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CASE REPORT

Utility of CT scan in patients with initial negative PCR for SARS-CoV2: a report of three cases

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Abstract
PCR-based viral RNA to confirm the diagnosis of SARS-CoV-2 infection has a sensitivity of around 70%. We report three cases of patients with negative initial PCR and CT scan lesions that led us to suspect COVID-19, but which one(s) are really COVID-19?

Keywords Coronavirus · COVID-19 · CT scan · Mycoplasma pneumoniae · SARS-CoV2

Introduction

In December 2019, a new coronavirus emerged in Wuhan and rapidly spread through China and around the world [1]. The first patient with Covid-19 in Besancon University Hospital (France) was identified on 5th March 2020. Given the rapid, exponential increase in COVID-19 patients, a specific ward for patients with suspected COVID was created in our hospital.

Clinical and laboratory characteristics of COVID19 are not easily distinguishable from pneumonia caused by common respiratory tract pathogens. However, chest computed tomography (CT) scans from COVID-19 patients were characterized by bilateral ground-glass opacities and patchy shadowing [1], and this pattern can be useful in the diagnosis of COVID-19 [2].

Currently, PCR-based viral RNA detection is almost the only way to confirm the diagnosis of SARS-CoV-2 infection in practice. However, its sensitivity is rather low (ranging from 67 to 88%), depending on the RT-PCR targets and the quality of the specimen [1–4].

We report three cases of patients with negative initial PCR and different CT scan lesions that led us to suspect COVID-19, but which one(s) are really COVID-19?

Case reports

The first case was a 24-year-old man with a history of coarctation of the aorta operated on 10 years previously. He was hospitalized with asthenia, cough and fever (39 °C) for 13 days. Amoxicillin was started 5 days previously without efficiency. There was no known contact with a COVID-19 patient. On admission, saturation was 92% with nasal oxygen therapy at 1 L/min, heart rate 73 beats per minute, blood pressure 125/70 mmHg, temperature 38 °C and respiratory rate 15/min. Pulmonary auscultation found crackles in the right base. The rest of the clinical examination was unremarkable. Biological tests found hemoglobin at 14.5 g/dL, platelets 394 G/L, leukocytes 6.9 G/L with lymphocytes at 1.44 G/L, creatinine 83 µmol/L, SGOT 43 IU/L, SGPT

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30 IU/L, total bilirubin 5 µmol/L, CRP 155 mg/L, PCT 0.04 ng/mL, lactate dehydrogenase 318 IU/L, and ferritin 340 ng/mL. HIV serology was negative.

Arterial blood gas analysis with oxygen therapy at 1 L/min showed PaO_2 at 10.6 kPa, PCO2 4.99 kPa, pH of 7.46 and bases at 27.1 mmol/L. A Legionella urinary antigen test was negative. Urinary and blood cultures were negative. Bacteriological sputum culture was positive for normal flora. A CT scan showed bronchiolar tree-in-bud opacities bilaterally, predominant in the middle and lower lobes of the right lung with parenchymal condensation of blurred contours and the presence of bilateral peribronchovascular thickening with mucoid impactions (Fig. 1a). Antibiotic therapy with ceftriaxone and spiramycin was introduced for severe community-acquired pneumonia. A nasopharyngeal swab PCR for SARS-Cov2 at admission (13 days after onset of symptoms) was negative.

Repeat SARS-Cov2 PCR from nasal swab and sputum were negative at day 2 and 4. Finally, *Mycoplasma pneumoniae* serology was positive for IgM (index IgM > 27) and was confirmed by PCR in a sputum sample.

Five days later, the patient was apyretic, the inflammatory syndrome decreased (CRP 20 mg/L), oxygen saturation on air was 95%. Spiramycin was continued alone for 5 days. The patient was discharged. After 15 days, there was no recurrence of infection.

The second patient was a 65-year-old man with a history of dyslipidemia. He had been suffering from asthenia, fever at 40 °C and headache for 10 days and was hospitalized due to the onset of shortness of breath. At admission, oxygen saturation was 90% requiring nasal oxygen therapy at 2 L/min. His heart rate was 90/min, blood pressure 130/80 mmHg, respiratory rate 17/min, temperature 37 °C. Pulmonary auscultation found bilateral crackles.

