

# On two cases of atypical respiratory distress in eastern Democratic Republic of the Congo months before the COVID-19 pandemic was declared: Could SARS-Cov-2 have been already spreading? Case report

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**Case report**

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# Abstract

## Background

Predictions have been made that Africa would be the most vulnerable continent to the novel coronavirus disease 2019 (COVID-19). Interestingly, the spread of the disease in Africa seems to have been delayed and initially slower than in many parts of the World. Here we report on two cases which make us suspect that COVID-19 might have been present in our region before the official declaration of the disease in December 2019.

## Case presentation

These two cases (one 55-year-old man and one 25-year-old woman) of acute respiratory distress secondary to atypical pneumonia were seen in Bukavu, in eastern Democratic Republic of the Congo (DRC), between September and December 2019. One patient had returned from China and the other had close contacts with travellers from China in the 2 weeks prior to the onset of symptoms. In either case, the aetiology could not be accurately determined. However, the two cases presented a clinical picture (progressive dyspnoea, preceded by dry cough and fever) and laboratory changes (procalcitonin within the normal range, slight inflammation, and lymphopenia) compatible with a viral infection. The chest X-Rays series of the first patient showed lesions (reticulations, ground glass, and nodules  $\leq 6$  mm) similar to those found in COVID-19. In addition, unlike the 25-year-old female patient who had no comorbidity, the 55-year-old male patient who had hypertension as comorbidity, developed a more severe acute respiratory distress which progressed to death.

## Conclusion

These cases bring to the attention a number of facts which make us suspect that the COVID-19 epidemic may have already been present in the region months before the official beginning of the pandemic.

## Background

The world is currently facing a devastating pandemic of the novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first declared in Wuhan, China, in December 2019 [1]. As of June 20, 2020, over 8.7 million cases of COVID-19 have been confirmed in 188 countries, including more than 461,000 deaths [2]. Predictions have been made that Africa would be the most vulnerable continent to COVID-19, because of various factors: dense population in many cities, high prevalence of chronic diseases (e.g., infections by human immunodeficiency virus (HIV), malnutrition, etc.) interfering with the immune defence, absent or poor infrastructures to diagnose or treat patients, and very frequent travels between China and Africa [3, 4]. The Democratic Republic of the Congo (DRC) is considered to be among the countries at highest risk, especially since the travels continued even after the pandemic was declared [3].

Interestingly, the spread of the disease in Africa seems to have been delayed and initially relatively slower than in many parts of the World. Since the first COVID-19 case was officially identified in Africa (in Egypt) on February 14, 2020 [5, 6], 208,535 confirmed cases and 4,750 deaths have been documented as of June 20, 2020, more than four months later [7]. These numbers are far below those recorded in other parts of the World. In the DRC, the first case has been reported on March 10, 2020, in Kinshasa (12 million inhabitants), but as of June 19, 2020, only 5,074 confirmed cases have been registered in the same city and 5,671 countrywide [8]. In Bukavu (about 1 million inhabitants, density: 16,600 inhabitants/km<sup>2</sup>), the capital city of South-Kivu, in eastern DRC, the first two COVID-19 cases were travellers who arrived on March 18 and 20, but despite a delay in the isolation measures (started on March 30, 2020), three months later the Province has registered only 193 confirmed cases of which 31 deaths [9].

The reasons for the initial low rate of COVID-19 propagation in Africa remain unknown. Actually, it is even possible that there was a longer delay before the appearance of first official cases in March 2020 and the currently observed spread of the disease. In this report, we present two patients who were admitted between September and December 2019 for acute respiratory distress in the Intensive Care Unit (ICU) of the "Hôpital Provincial Général de Référence de Bukavu" (HPGRB), in Bukavu. For both patients, a diagnosis of atypical viral pneumonia was made. Although they were not tested for COVID-19 (as the disease was not yet known at that time) the clinical presentation, radiological findings, and the course of the disease are compatible with COVID-19.

