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Case report

Co-infection of SARS-CoV-2 and *Bordetella bronchiseptica* in a young man with idiopathic non-cystic bronchiectasis and vitamin D_3 deficiency

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ABSTRACT

This is the first reported case, to our knowledge, of co-infection of *Bordetella bronchiseptica* and SARS-CoV-2 in a young patient with underlying idiopathic bronchiectasis and vitamin D_3 deficiency that was treated successfully with a combination therapeutic regime integrating doxycycline, empiric therapies for COVID-19, vitamin D supplementation, and supportive ICU care. Large prospective studies are required to investigate further the role of co-infections in COVID-19 patients with bronchiectasis. Randomized control trials should examine the putative beneficial role of vitamin D supplementation in patients with COVID-19.

1. Introduction

The novel SARS-CoV-2 disease (COVID-19) has affected almost every national health care system in the world [1]. Bacterial co-infection rates in patients with COVID-19 have been reported to be lower compared to flu pandemics in a recent meta-analysis integrating four thousand COVID-19 patients [2]. However, scarce data exist about co-infection rates in COVID-19 patients with underlying lung pathology. Non-cystic bronchiectasis (bronchiectasis) has been remotely identified, mainly in elderly COVID-19 patients, by chest computed tomography (CT) studies [3–8]. Idiopathic bronchiectasis is a chronic irreversible airway dilatation of unknown underlying causes, which occurs more frequently in younger patients, and accounts for approximately 50% of all bronchiectasis etiologies [9,10]. Patients with idiopathic bronchiectasis could accumulate thick mucus within their enlarged bronchi making them susceptible to various infectious pathogens. Notably, it has been speculated that vitamin D_3 supplementation may reduce the infection risk in idiopathic bronchiectasis as well as ameliorate the severity of symptoms in COVID-19 [11,12]. We are briefly presenting a rare co-infection of *Bordetella bronchiseptica* and SARS-CoV-2 in a young man with underlying idiopathic bronchiectasis and vitamin D_3 deficiency.

2. Case presentation

In June 2020, a 30 year old man with a past medical history of idiopathic bronchiectasis was admitted to the emergency department (ED) due to recent onset fever (38.6 °C), productive cough, chest pain, dyspnea, and anosmia. The patient has been living alone with his pet dog; however, he had recent contact with his friend who has just recovered from COVID-19. Hence, nasopharyngeal swabs were derived and sent for SARS-CoV-2 testing as per hospital protocol. Physical examination showed bilateral crackles at the lower lobes. The saturation of peripheral oxygen (SpO_2) was 65%, on room air, but the patient had no respiratory distress. He was connected to a high flow nasal cannula [(HFNC) with a flow of 60 L/min, and fraction of inspired oxygen (FiO2) of 60%] maintaining SpO_2 of 82%. Chest X-ray showed peripheral infiltrates (Fig. 1). Soon after, the patient desaturated (SpO_2: 55%), and thus he was intubated and connected to mechanical ventilation (MV). Nasopharyngeal swabs confirmed COVID-19 by Real-Time-Polymerase-

Abbreviations: SARS-CoV-2 disease, COVID-19; ED, emergency department; ICU, intensive care unit; RT-PCR, Real-Time-Polymerase-Chain-Reaction; CT, computed tomography; HFNC, high flow nasal cannula; MV, mechanical ventilation; SpO_2/FiO_2, partial arterial pressure of oxygen to fractional inspired concentration of oxygen.

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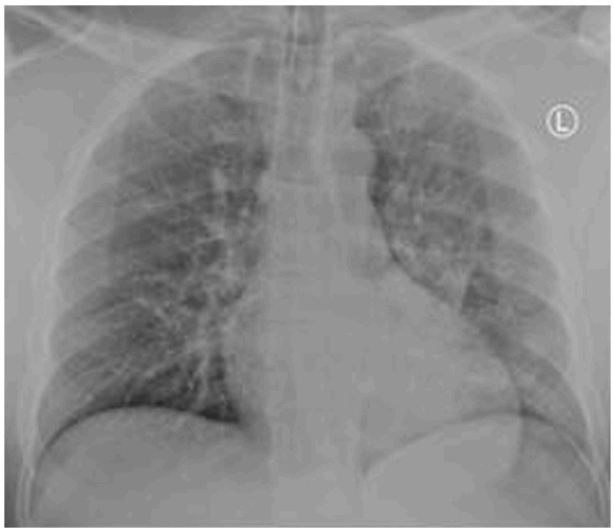

Fig. 1. Chest X-ray depicting infiltrates (distributed mainly on the left lung) in our COVID-19 patient.

