Positive Chest CT and Negative RT-PCR Testing in a Case of Suspected COVID-19

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Abstract

Both chest computerised tomography (CT) and real time-polymerase chain reaction (RT-PCR) from swab samples are used in the diagnosis of 2019 novel coronavirus disease (COVID-19). RT-PCR is associated with increasingly high false-negative rates, and sensitivity is dependent on how samples are taken. Chest CT is a more sensitive test, and the characteristic findings of ground-glass opacification are often found before positive RT-PCR results. Here, we present a 61-year-old female patient admitted with pyrexia and diarrhoea, with a recent travel history from Egypt. She was initially managed with intravenous antibiotics, but went into severe acute respiratory distress syndrome and was intubated. Serial chest X-ray (CXR) revealed patchy opacification correlated with severity of symptoms. Chest CT showed widespread extensive ground glass opacification resembling COVID-19 pneumonia. Two RT-PCR analyses from COVID-19 swabs were negative, as were investigations for other possible causes of ground glass opacification. She had supportive treatment for her symptoms, responded to this well, and was discharged home with no sequelae of disease. This case demonstrates the diagnostic pathway for COVID-19, differential diagnoses for radiological findings associated with COVID-19, and emphasises the advantage of CT as a diagnostic modality over RT-PCR in a subsection of cases.

Keywords: *COVID-19; Chest computerised tomography; RT-PCR; SARS-CoV-2*

1. Introduction

2019 novel coronavirus disease (COVID-19) is caused by SARS-COV-2 virus, and manifests itself through a clinical spectrum from asymptomatic to severe acute respiratory distress and death. Treatment is supportive, though various lysosomotropic and antiviral agents, like hydroxychloroquine and remdesivir respectively, are being investigated in various trials all over the world [1].

Initial studies from China have identified fever as the most common clinical symptom, with 83%-98% of patients developing fever during their disease course [2-4]. However, other clinical symptoms are also encountered in COVID-19, including cough, fatigue, shortness of breath, sore throat, and diarrhoea [3]. Biochemical markers have also been associated with COVID-19, and are often used clinically in the diagnostic pathway. These include lymphocytopenia (63%), elevated transaminases (37%), and elevated hypersensitive troponin I (12%) [5]. Derangement of these biomarkers are found more frequently in more severe cases and in deceased patients [3,6].

Currently COVID-19 infection is diagnosed through swabs taken from nasal and throat mucosa using real time-polymerase chain reaction (RT-PCR), however, the sensitivity of this assay is reliant on sample taking, and is estimated at only 66%-80% [7]. The most sensitive investigation seems to be chest computerised tomography (CT); 100% of COVID-19 positive patients in the Huang et al. study had chest CT changes, and 96% of COVID-19 positive patients in the Guan et al. study had abnormal chest CT [2,3]. Previous studies have demonstrated CT findings of ground glass opacities with multilobe and posterior involvement [8].

Here, we present a case of a patient with two negative COVID-19 RT-PCR swabs, but with radiological findings on chest X-ray (CXR) and chest CT suggestive of COVID-19. We have outlined her journey from presentation, development of respiratory symptoms, intubation on an intensive care unit (ICU), extubation, to discharge. We have included pertinent investigations for the cause of her respiratory presentation in the 'Investigations' section of this case report.

2. Case Presentation

A 61-year-old Caucasian female presented to a hospital in the United Kingdom in early March 2020 with pyrexia, diarrhoea and cough. She had a background of essential hypertension, polymyalgia rheumatica, osteoporosis, and hypothyroidism, and had recently returned after a holiday to Egypt.