## Case Presentation

**Case 1:** A 55-year-old man, with a 10-year history of hypertension and a 5-year history of pigeon breeding, was seen in the Department of Internal Medicine on September 20, 2019, for dry cough, after returning from China 2 weeks before. A diagnosis of non-specific interstitial pneumonia was evoked based on a chest X-Ray (CXR) showing bi-basal and posterior densification (25-30% of total chest height), blurring heart borders and diaphragm, associated with trabecular bands and ground-glass zones on the mid third of the lungs (Fig 1a, b). He was sent back home with oral azithromycin (500 mg daily for five days), acetaminophen and an antitussive drug.

Despite treatment, coughing was exacerbated, and fever and dyspnoea occurred two weeks later. On October 10, 2019, he was admitted in the Emergency ward. The clinical evaluation noticed polypnea (30 breaths/min), tachycardia (100 beats/min) and fever (38°C). Oxygen saturation (SaO<sub>2</sub>) was 54 % [normal range: 95-100 %]. The patient presented a respiratory distress (nose flaring, chest retractions and cyanosis) and had fine crackles at both lung bases. Cardiovascular examination was normal. Laboratory results showed a moderate inflammatory syndrome with hyperleukocytosis (11,600 leucocytes/ $\mu$ l [4,000-10,000/ $\mu$ l] of which 9,700 neutrophils [1,500-7,000/ $\mu$ l] and 1,300 lymphocytes [1,500-4,500/ $\mu$ l]) and increased C-reactive protein (CRP, 54.9 mg/l [0-3 mg/l]). Procalcitonin levels were normal [below 0.1 ng/ml]. An arterial blood gas (ABG) analysis revealed the presence of severe hypoxemia (P<sub>a</sub>O<sub>2</sub> 33 mmHg [75-100 mmHg]) and respiratory alkalosis (pH 7.58 [7.35-7.45], P<sub>a</sub>CO<sub>2</sub> 29.7 mmHg [35-45 mmHg], P<sub>a</sub>O<sub>2</sub>/FiO<sub>2</sub> ratio 157 mmHg [400-500 mmHg], bicarbonate 27.1 mmol/l [22-26 mmol/l], and lactates 1.89

mmol/l [ $< 2$  mmol/l]). Other laboratory results were normal. Bacteriological investigations were all negative. Tuberculosis was unlikely given a Ziehl-Neelsen stain of sputum which was negative for three samples collected at different times. HIV serological tests were negative. A second CXR showed persistence of the aforementioned findings, except for the trabeculae hidden by the alveolar densification that had progressed up to the level of the main bronchi, overhung by a well delimited ground glass zone without encroachment upon the apices (Fig 1c).

The patient was hospitalized in the ICU for acute respiratory distress syndrome (ARDS) secondary to viral pneumonia with probable bacterial surinfection. He received oxygen by mask (5 litres/min) and intravenous antibiotics (combination of amoxicillin and clavulanic acid 1/0.25 g thrice daily). Despite this treatment, continuous fever (average temperature: 38.5°C) and hypoxemia persisted, and lactates increased to 4 mmol/l. So, two days later, amoxicillin and clavulanic acid were replaced by levofloxacin (500 mg) and ceftriaxone (1 g), both twice daily, in addition to intravenous dexamethasone (16 mg thrice daily).

Four days later, no improvement was observed. The oxygen flow was increased to 10 litres/min and dexamethasone replaced by methylprednisolone (125 mg twice daily for 5 days). During the following week, there was a slight improvement of the dyspnoea and fever, but on October 23, 2019, fever reappeared, and the respiratory distress worsened. A new CXR showed a reduction of the alveolar consolidation to the advantage of an interstitial syndrome (reticulations, ground-glass, and nodules  $\leq 6$  mm) extending to lung tops (Fig 1d). Meanwhile, the CRP was 49 mg/l and procalcitonin 0.62 ng/ml. A diagnosis of respiratory zoonosis was considered, given the history of pigeon breeding. Intravenous methylprednisolone (125 mg twice daily) was reintroduced and Duovent® (combined ipratropium and fenoterol) was administered in nebulization, without any improvement. SaO<sub>2</sub> remained at 40 %, P<sub>a</sub>O<sub>2</sub>/F<sub>i</sub>O<sub>2</sub> ratio decreased to less than 70 mmHg, lactacidemia increased to 12.3 mmol/l, and the patient became confused.

