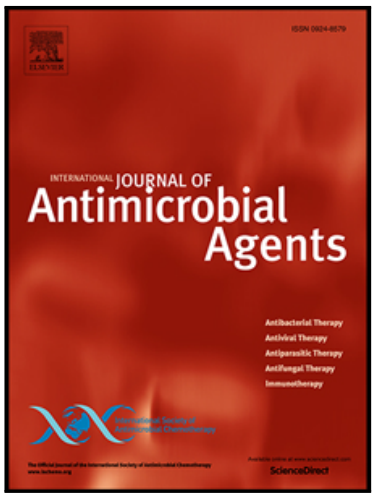

SARS-COV-2 was already spreading in France in late December 2019

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Highlights

- Covid-19 was already spreading in France in late December 2019, a month before the official first cases in the country
- Early community spreading changes our knowledge of covid-19 epidemic
- This new case changes our understanding of the epidemic and modeling studies should adjust to this new data

SARS-COV-2 was already spreading in France in late December 2019

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Key words: COVID-19, Intensive Care Unit,

Abstract

The COVID-19 epidemic is believed to have started in late January 2020 in France. We report here a case of a patient hospitalized in December 2019 in our intensive care, of our hospital in the north of Paris, for hemoptysis with no etiological diagnosis and for which RT-PCR was performed retrospectively on the stored respiratory sample which confirmed the diagnosis of COVID-19 infection. Based on this result, it appears that the COVID-19 epidemic started much earlier.

Introduction

After its onset in December 2019 in China, the new coronavirus (SARS-COV-2) spreads widely in several countries, causing COVID-19 illness.[1] World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020.[3] France reported the first cases of SARS-COV-2 related infection on January 24, 2020.[5] Both cases had a history of travel to Wuhan.[6] To the best of our knowledge, these 2 cases are believed to be the first confirmed cases in France. COVID-19 most commonly present with influenza-like illness (ILI).[7] While China was facing COVID-19 outbreak, European countries were struggling with seasonal influenza.[8] Clinical symptomatology between COVID-19 and ILIis similar,we therefore decided retrospectively to look for SARS-COV2 in respiratory samples collected in the intensive care units (ICUs) of our hospital near Paris.

Methods - Retrospective analysis

Selected records

We reviewed medical record of ICUs patients admitted for ILI between December 2, 2019 and January 16, 2020, with a negative RT-PCR performed at admission. Every respiratory sample collected in our hospital are frozen at -80°C in ThermoScientific -86°C freezer and stored for four years in case of a need for further analysis. Samples taken from patients with both ILI symptoms (fever higher than 38.5°C, cough, rhinitis, sore throat or myalgia) and ground glass opacity according to their medical record underwent SARS-COV-2 RT-PCR. A description of sample selection is available in Figure 1.

Testing for COVID-19

SARS-COV-2 RT-PCR was performed on the 14 selected biobanks between April 6 and 9, 2020. RT-PCR was performed strictly according to the Charité protocol[11] targeting the E gene, coding for envelope protein, pangenomic of SARS-COV-1 and SARS-COV-2, on a QuantStudio7 (Thermofisher) device. Positive result (Figure 2) was confirmed with the Gene finder® COVID19 Plus RealAmp kit (IFMR-45) according to the manufacturer's recommandations. This test targets 3 viral genes (RdRp, E and N coding respectively for the viral RNA-dependant RNA polymerase, envelope and nucleocapsid protein), and the cellular RNAse P gene, in order to confirm the quality of the respiratory sample.

Results:

During the study period, 14 (24%) patients out of 58 admitted for ILI were included in our analysis (Table 1).One sample was positive taken from a 42 years old manborn in Algeria, who lived in France for many years, and worked as a fishmonger. His last trip was in Algeria during August 2019. One of his child presented with ILI prior to the onset of his symptoms. His medical history consisted in asthma, type II diabetes mellitus. He presented to the emergency ward on December 27 2019 with hemoptysis, cough, headache and fever, evolving for 4 days. Initial examination was unremarkable and the performed CT scan revealed bilateral ground glass opacity in inferior lobes (Figure 3).

at admission he had a lymphopenia, an elevated C-Reactive Protein and fibrinogen while Pro Calcitonin was in normal range value. No pathogen was identified on sputum sample collected in the emergency ward. The patient was admitted to the ICU with antibiotic therapy, and evolution was favorable until discharge on December 29,2019

Discussion

We report an observation of a patient infected with COVID-19 one month before the first reported cases in our country. On admission, the patient presented clinical signs and radiological patterns frequently seen previously in the Chinese[12] and Italian[13] cohorts. Identifying the first infected patient is of great epidemiological interest as it changes dramatically our knowledge regarding SARS-COV-2 and its spreading in the country. Moreover, the absence of a link with China and the lack of recent travel suggest that the disease was already spreading among the French population at the end of December, 2019.