Chain-Reaction (RT-PCR) assays using QuantiNova Probe RT-PCR kit (Qiagen) in a Light-Cycler 480 real-time PCR system (Roche, Basel, Switzerland) [13–15]. Electrocardiogram, cardiac enzymes, and echocardiography were normal. Baseline laboratory findings were normal apart from leukocytosis (17.9 × 10^9/L, normal 4–10 × 10^9/L) with lymphocytopenia (0.42 × 10^9/L, normal: 1.1–3.2 × 10^9/L), and increased D-dimer (3.3 mcg/ml, normal: 0 to 0.5 mcg/ml), C-reactive protein (245 mg/liter, normal: 0–7 mg/liter), lactate dehydrogenase (904 units/liter, normal: 100–190 units/liter), and ferritin (883 ng/ml, normal: 23–336 ng/ml). Contrast chest CT scans excluded pulmonary embolism and revealed bilateral peripheral ground-glass opacities, which were distributed mainly on the left lung, with associated bronchiectasis (Fig. 2). The patient was admitted to our polyvalent COVID-19 designated intensive care unit (ICU). The patient underwent a full diagnostic work-up for other viral and bacterial infections; moreover, serum 25(OH) D levels were measured using a competitive electrochemiluminescence assay kit (Elecsys, Roche Diagnostics, Burgess Hill, UK). The latter was deemed necessary as the patient stated that he has not moved outside his house for three months due to the imposed lockdowns for COVID-19 in the Kingdom. Empiric therapy for COVID-19 with ribavirin, ceftriaxone and azithromycin, prophylactic anti-coagulation, acute respiratory distress syndrome (ARDS)-net and prone position ventilation (positive end-expiratory pressure of 10 cm H_20), and supportive ICU care was administered [16].

On day-3 post-ICU admission, the patient's respiratory status on MV did not show any improvement [partial arterial pressure of oxygen to fractional inspired concentration of oxygen (SpO_2/FiO_2) ratio: 160]. However, quantitative cultures of endotracheal aspirates, which were derived on day-1, revealed $\geq 10^5$ colony-forming-units (cfu)/ml of *Bordetella bronchiseptica* that was sensitive to doxycycline [17,18]. Hence, the antibiotic regime was adjusted accordingly. The patient received doxycycline for approximately two weeks. Also, his serum 25 (OH) D levels revealed severe vitamin D deficiency (25 nmol/L, normal: $>$ 50 nmol/L). Thus, the patient received an initial vitamin D_3 bolus dose of 100,000 IU, and thereafter a weekly vitamin D_3 dose of 25,000 IU was prescribed. On day-15, he was extubated. On day-18, RT-PCR for COVID-19 and microbiology were negative. The patient was finally discharged to home isolation twenty days post-ICU admission. He was asked to monitor his pet dog for any symptoms of "kennel cough", and review his vitamin D supplementation prescription as well as his dietary habits with his family physician.