On October 25, 2019, the patient underwent orotracheal intubation for mechanical ventilation. This improved the SaO<sub>2</sub> to 90-94 % but on October 29, 2019, the patient developed a shock followed within a few hours by cardiac arrest irresponsive to resuscitation.

**Case 2:** A 25-year-old woman, with no history of recent travel, was admitted at the Emergency ward on December 18, 2019, for a one-week progressive dyspnoea, preceded by dry cough and fever. She had no particular medical history and was a nurse in a hospital where Chinese employees from a multinational mining company are treated, of whom some had recently travelled from China. On admission, she could not complete sentences due to dyspnoea. At ambient air, she presented a SaO<sub>2</sub> of 82 % and signs of respiratory distress without cyanosis. Her pulmonary auscultation was normal.

The CXR showed reticular lines and peribronchovascular haziness in the infrahilar and retrocardiac regions, bilaterally. This suggested a mild interstitial pneumonia (Fig 2a, b). Laboratory results showed a slight inflammation with CRP at 14.5 mg/l, lymphopenia (700 lymphocytes/ $\mu$ l) and normal

procalcitoninemia. The ABG showed a hypoxemia ( $P_aO_2$  60 mmHg) and a respiratory alkalosis (pH 7.51,  $P_aCO_2$  35 mmHg,  $P_aO_2/F_iO_2$  286 mmHg, bicarbonate 27.1 mmol/l, and lactates 1.50 mmol/l). Creatinine, blood urea nitrogen and blood electrolytes were normal. HIV serology was negative.

A diagnosis of moderate ARDS secondary to a viral pneumonia was retained and the patient was admitted in the ICU, receiving oxygen (4 litres/min), azithromycin (500 mg once daily for 5 days) and Duovent® in nebulization. Three days later, she was eupnoeic with normal  $SaO_2$  at ambient air. She was discharged from hospital five days after admission.

## Discussion

In this report, we present two cases of acute respiratory distress secondary to atypical pneumonia in eastern DRC. One patient had returned from China and the other had had close contacts with travellers from China in the 2 weeks prior to the onset of symptoms. In either case, the aetiology could not be accurately determined. COVID-19 was not yet known when these patients were hospitalized. However, when viewed retrospectively the two cases presented a clinical picture and laboratory changes (procalcitonin within the normal range, slight inflammation, and lymphopenia) compatible with a viral infection. The CXRs series of the first patient showed lesions similar to those found in COVID-19 [10]. In addition, unlike the 25-year-old female patient who had no comorbidity, the 55-year-old male patient who had hypertension as comorbidity, developed a more severe acute respiratory distress which progressed to death. For COVID-19, available data show that older age and comorbidities such as cardiovascular diseases, diabetes, hypertension, chronic respiratory diseases and cancer are associated with an increased risk of death [11, 12]. A diagnosis of psittacosis can hardly be sustained in view of the lack of response to antibiotics, and the dramatic evolution to death, uncommon in this disease. In retrospect, especially given the context of travel to China or of contact with travellers from China, the question can thus be raised as to whether these cases could have been COVID-19 infections.

The two cases and a number of other facts make us suspect that COVID-19 may have already been present in some regions of eastern DRC before the official beginning of the pandemic. The cases presented here are illustrative of (unpublished) observations made by clinicians in Bukavu during the last term of 2019. During that period, an abnormally high number of patients presented to local hospitals with symptoms of cough and fever, which were diagnosed as flu or atypical pneumonia for those who could have a chest radiography. Below are additional arguments that support the above hypothesis, although a confirmation cannot be provided.