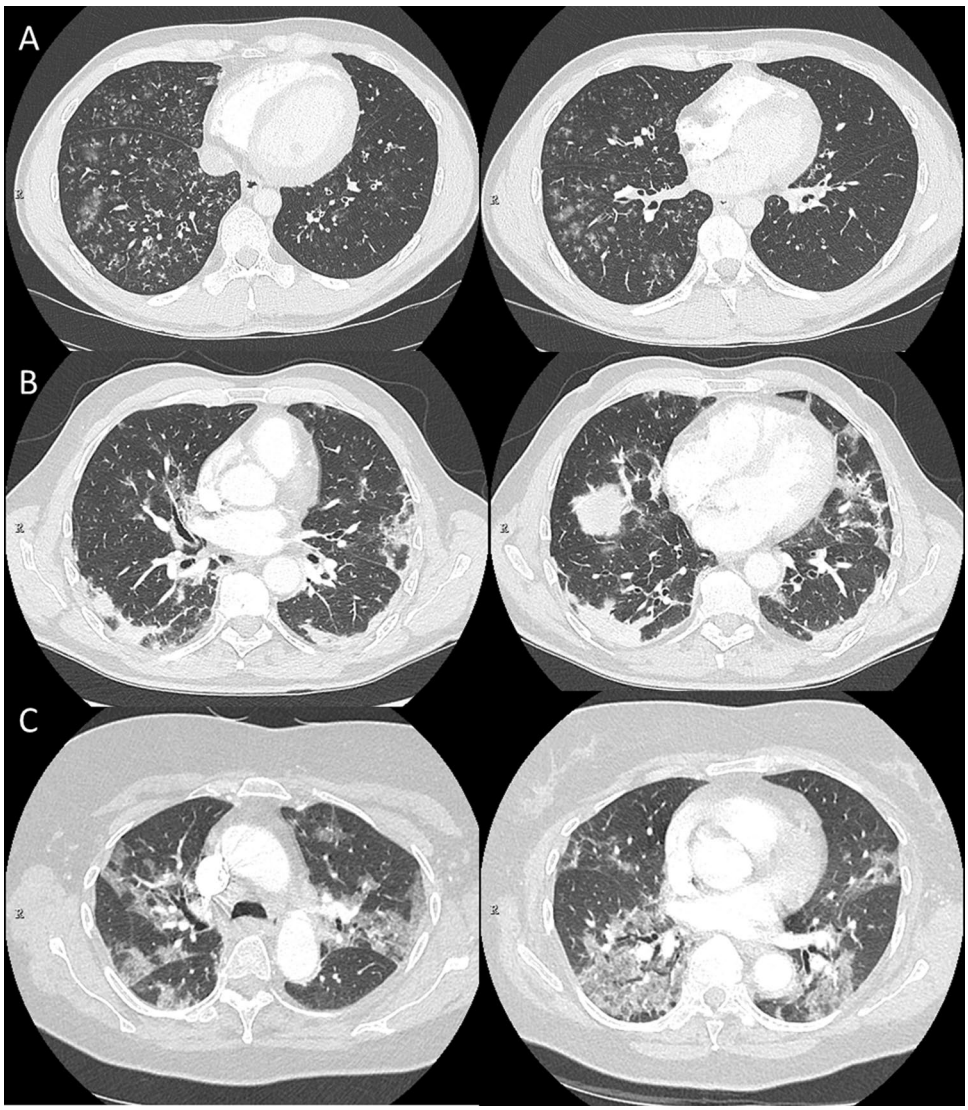

Fig. 1 Thoracic computed tomography scan of three patients with pneumonia and suspected COVID-19. **a** The CT scan of the first patient showed bronchiolar tree-in-bud opacities bilaterally predominant in the middle and lower lobes of the right lung with parenchymal condensation of blurred contours. The final diagnosis was *Mycoplasma pneumoniae* pneumonia. **b** The CT scan of the second patient showed peripheral, diffusely distributed subpleural ground glass opacities associated with alveolar condensation of peripheral distribution predominant in the lower lobes. The final diagnosis was COVID-19. **c** The CT scan of the third patient revealed bilateral patchy ground-glass opacities with areas of thickened septal lines (forming a crazy paving pattern), predominant in subpleural areas. The final diagnosis was COVID-19

Chest CT at admission revealed peripheral, diffusely distributed subpleural ground glass opacities associated with alveolar condensation of peripheral distribution, predominant in the lower lobes (Fig. 1b). On biological tests, hemoglobin was 13 g/dL, platelets 417 G/L, leukocytes 6.4 G/L with lymphocytes 1.05 G/L, creatinine 84 µmol/L, SGOT 87 IU/L, SGPT 83 IU/L, total bilirubin 10 µmol/L, CRP 88 mg/L, PCT 0.21 ng/mL, lactate dehydrogenase 451 IU/L, and ferritin 3173 ng/mL.

Arterial blood gas analysis with oxygen therapy at 3 L/min showed PaO_2 at 14 kPa, PCO_2 5.03 kPa, pH of 7.48 and bases at 27 mmol/L.