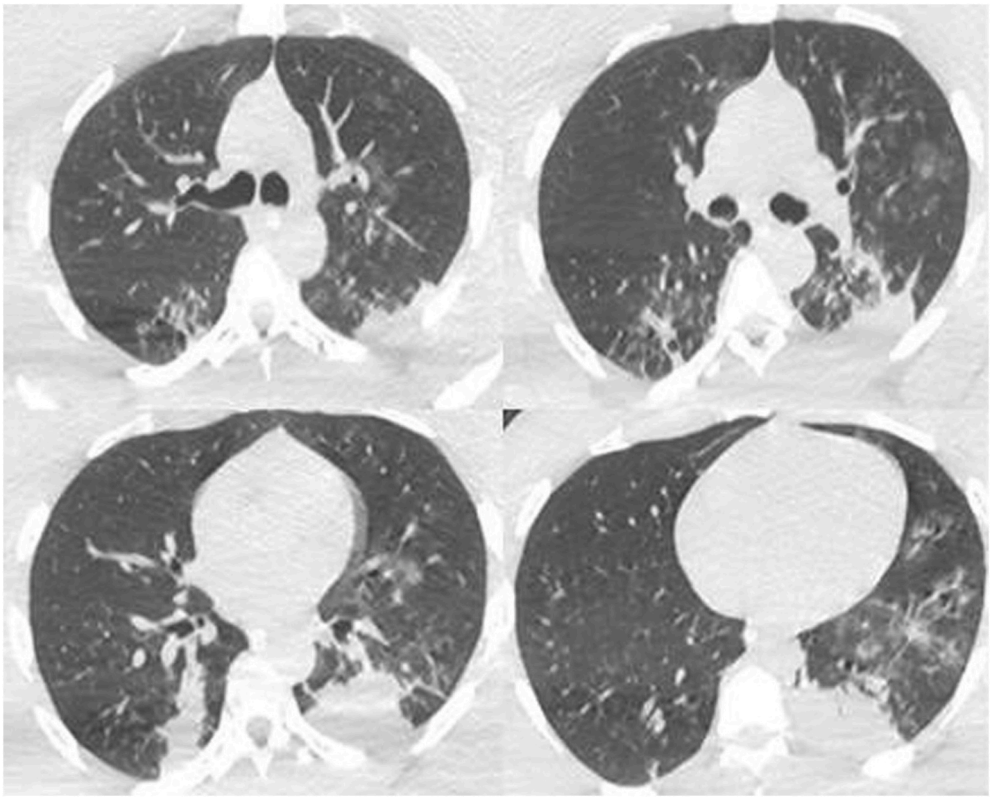

Fig. 2. Contrast chest computed tomography depicting scattered bilateral ground-glass opacities (distributed mainly on the left lung) and bronchiectatic changes. Pulmonary embolism was excluded.

3. Discussion

A minority of COVID-19 patients have critical illness characterized by ARDS, sepsis, thromboembolic disease, and multi-system organ failure [19]. An important risk factor for developing critical illness is age of more than 65 year old [20]. Notably, bronchiectasis is an uncommon comorbid disease found in COVID-19 [19,20]. Our patient was a young healthy man who presented with happy hypoxemia (very low oxygenation without respiratory distress; or type L COVID-19 pneumonia) and cytokine storm [21,22].

Interestingly, *Bordetella bronchiseptica* was depicted from the cultures of bronchial aspirates. This is a gram-negative aerobic pathogen, which can be transmitted to humans from pets [23], and rarely causes respiratory tract infections. Notwithstanding, the clinical manifestations of *B. bronchiseptica* could range from asymptomatic carriage to severe infection or even death [24]. The dilated bronchi of patients with bronchiectasis could be colonized by this pathogen, which is extremely difficult to be, thereafter, eradicated. In our previously healthy young patient, the possible exacerbation of *B. bronchiseptica* infection, which was treated successfully by doxycycline, along with the severe presentation of COVID-19 pneumonitis on the grounds of idiopathic bronchiectasis might have at least be partially responsible for his fulminant clinical presentation.

Also, in our patient, extremely low serum 25(OH) D levels were detected. Vitamin D deficiency has been previously linked to chronic bacterial colonization and disease severity in patients with bronchiectasis [25]. Interestingly, vitamin D supplementation has been suggested to reduce the incidence of respiratory tract infections in patients with asthma and chronic obstructive pulmonary disease [26–28]. Recent studies of vitamin D supplementation have shown promise in improving the symptoms of patients with bronchiectasis [29]; while, the therapeutic potential of vitamin D has been also suggested for SARS-CoV-2 infection [11]. Nevertheless, the latter remains a mere speculation. Our patient has improved on a combination treatment of doxycycline for *B. bronchiseptica*, empiric therapy for COVID-19, vitamin D supplementation, and supportive ICU care. We are uncertain whether this combination therapy was responsible for his improvement, but given the severity of his clinical picture, we speculate that it might have helped.

This is the first reported case, to our knowledge, of co-infection of *B. bronchiseptica* and SARS-CoV-2 in a young patient with underlying idiopathic bronchiectasis and vitamin D_3 deficiency. The patient was treated successfully by a combination therapeutic regime integrating vitamin D administration. Large prospective studies are required to investigate further the role of co-infections in COVID-19 patients with bronchiectasis. Randomized control trials should examine the putative beneficial role of vitamin D supplementation in patients with COVID-19.

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Ethical approval

The study was approved by the Institutional Review Board of King Saud Medical City, Riyadh, Kingdom of Saudi Arabia [H-01-R-053, IORG0010374, H1RI-May20]. Written informed consent was obtained from the patients.

CRediT authorship contribution statement

Fahad Faqihi: Investigation, Validation, Writing - original draft. **Abdulrahman Alharthy:** Investigation, Validation, Writing - original draft. **Pattarin Pirompanich:** Validation, Writing - original draft. **Alfateh Noor:** Investigation, Validation. **Ahmad Shahzad:** Investigation, Validation. **Nasir Nasim:** Investigation, Validation. **Abdullah Balhamar:** Investigation, Validation, Writing - original draft. **Ziad A. Memish:** Validation, Supervision, Writing - review & editing, Conceptualization, Writing - original draft.

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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