First, the COVID-19 epidemic has apparently been late to hit Africa, relative to the starting dates in Asia or Europe. This is not due to lack of contacts with China, known to be the origin of the pandemic. During the past two decades business exchanges between many regions of Africa, especially the eastern part of the continent, with Asia, and in particular with China, have been on the increase [13]. Even after the official declaration of the pandemic, many persons from Africa continued to travel to China, to secure the import

of various goods. The apparent delay in the outbreak of COVID-19 cannot therefore be explained solely on the grounds that there is a low level of traveling between Africa and China.

Secondly, despite the evidence of community spread of COVID-19 in DRC since more than 3 months, the progression of the number of such cases has been relatively slower compared to Europe, the USA and Latin America. One reason for the small number of reported positive cases could arguably be due to the low level of testing. However, indirect evidence of the local propagation of the disease could consist in the occurrence of an increased number of people consulting for cough, fever, dyspnoea and eventually for severe respiratory distress requiring respiratory assistance as it has been the case since the last week of May 2020. Before this period, such an increased incidence of cases of acute respiratory distress was not observed locally, suggesting that there was likely a silent epidemic instead of the expected rapid spread of COVID-19, probably due to protective factors such as the generally young age of the population, other immunizations (Bacille Calmette-Guérin vaccination, measles, etc.), some environmental or genetic factors, etc.

In view of the above-mentioned observations, it is tempting to suggest that SARS-CoV-2 infection might have already been present in the region. This hypothesis can only be examined by testing for the presence of anti-SARS-Cov-2 antibodies in the population. If this were to be true, then it would raise the questions as to whether the pandemic really started in China in December 2019 and why the disease did not develop into an epidemic for so many months (till very recently).

However, only a retrospective analysis of blood samples from the population, initially targeting recalled known cases of atypical pneumonia but also common people would provide solid arguments.

## Conclusion

This case report highlights a number of facts suggesting that COVID-19 may have already been present in parts of eastern DRC (and possibly other parts of East Africa) months before the official start of the pandemic. Larger studies, including retrospective microbiological and serological investigations in local communities are needed to test this hypothesis. There is also a need to develop more robust epidemiological surveillance systems in Africa, sensitive to the threat of pandemics as a consequence of increased international traffic and globalisation.

## Abbreviations

ABG

Arterial blood gas

ARDS

Acute respiratory distress syndrome

COVID-19

The novel coronavirus disease 2019

CRP  
C-reactive protein  
CXR  
Chest X-Rays  
DRC  
The Democratic Republic of the Congo  
HIV  
Human Immunodeficiency Virus  
HPGRB  
Hôpital Provincial Général de Référence de Bukavu  
ICU  
Intensive Care Unit  
SaO<sub>2</sub>  
Oxygen saturation  
SARS-CoV-2  
Severe acute respiratory syndrome coronavirus 2

## **Declarations**

### **Ethics approval and consent to participate**

All patients admitted in the “Hôpital Provincial Général de Référence de Bukavu” consent that their clinical and imaging data can be used for publication or education purpose. All procedures performed were in accordance with the ethical standards of the institutional ethical committee and with the 1964 Helsinki declaration and its later amendments

All patients admitted consent that their clinical and imaging data can be used for publication or education purpose.

### **Consent for publication**

Written informed consent for publication of the clinical details and/or clinical images was obtained from the patients or the next of kin (for the deceased patient).

### **Availability of data and materials**

All data generated or analysed during this study are included in this manuscript.

### **Competing interests**

The authors declare that they have no competing interests

### **Funding**

There was no funding source for this study.

## Authors' contributions

All authors contributed to the study conception and design. GQM, PM, SM, AB and BF contributed to the clinical patient care and management. Chest X-Rays were performed and interpreted by FN and GM. All authors contributed to the literature search. The first draft of the manuscript was written by MB and PM and all authors contributed to subsequent versions of the manuscript. All authors read and approved the final manuscript.

