemia'. In a limited number of patients a sudden deterioration occurs during the course of illness, with an increase in oxygen demand when fatigue and dyspnea set in. We hypothesized that dysfunction of the diaphragm could be a contributing factor in the clinical course of patients requiring admission to the ICU.

2. Case description

A 67-year-old man (1.86 m, 84 kg) came to our hospital on 03-04-2020 because of fever, progressive dyspnea and coughing since a week. His medical history indicated slight bronchial hyper-responsiveness and a hip prosthesis. On admission, the patient had a SaO2 of 82% while breathing air at 30 breaths/min. He was tachycardic (106 bpm) with a blood pressure of 160/86 mmHg and a temperature of 39.4 °C. SaO2 improved to 98% on a non-rebreathing oxygen mask (ABG: pH 7.56, pCO2 3.6 kPa, pO2 16.2 kPa, P/F ratio 18). A chest CT showed extensive bilateral ground glass attenuation and consolidations (Fig. 1) with a CT severity score of 22. A PCR test for Covid-19 was positive. Admission to the ICU was deemed unnecessary as the respiratory rate had declined to 18 breaths/min while the patient felt better and expressed no fear of exhaustion. The patient was admitted to a Covid-19 ward and treated with supplemental oxygen, ceftriaxone, chloroquine and prophylactic nadroparine. Laboratory data showed leucocytosis (15.5 × 10ˆ9/nL), lymphocytes 0.38 × 10ˆ9/nL and CRP 388 mg/L. Within 12 hours after admission a sharp decline in SaO2 occurred with coughing. Breathing frequency had increased to 34 bpm with the use of accessory respiratory muscles. Arterial blood gas analysis showed a pH 7.49, pCO2 4.4 kPa, pO2 8.1 kPa and P/F ratio 16.1.

The patient was taken to the ICU on 04-04-2020. An ultrasound examination indicated bilateral diaphragm dysfunction prior to intubation and the start of lung protective mechanical ventilation (Figs. 2 and 3). Oxygenation improved with mechanical ventilation (PRVC, 16 × 480 ml, PEEP 16 cm H2O, FiO2 45%), reaching a P/F ratio of 37.8 (respiratory parameters for the fist ten days following admission are shown in Table 1). One day later CRP had increased to 400 mg/L with temperatures fluctuating between 37 and 40 °C. After 34 hours of

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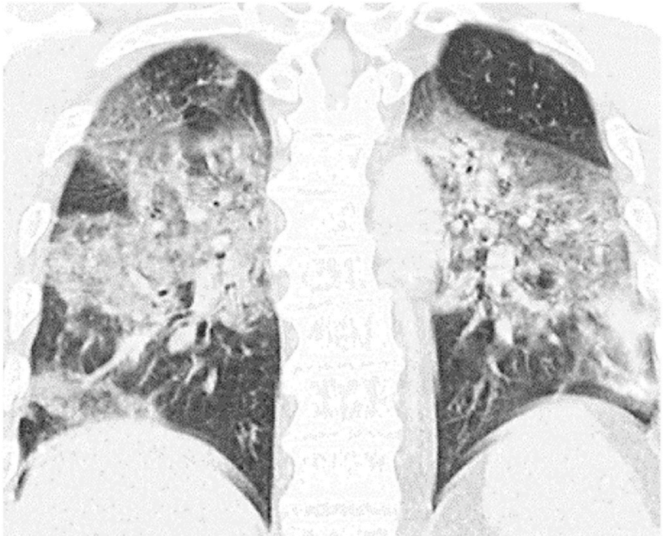

Fig. 1. Frontal section of CT-image on admission showing a mixture of bilateral ground glass attenuation and consolidations. In retrospect, the highly convex diaphragm contours may have been an indication of poor function.

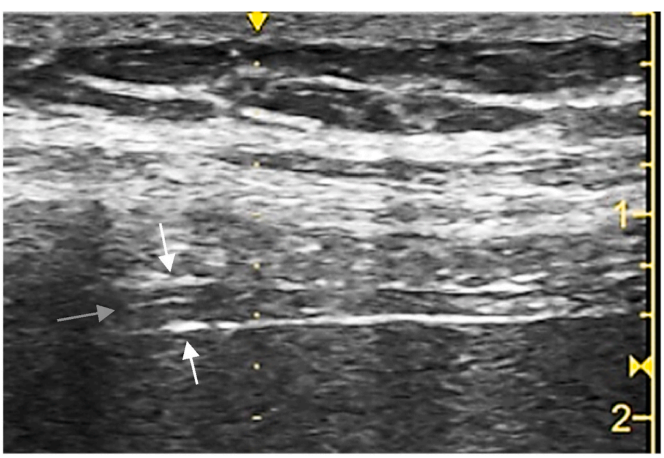

Fig. 2. B-mode ultrasound image of the diaphragm at the opposition zone. Borders of the diaphragm are indicated by white arrows. The central fibrous layer is indicated by the horizontal gray arrow.