Admission blood tests showed mild hypokalaemia, a mildly raised C-reactive protein of 19, and mild uncompensated respiratory alkalosis. CXR on admission showed no consolidation or collapse (FIG. 1A). She was therefore initially managed as traveller's diarrhoea with intravenous ciprofloxacin according to local guidelines, but within few days she started to develop shortness of breath and her cough increased in frequency, still dry in nature.
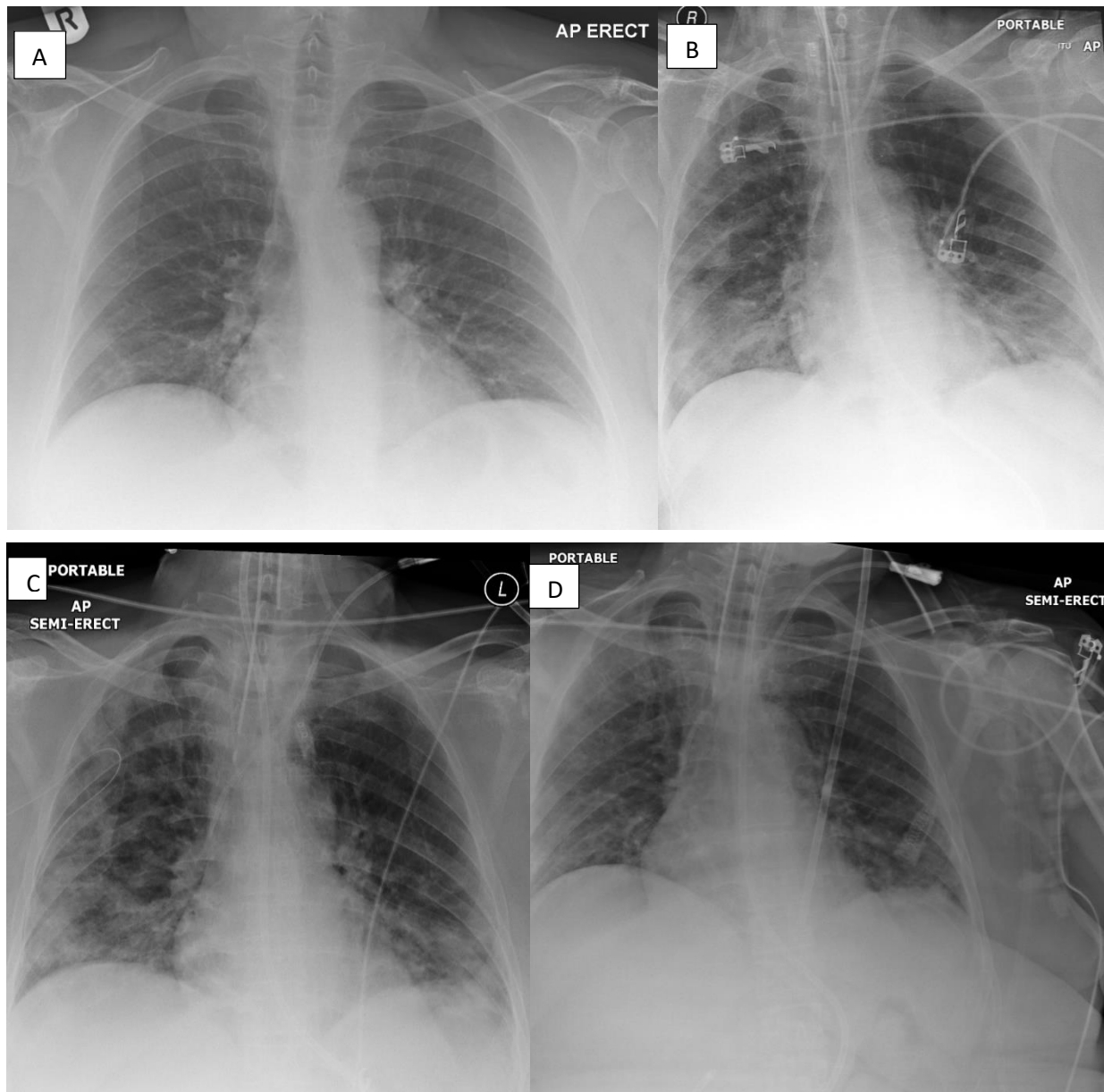
FIG. 1. **Serial chest X-ray during patient admission. (A) no obvious consolidation or collapse taken at the time of admission. (B) Patchy bilateral opacification taken before intubation. (C) Increase in bilateral opacification in both lungs, taken while the patient was intubated in the intensive care unit and the condition was at worst. (D) Resolving of opacifications, taken before discharge.**

Repeat CXR (FIG. 1B) showed interval appearance of patchy air spaces in bilateral lower zones. She was managed for community acquired pneumonia, but continued to desaturate and had increasing oxygen demands which dictated the need to consider alternative diagnoses. Swabs were taken for upper respiratory panel, Influenza A and B, and COVID-19, blood cultures were taken, and she was also tested for malaria, dengue fever, and HIV. Further evaluation with chest CT (FIG. 2) showed extensive areas of ground glass opacities which were highly suspicious of COVID-19.

FIG. 2. **Computed Tomography of the Chest taken 4ᵗʰ day post admission showing widespread extensive patchy opacification involving almost whole of the right lung and middle lower zone of the left lung.**

On the 7th day post admission she was intubated in ICU due to sudden deterioration and dropping saturations. All previous investigations were negative and there was no causative organism identified on blood culture. Due to high clinical suspicion, she was treated as COVID-19 and re-swabbed. She was managed with supportive therapy and received intravenous antibiotics to cover for bacterial co-infection. Other infective and rheumatological causes of ground glass opacities were investigated, but all investigations including repeat COVID-19 RT-PCR were negative.