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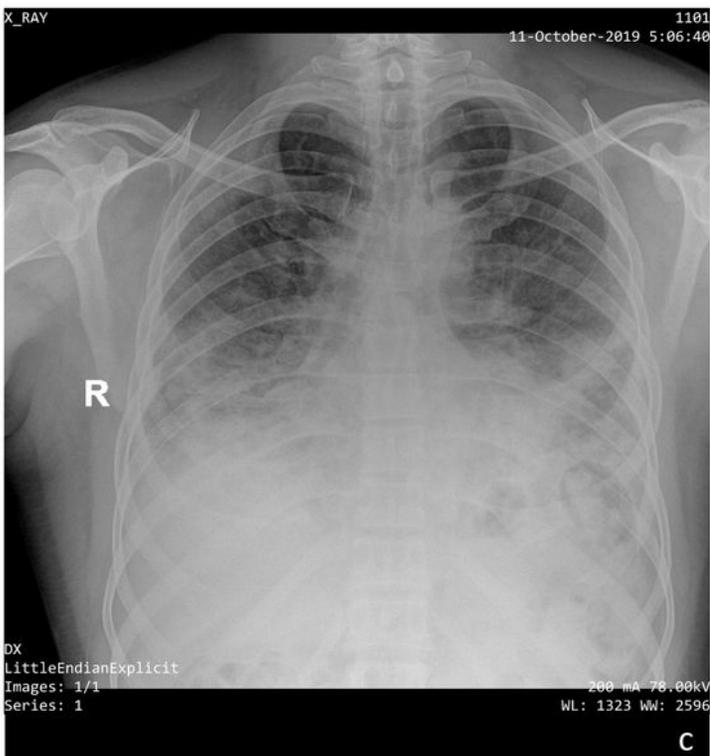
Not applicable.

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## Figures



**Figure 1**

Serial Chest X-Rays of Patient 1. Multifocal then diffuse airspace disease in a 55-years-old man. Bibasal lung consolidation with assorted trabeculae, especially in the posterior regions, overhung by discreet hazy opacities (a, b). Follow-up showing a cranially progress of the predominant inhomogeneous consolidation still coexisting with a clearly diffuse ground-glass (c). Notice the apparent replacement of alveolar densification by diffuse reticular interstitial marks with some few parahilar nodules (d)

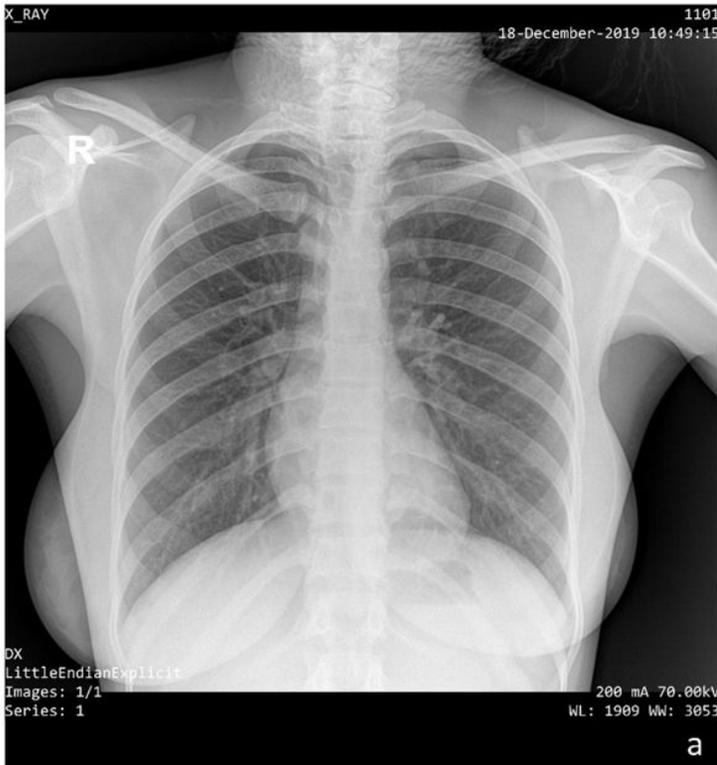


Figure 2

Chest X-Rays of Patient 2. Subnormal CXR of a 25-year-old female. Discrete peribronchovascular blur in the posterobasal regions. Normal aspect of the hila and the costophrenic angles.