controlled mechanical ventilation, sedation was reduced and the patient was put on pressure support ventilation (PSV). Ultrasound examination on 06-04-2020 showed an increase in both thickness and inspiratory thickening of the diaphragm. Maximal diaphragm thickness on expiration/inspiration was 2.1/3.1 mm for the right and 2.0/2.7 mm for the left hemidiaphragm (thickening fractions respectively 0.48 and 0.35. Two days later similar contractions of the diaphragm were observed (Fig. 4). Because of worsening oxygenation (P/F ratio 14.3), with a CTA showing pulmonary emboli and increased ground glass attenuation, the patient was subsequently put on PRVC ventilation in prone position. An additional measurement of the right hemidiaphragm taken in recumbent position on 10-04-2020 showed an increase in thickening fraction to 0.94 (Fig. 5). Conditions for this last measurement differed slightly as they were made during an episode of controlled ventilation by temporarily switching to pressure support, 6 hours after discontinuing rocuronium infusion. With further respiratory complications including severe mucus impactions requiring bronchoscopy, signs of progressive pulmonary fibrosis and a pneumothorax the patient ultimately died 24 days after admission to the ICU.

3. Discussion

We describe the finding of bilateral diaphragm dysfunction in a patient with a Covid-19 pneumonia within 12 hours following admission to the hospital. Diaphragm dysfunction was initially not suspected due to the decline in respiratory rate with supplemental oxygen, a mild respiratory alkalosis and the patient expressing confidence in his respiratory stability. Yet impending respiratory failure was revealed by a combined increase in pCO_2 despite worsening oxygenation and the patient's use of accessory respiratory muscles. With the shortage of available ICU beds during the Covid-19 pandemic, patients with an indication for closer monitoring of respiratory function are frequently treated on general wards. Chances are that by doing so, patients with occult diaphragm dysfunction will damage their diaphragm due to over-exertion while exposed to severely increased inflammatory mediators. This will likely translate into a prolonged ICU stay and difficulty in weaning from the ventilator [2,3]. Ultimately, this could affect the number of patients that can be treated with mechanical ventilation. Monitoring of respiratory muscle performance in Covid-19 patients prior to ICU admission has recently been proposed [5] A routine assessment of diaphragm function in Covid-19 patients with severe bilateral pulmonary involvement may allow more timely intervention in vulnerable patients. The clinical observation of a breathing pattern disorder may help to identify such patients while point of care ultrasound allows repeated measurement of the diaphragm and its contractility. A ventilation strategy aimed at preventing further harm to intubated patients should subsequently be pursued [4].

In this case report early intubation followed by two days of controlled mechanical ventilation before switching to pressure support ventilation may have been beneficial to the recovery of diaphragm function. However, repeated measurements of diaphragm thickening revealed a strong respiratory drive, likely related to hypoxemia and a physiological defense against the loss of end expiratory lung volume. Large thickening fractions of the diaphragm have been linked to prolonged duration of mechanical ventilation [6]. In our patient we cannot exclude the possibility that self inflicted lung injury during mechanical ventilation has contributed to further pulmonary complications. The very large thickening fraction measured on day six could indicate an additional effort by the patient after a brief switch from pressure control to pressure support ventilation at low values for dynamic respiratory compliance (Table 1). Although we should be cautious when interpreting dynamic compliance, review of the patients records indicated that a muscle relaxant (rocuronium) was started 36 hours prior to the ultrasound investigation on day six because of pulmonary deterioration and active breathing of the patient which was considered harmful. A presumed loss of lung volume despite increased PEEP and forceful inspiration by the patient upon temporary discontinuation of muscle relaxation indicate a detrimental side effect of this treament which is commonly used in severe ARDS. It is not known how long these very forceful contractions would have persisted if the patient had been kept on pressure support at that time, but it is clear that such contractions would have contributed to self inflicted lung injury. While respiratory parameters indicated a loss of dynamic compliance, a loss of lung volume was not evident from a chest X-ray on day six as this was performed in supine position with temporary discontinuation of rocuronium. The very strong diaphragm contractions may have restored lung volumes at the time of the X-ray. More sophisticated respiratory monitoring using EIT and esophageal pressure measurements might have revealed problems in maintaining lung volume upon starting the muscle relaxant.