Further studies are required to evaluate SARS-COV-2's actual onset on French territory, the actual extent of SARS-COV-2 contamination in the population during late 2019 and January 2020, and explore the potential unnoticed deaths that could have happen at the time. COVID-19 is considered to be responsible for 86334 cases and 12210 deaths as of April 10, 2020[4] in France, but our findings suggest that these numbers could be underestimating the actual burden of COVID-19. Two recent studies suggested that around 18 to 23% infected with SARS-COV-2 were asymptomatic[16] and that around 55% of infected were caused by unidentified infected persons.[17] Our results strongly support these two assumptions, suggesting that many asymptomatic patients were not diagnosed during January 2020 and contributed to the spread of this epidemic.

Furthermore, since these results change our understanding of the dynamic of the epidemic, it also means that several models used to predict the evolution and outcomes of the SARS-COV-2 propagation might be based on biased data and would need to be adjusted to the actual profile of the epidemic.[18]

Our study presents several limitations. Firstly, due to the retrospective nature of the analyses carried out, medical records were not exhaustive and some relevant information might have been missing. Secondly, we are not able to rule out false negative results due to the sensitivity of RT-PCR[19] and a technique of storage that possibly damage the quality of the samples.[20] To avoid any false positive result we have taken all the usual precautions and we also confirmed it by two different, techniques and staff. Thirdly we restricted our analyses to only a few samples and we chose to limit the selected records to ICU patients with compatible symptoms and CT, even though most patients actually have mild symptoms. Fourthly, we restricted our analyses to patients with a negative multiplex PCR at the time even though cross contamination has been described in literature.[9] Finally, we conducted a monocentric study in the Northern Paris area, which faced a particularly high burden in this epidemic.[21] These limitations could explain why we were only able to identify one person infected with SARS-COV-2, in our population.

