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Title:

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Abbreviations

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; MAFLD, metabolic associated fatty liver disease; OSAHS, obstructive sleep apnoea hypopnea syndrome.

Introduction

The outbreak of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been declared a pandemic by the World Health Organization[1]. Obesity is a common cause to aggravate the severity of respiratory diseases [2] which may place obese patients infected by SARS-CoV-2 at risk for pulmonary complications.

Case presentation

We here report the case of a 23-year-old man who attended our hospital (on January 21, 2020) after five days of fever, chills, headache, nasal congestion, cough and mild dyspnoea. Other medical comorbidities included metabolic associated fatty liver disease (MAFLD)[3] for five years, obstructive sleep apnoea hypopnea syndrome (OSAHS) for two years, and gout for one year, the latter treated with oral benzbromarone and bicarbonate. At the time of hospital admission, the most relevant clinical findings at baseline included a body mass index (BMI) of 37·3 kg/m^2 and body temperature of 39·4 ºC, white blood cell (WBC) count of $4{\cdot}8 \times 10^9$/L, neutrophil count of $3{\cdot}1 \times 10^9$/L, lymphocyte count of $1{\cdot}2 \times 10^9$/L, platelet count of 217×10^9/L, C-reactive protein (CRP) of 37·8 mg/L, fasting blood glucose of 4·9 mmol/L, total cholesterol of 4·38 mmol/L, high-density lipoprotein of 0·62 mmol/L, low-density lipoprotein of 1·62 mmol/L, lactic acid dehydrogenase of 271 U/L, uric acid of 602 μmol/L, ferritin of 796 μg/L, lactate of 2·2 mmol/L, and PaO_2/FiO_2 of 205 mmHg. His chest computed tomography (CT) scan showed bilateral ground-glass opacities (Figure 1A). On the suspicion of COVID-19, the attending physician ordered salivary testing which was positive for SARS-CoV-2 by real-time RT-PCR assay (RT-PCR).

The patient was immediately transferred to the isolation ward and commenced on nebulized α-interferon (5,000,000 IU) twice per day, oral lopinavir/ritonavir (200 mg /50 mg) twice per day, and oral arbidol (200 mg) thrice per day as recommended by the Chinese COVID-19 Interim Management Guidance (3rd edition) [4]. Because of the increased serum CRP, the patient was suspected to have a bacterial co-infection and empirical treatment with intravenous amoxicillin sodium and clavulanate potassium (1·2 g) thrice per day was commenced. Given his worsening dyspnoea and continued PaO_2/FiO_2 of less than 300 mm Hg, the patient was subsequently given continuous high-flow oxygen inhalation (6 L/min) via a nasal catheter. Of note, the dyspnoea improved with arterial PaO_2 fluctuating between 94·5-127·5 mm Hg, while the arterial $PaCO_2$ remained high (46·8-53·9 mm Hg). Several attempts over the next 72 hours to improve the $PaCO_2$ levels by lowering the oxygen therapy flow rate was to no avail. On day nine, the patient had significant improvement in symptoms with $PaCO_2$ <40 mm Hg. A follow-up chest CT scan showed marked improvement in pulmonary infiltration (Figure 1B). Subsequently, a follow-up CT of the chest on day twenty-one showed evidence of further improvement (Figure 1C) and he was discharged after two negative oropharyngeal swab tests and one faecal nuclei acid test for the virus by RT-PCR. On follow-up two weeks after discharge, his chest CT showed resolution of the pulmonary infiltrates (Figure 1D).

Discussion

This patient was diagnosed with type II acute respiratory failure as the likely result of COVID-19 in the context of other comorbidities including obesity and MAFLD. This is an interesting case in that up to now, only type I acute respiratory failure has been reported in severe COVID-19 patients[5]. Our patient's $PaCO_2$ levels remained elevated despite multiple attempts to adjust his

oxygenation therapy. Fortunately, his hypercapnia improved on day nine which we believe was due to the improvement in pulmonary infiltrates. Previous studies have shown that obesity may cause restrictive lung disease with reduced vital capacity.[6] In our patient, obese hypoventilation syndrome (i.e. BMI ≥30 kg/m^2 and $PaCO_2$ >45 mm Hg) was observed, possibly the result of combined severe pulmonary viral and bacterial infection; this can progress to malignant hypoventilation syndrome, a condition typically characterized by a poor prognosis[6]. The current practice guidance for treatment of COVID-19 suggests non-invasive oxygenation management targeting dyspnoeic individuals with PaO_2/FiO_2 levels below 300 mm Hg or primarily in those with type I acute respiratory failure. However, no strategies exist for managing COVID-19 patients with obesity, chronic obstructive pulmonary disease or other diseases that may cause type II acute respiratory failure.

In this patient, worsening hypercapnia might have led to serious sequelae if he had not recovered from his illness. Potential management strategies in deteriorating patients includes the use of different oxygenation therapies. In high-flow oxygenation therapy, a moisturized and temperature-controlled airflow provides appropriate respiratory support with moderate positive airway pressure and helps remove mucus plugs to facilitate better oxygen exchange in the lungs and, thereby, increasing PaO_2/FiO_2. However, its effect on improving simultaneous hypercapnia is uncertain. Alternatively, non-invasive ventilation with an oxygen mask might significantly improve both hypoxemia and hypercapnia, in addition to managing the OSAHS. However, non-invasive ventilation is often uncomfortable and is associated with non-compliance and increases the risk of mucus plug accumulation in the lungs. Invasive ventilation may be the most effective strategy for these patient in that all the abovementioned complications can be appropriately

managed, especially when the arterial blood gas pH is <7·3 (or correspondingly increased $PaCO_2$ levels). However, the risk that needs to be balanced is of nosocomial infection through prolonged intubation and transmission risk to healthcare providers of SARS-CoV-2. Overall, in obese patients combined with SARS-CoV-2 infection, especially in slow to recover patients, early invasive ventilation therapy might be a more appropriate strategy for managing a rapidly deteriorating pulmonary function.