4. Conclusion

Careful review of repeated ultrasound examinations of the diaphragm both in spontaneously breathing and in mechanically ventilated patients may yield substantial clinical information. Future studies of diaphragm function in patients with severe pneumonia may help to

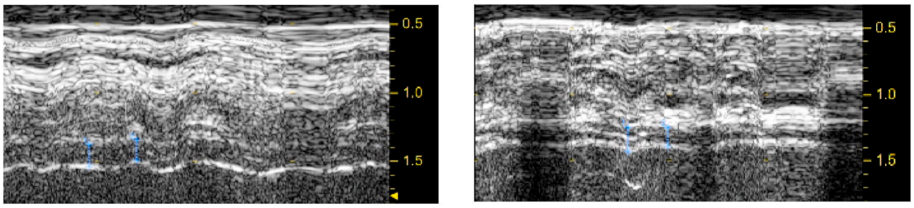

Fig. 3. M-mode images of the right and left hemidiaphragm prior to intubation. Images show parallel vertical movement of the borders of the diaphragm without thickening of the muscle in a clear respiratory pattern. The diaphragm moves synchronous to subcutaneous tissue, likely due to auxiliary respiratory muscle activity. Measures of diaphragm thickness ranged from 1.5 to 1.7 mm on the right and from 1.4 to 1.8 mm on the left side (values below average, but corresponding to the lower 5th percentile of normal values for ventilation at rest [1].

Table 1
Respiratory parameters for the first ten days following admission: RR = respiratory rate, TVe = measured expiratory tidal volume, PEEP = positive end expiratory pressure, P/F ratio = PO2 (kPa)/FiO2, Cdyn = dynamic compliance, PRVC = pressure regulated volume support, PS = pressure support. Respiratory parameters were averaged from 2 to 3 available values within 1 h from arterial blood gas analysis. The days of ultrasound analysis of the diaphragm are greyed.
*) Dynamic compliance increased to a value of 43 during the day while rocuronium was temporarily discontinued.

day nr	ventilation mode	position	rocuronium	RR	Tve (ml)	PEEP (cm H2O)	P/F ratio	Cdyn (L/bar)
0	Spontaneous	Supine	-	34	-	-	16	-
0	PRVC 16 x 480 ml	Supine	-	20	536	16	31	38
1	PRVC 16 x 480 ml	Supine	-	17	539	16	38	49
2	PRVC 16 x 480	Supine	-	19	605	14	28	55
2	PS 10 cm H2O	Supine	-	31	505	14	-	41
3	PS 12 cm H2O	Supine	-	29	598	14	20	45
4	PS 12 cm H2O	Supine	-	31	676	14	18	52
5	PRVC 28 x 480 ml	Prone	+	28	468	16	14	26
6	PRVC 28 x 480 ml	Prone	+	28	529	16	14	28*
7	PRVC 28 x 480 ml	Supine	+	28	531	15	15	31
8	PS 16 cm H2O	Prone	-	36	598	15	14	35
9	PRVC 28 x 480	Prone	+	28	524	18	19	29
10	PRVC 28 x 480	Supine	-	29	472	18	19	30

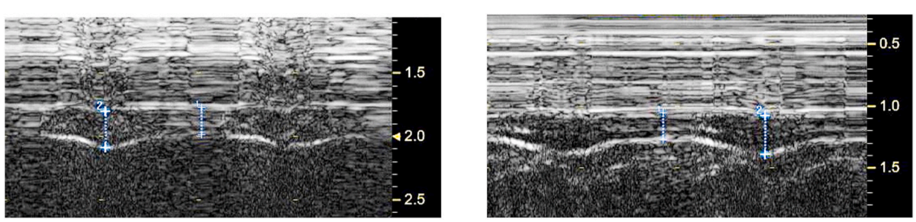

Fig. 4. M-mode images of the right and left hemidiaphragm with pressure support ventilation on day four following admission. Measures of diaphragm thickness during expiration and inspiration: 2.2/3.0 mm (36% thickening fraction) on the right side and 2.2/3.1 mm (41% thickening fraction) on the left side. Note that there is no vertical movement of subcutaneous tissue with interrupted activity of auxiliary respiratory muscles.

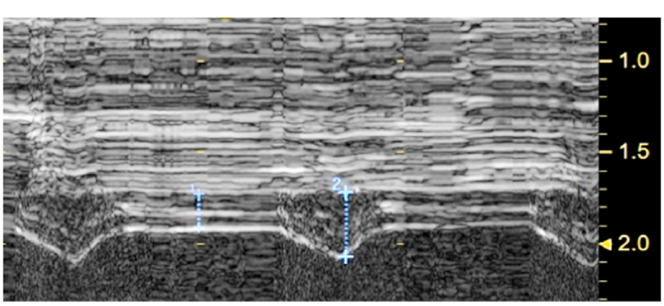

Fig. 5. M-mode image of the right hemidiaphragm on day 6 following intubation. Diaphragm thickness: 1.8 mm in expiration and 3.5 mm during inspiration (thickening fraction 0.94). Measurements were made during a brief switch from pressure control to pressure support ventilation.

improve the timing of a switch to mechanical ventilation as well as strategies for monitoring and treatment in ventilated patients.

Declaration of competing interest

The authors have no conflict of interest and have no financial disclosures in relation to the research in this article.

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