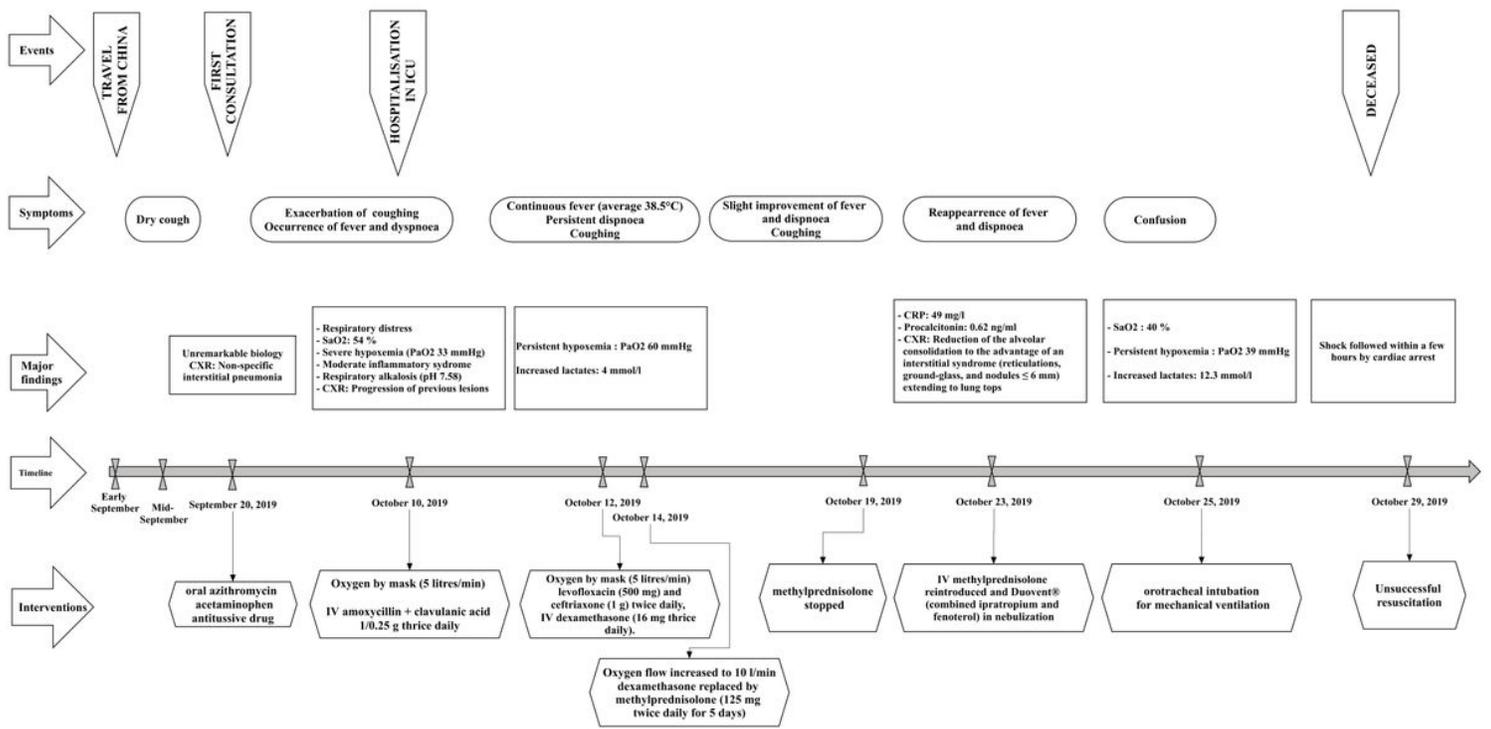
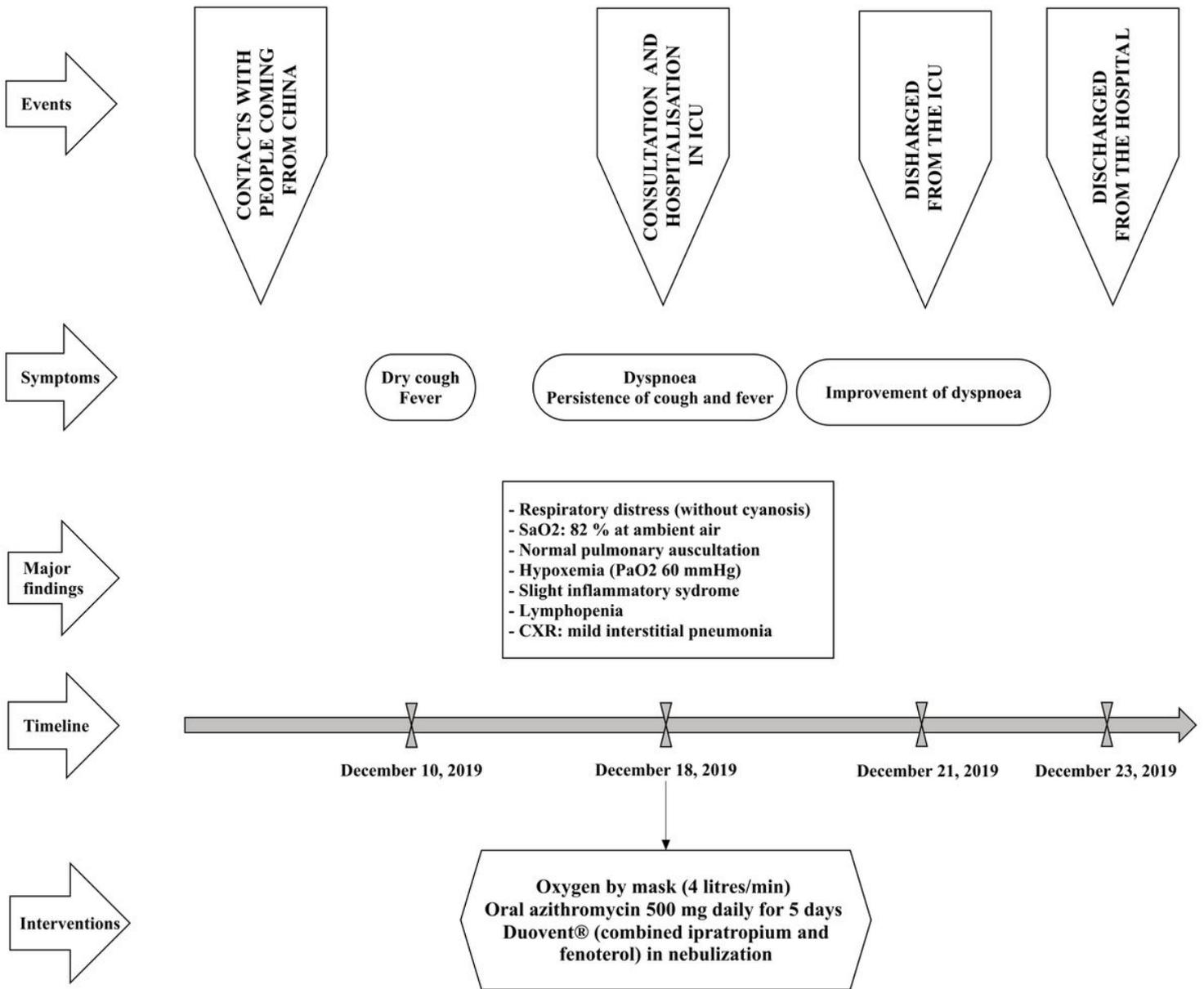


Figure 3

Summary of the 55-year-old patient's information and care organized as a timeline



**Figure 4**

Summary of the 25-year-old patient's information and care organized as a timeline

## Supplementary Files

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