That said, it is reasonable to speculate that obesity with coexisting COVID-19 may predispose patients to the risk of more severe conditions such as obese hypoventilation syndrome. This is more likely in those that are older and with multiple comorbid diseases such as MAFLD, dyslipidaemia and OSAHS, and therefore less likely to be have adequate compensatory organ capacity. Future studies are needed to confirm these observations and to better understand the underlying mechanisms linking SARS-CoV-2 infection with the occurrence of type II acute respiratory failure in obese patients.

Contributors:

J-FH, X-BW and KIZ contributed equally to the study. M-HZ, J-FH, X-BW, KIZ, W-YL, J-JC and JG were involved in design and data interpretation. KIZ wrote the manuscript. M-HZ and JG conducted critical revision of the manuscript. All authors reviewed and commented on the manuscript and approved the final version. Written informed consent to publication was obtained.

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Conflicts of interest

The authors have no conflicts of interest related to this article.

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None.

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Figure Legends

Figure 1. Chest computed tomography of the patient at hospital admission (A) and during the hospital stay on days nine (B), twenty-two (C) and on follow-up two weeks after discharge (D).

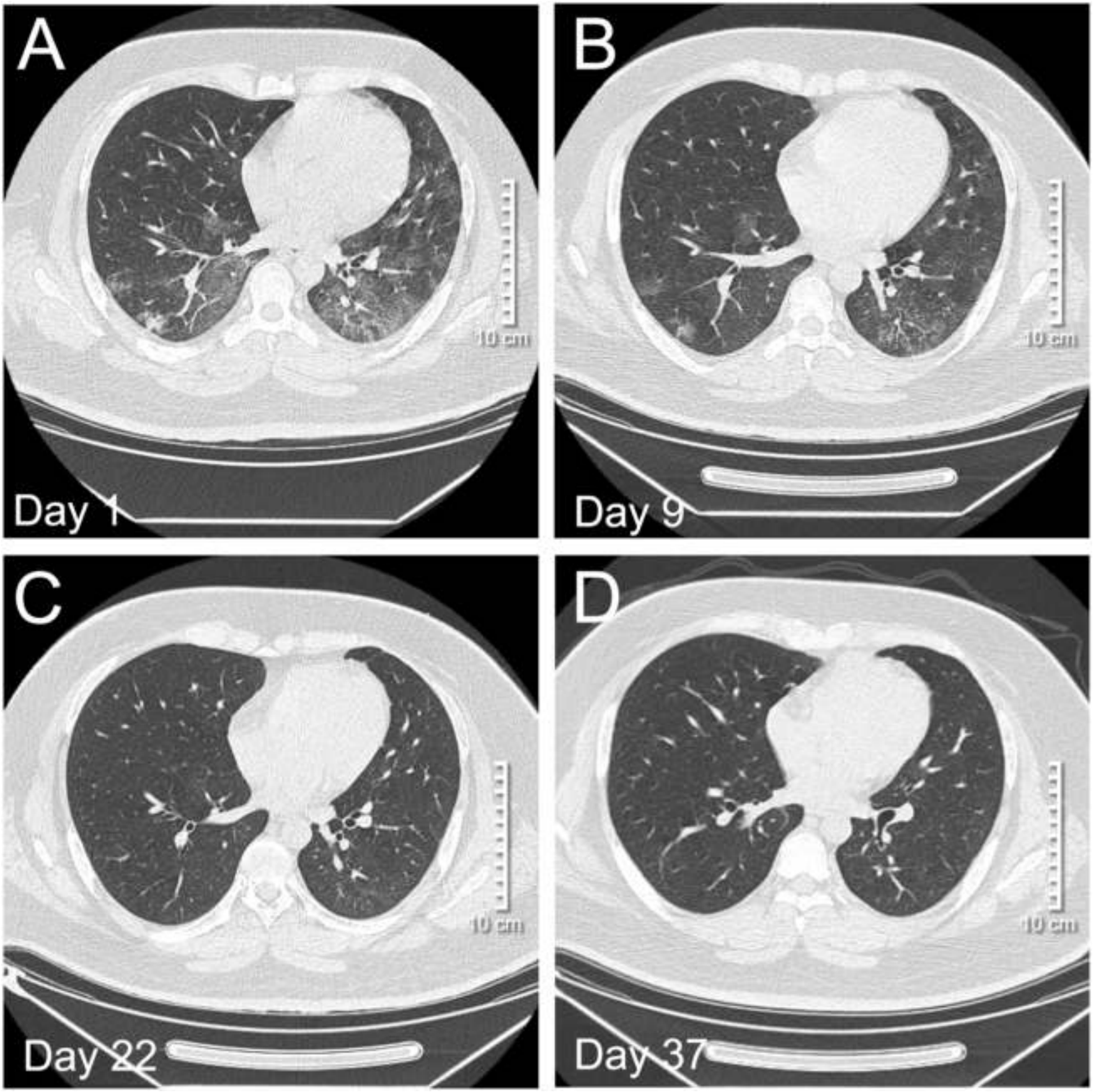

Figure 1