Declarations

Funding: No

Competing Interests: None

Ethical Approval: Not required

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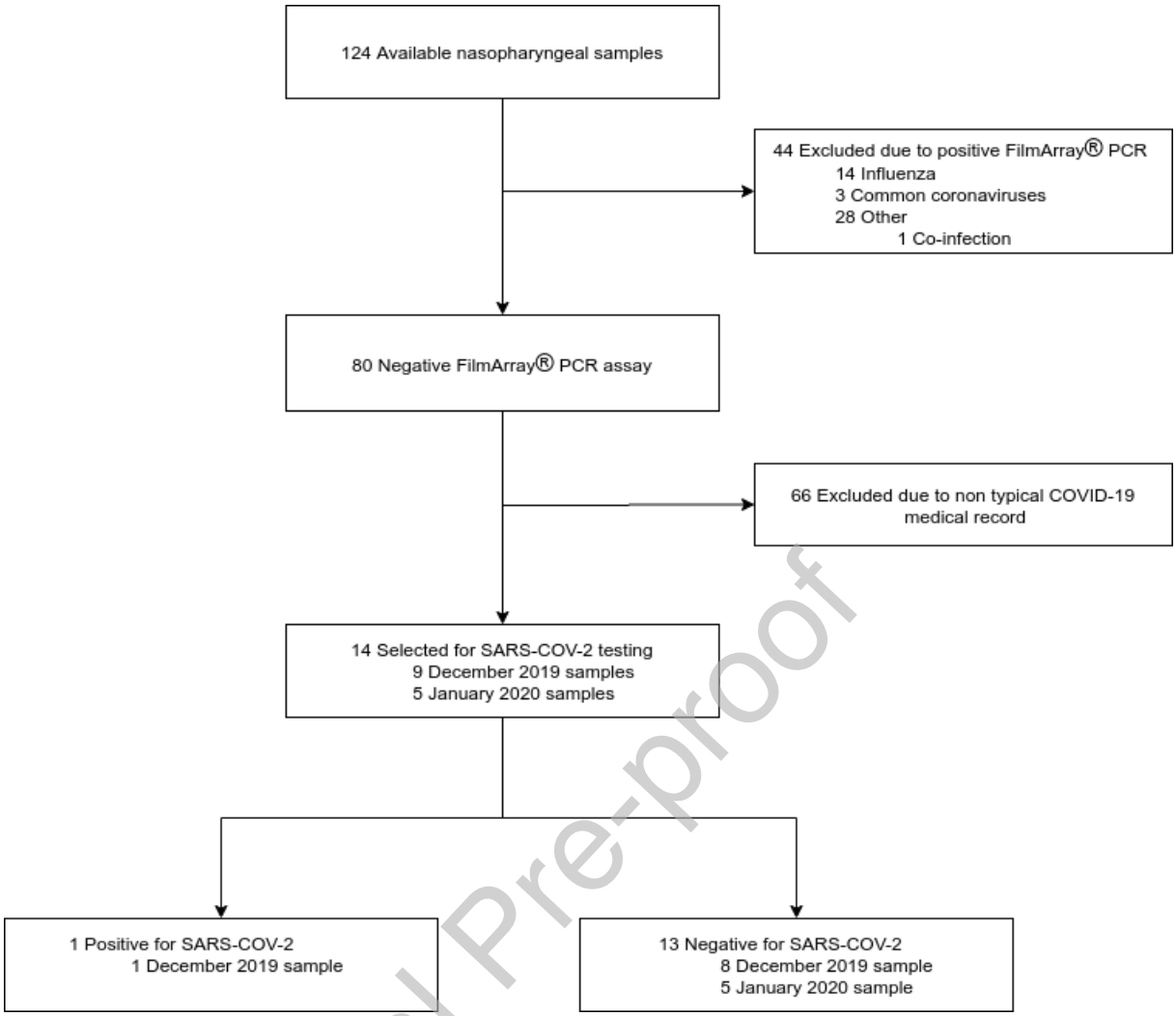

Figure 1. Selection process for testing.

SARS-COV-2 : severe acute respiratory syndrome coronavirus-2

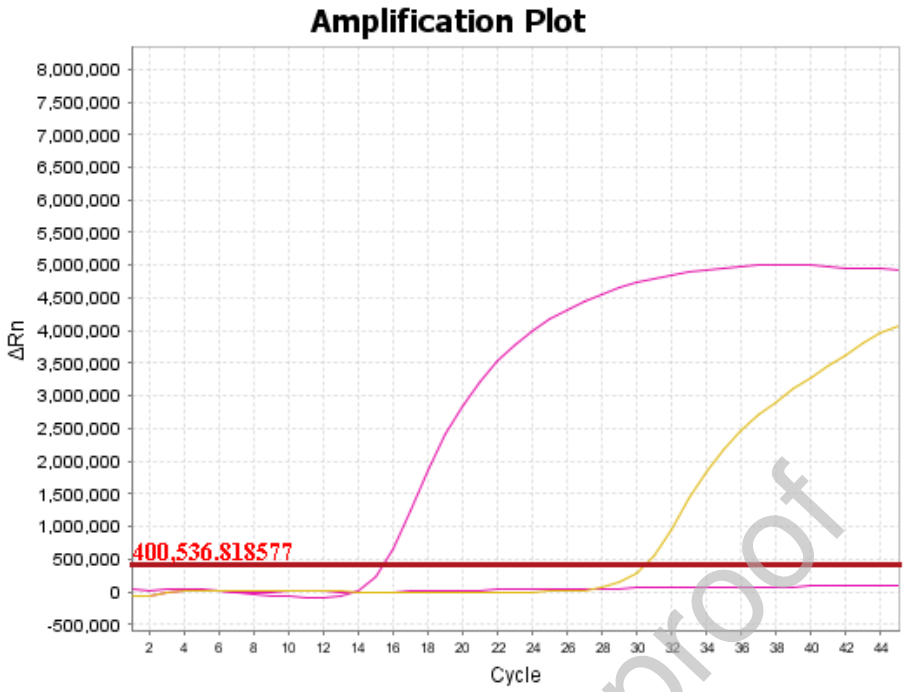

Figure 2. Result of Charite Protocol RT-PCR assay.
Patient's curb in yellow, Positive and negative test sample in purple)