A nasopharyngeal swab PCR for SARS-Cov2 performed at admission (10 days after onset of symptoms) was negative. Antibiotic therapy with ceftriaxone was introduced. Repeat PCR at day 3 was positive for SARS-Cov2. Four days later, the patient's clinical state improved with oxygen withdrawal and the fever disappeared. No specific therapy was given for COVID-19.

The third patient was a 63-year-old woman with a history of arterial hypertension. Symptoms had begun 10 days previously, with cough and fever at 38.5 °C. Two days later, the patient consulted her general practitioner, and a diagnosis of pneumonia was retained. Antibiotic therapy with amoxicillin was introduced. Seven days later, the patient developed dyspnea with minimal effort and oxygen saturation of 90%. The patient was then admitted to hospital. On biological tests, hemoglobin was 13.4 g/dL, platelets 309 G/L, leukocytes 7.1 G/L with lymphocytes at 1.62 G/L, creatinine 60 µmol/L, SGOT 51 IU/L, SGPT 28 IU/L, total bilirubin 7 µmol/L, CRP 220 mg/L, PCT 0.68 ng/mL, lactate dehydrogenase 537 IU/L, and ferritin 1738 ng/mL. Arterial blood gas analysis with oxygen therapy at 1L/min showed PaO_2 of 9 kPa, PCO_2 3.95 kPa, pH of 7.49 and bases at 26 mmol/L.

Chest CT scan showed bilateral patchy ground-glass opacities with areas of thickened septal lines (forming a crazy paving pattern), predominant in subpleural areas (Fig. 1c).

A nasopharyngeal swab PCR for SARS-Cov2 performed at admission (10 days after onset of symptoms) was negative, but repeat PCR at day 2 was positive. Corticosteroid therapy was introduced (1 mg/kg) for seven days. Three days later, oxygen therapy was stopped. The patient improved on day 8 and was discharged.

Discussion

We describe three different CT scan patterns of patients hospitalized for pneumonia during the Covid-19 pandemic with negative initial PCR for SARS-CoV2. Ground glass opacities and condensation, with peripheral and sub-pleural distribution are typical of COVID-19, whereas tree-bud lesions should suggest another diagnosis. In the context of the pandemic, and in the absence of a proven antiviral therapy for COVID-19, effective infection control measures, including patient isolation, are critical. Hence, precise diagnostic criteria are essential.

Moreover, other infectious agents responsible for pneumonia, which requires specific treatment, should continue to be investigated.

Currently, PCR-based viral RNA detection is almost the only way to confirm the diagnosis of SARS-CoV-2 infection in practice, but its sensitivity remains insufficient [5]. The performance of RT-PCR depends on many factors, such as the sample types, the stage of infection of the patient, the skill with sample collection, and the quality and consistency of the PCR assays [5, 6]. In this study, samples were taken from nasopharyngeal swabs performed by trained nurses. Only one sample from patient 1 was taken from sputum. All nurses working in the COVID unit were trained by a medical health officer to perform nasopharyngeal swabs.

Many cases that were strongly epidemiologically linked to SARS-CoV-2 exposure and with typical lung radiological findings remained RNA negative in their upper respiratory tract samples.

The chest CT scans of COVID-19 patients are characterized by ground-glass opacities and bilateral patchy shadowing in peripheral and sub-pleural areas, with bilateral lower lobe infiltration [7]. Xu et al. reported 50 patients with confirmed COVID-19 and found that the CT imaging on admission mainly presented patchy ground glass opacities in the peripheral areas under the pleura and infiltration of bilateral lower lobes [8].

Different studies confirm the primary pattern on CT imaging of COVID-19 pneumonia is ground glass opacities of different subtypes, with prominence of the distribution in the lower, posterior and peripheral lung, which can quickly change during hospitalization with the appearance of condensations [8, 9]. CT scan has an important role in the diagnosis of COVID-19, facilitating patient triage according to severity, and early implementation of quarantine or treatment, depending on the clinical presentation. The CT scan of our first patient was not typical of COVID-19, with the absence of a peripheral distribution, and the absence of ground glass opacities. However, parenchymal condensation of blurred contours could wrongly lead us to a diagnosis of COVID-19.

For laboratory tests, it has been reported that most patients had lymphopenia and elevated C-reactive protein [10]. Elevated ferritin has also been associated with ARDS [11]. However, no biological analysis was specific for COVID-19.

Conclusion

Chest CT scan plays an important role in the diagnosis of COVID-19, especially in patients with negative PCR. Other etiologies of pneumonia should not be overlooked because of the COVID-19 pandemic.

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Author contributions KB, CP, CC, SH, AM, FG designed the study. KB, FG collected the data and wrote the initial draft. KB performed the statistical analysis. All authors participate in editing, and approved the final version of the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare no competing financial interest and received no grants related to this study.

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