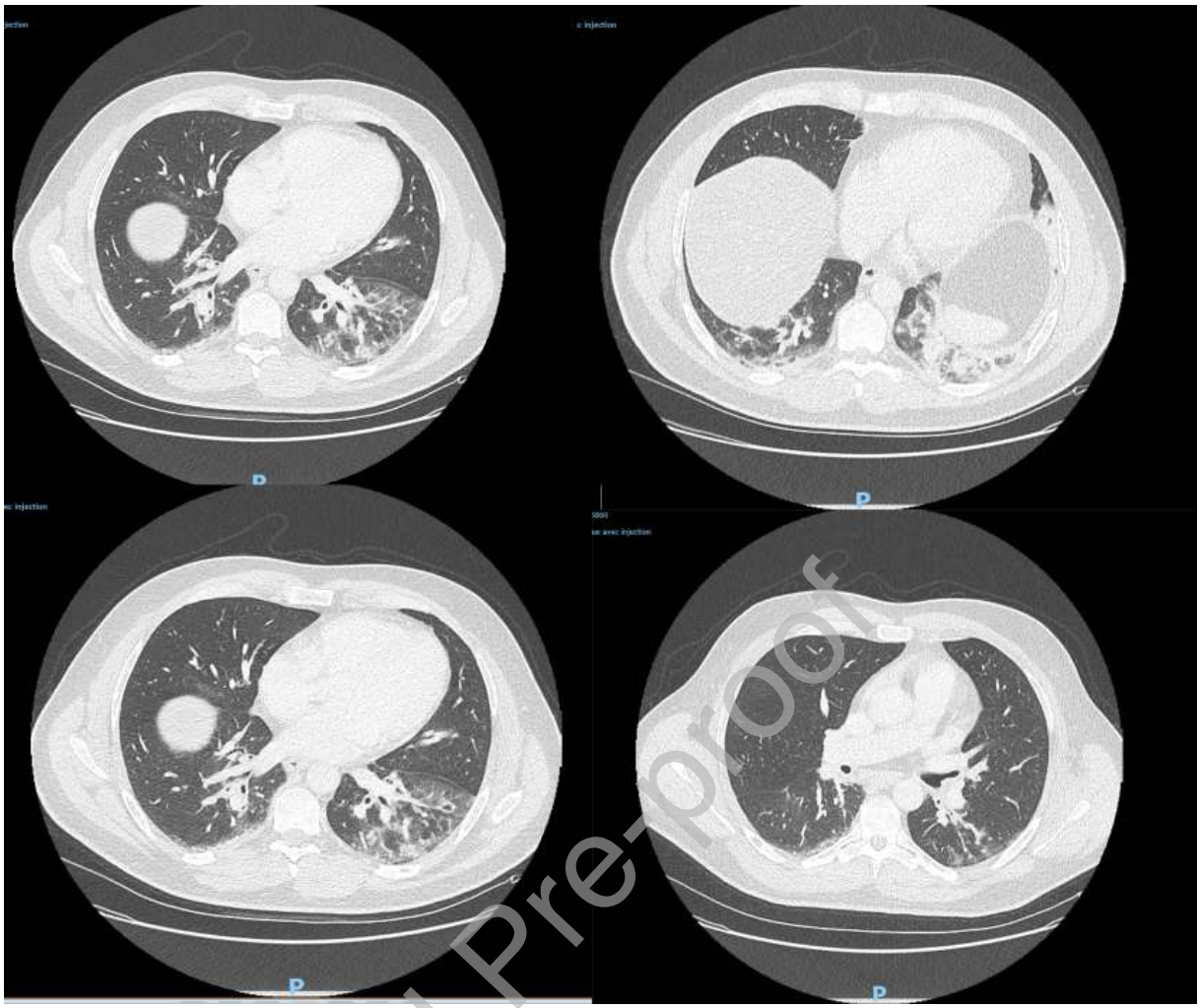

Figure 3. Chest computed tomography performed at baseline.
Bilateral ground glass opacities appear in inferior lobes