She had three extubation attempts. On first extubation she developed a small pneumothorax that required a chest drain, while on second extubation she developed vocal cord oedema for which she received intravenous steroids. During her stay in the hospital her progress was monitored with regular blood tests and serial CXRs, which showed improvement with time (FIG. 1C, 1D). On the 17th day post admission, after being intubated for 10 days, she had a successful extubation with no complications. She was stepped down to a medical ward for four days, where she was discharged home after an uneventful recovery.

3. Investigations

3.1 Biochemistry

Biochemical markers	Admission	Pre-Intubation	During Intensive care stay	Post-extubation	Before Discharge
C-Reactive protein (mg/dL)	12.8	347.5	312.4	37.2	59.5
Lymphocytes ($\times 10^9$/L)	1.8	1.5	0.9	2.8	3.5
Neutrophils ($\times 10^9$/L)	2.9	5.7	5.4	10.1	7.4
White Blood cells ($\times 10^9$/L)	5.0	7.5	6.9	14.0	11.9

3.2 Rheumatologic Investigations

1) Rheumatoid Factor 10.8 IU/mL (within reference range)
2) *CCP* Antibody 2.0 U/mL (within reference range)
3) *IgE* level 67 kU/L (within reference range)
4) *ENA* antibody level negative (tested for *Ro, La, Sm, RNP, Jo-1, Scl-70*, and *CENP-B*)
5) Antinuclear antibody screen negative (tested for *U1RNP, SS-A/Ro*(60 kDa, 52 kDa), *SS-B/La, Centromere B, Scl-70, Jo-1 Fibrillarin, RNA Pol 3, Rib-P, Pm-Scl, PCNA, Mi-2 proteins, Sm proteins and dsDNA*.)
6) Antineutrophil cytoplasmic antibodies not detected

3.3 Microbiology

1) Two negative COVID 19-swabs.

2) HIV 1 and 2 *AB* and *P24 Ag* not detected.

3) Complete Dengue virus RNA screen negative.

4) Upper respiratory panel screen tested through PCR: *Adenovirus, Coronavirus HKU1, Coronavirus NL63, Coronavirus 229E, Coronavirus OC43, human Metapneumovirus, Human Rhinovirus/Enterovirus, Influenza A, Influenza A/H1, Influenza A/H3, Influenza A/H1-2009, Influenza B, Parainfluenza Virus1, Parainfluenza Virus2, Parainfluenza virus 3, parainfluenza virus 4*, Respiratory Syncytial Virus, all not detected.

5) *Influenza A & B* not detected.

6) Four Blood Cultures: only the second blood culture showed growth from contaminant (mixed skin organisms).

7) MRSA MCS swab negative from nose, axilla and groin.

8) Pneumococcal and Legionella Antigen not detected.

9) MCS sputum for Acid fast bacilli negative for three consecutive early morning sputum samples.

10) MCS Faeces: *Cryptosporidium*, *Giardia lamblia*, *Salmonella* Species, *Shigella* species, *Campylobacter* species, *E. coli* species all not detected.

11) Hepatitis E *IgM* not detected.

12) Hepatitis A Antibody not detected.

13) *Aspergillus* Antibody level not detected.

14) Acid fast bacilli screen from bronchial washing showed no AFB detected.

15) Avian precipitins blood: *IgG* to budgerigar, pigeon, and parrot not detected.

16) *Coxiella burnetii* nucleic acid screen negative.

3.4 Echocardiogram

Portable study performed on ward.

Overall left ventricular systolic function good. Ejection Fraction >55%.

No significant valve pathology.

4. Discussion

Our case is unique due to the patient's initial clinical presentation of diarrhoea, the extensive negative investigations for an infectious or autoimmune cause for her respiratory symptoms, and the chest CT showing ground-glass appearance suggestive of COVID-19. The focus on her diarrhoea symptoms took precedence initially due to patient concern and the date of presentation, when the United Kingdom had relatively few COVID-19 cases. However, when retrospectively analysed, she had presented with the most common symptoms of COVID-19, namely fever and dry cough. Travel history was also a concern, and may point a clue on how she acquired the infection through social contact. Sudden deterioration with respiratory symptoms and characteristic changes on chest CT suggested COVID-19 infection, but the COVID-19 RT-PCR test was negative twice, leading to extensive further investigation of other differentials.

Overall, the ground glass opacification found on CT could be divided into various categories by different sets of classification. Broadly, we can split this into infectious processes, chronic interstitial diseases, acute alveolar diseases, and other causes. In the diagnostic workup we investigated for possible causes for her respiratory and CT findings, which included aspergillosis, *C. burnetii* infection, viral causes of pneumonia, and rheumatological causes including vasculitis. We conducted RT-PCR for COVID-19 twice but the viral load was undetected on both of the taken samples. Since most of possible causes of the ground glass opacification were ruled out, the diagnosis has to take into account the clinical presentation. Hence, COVID-19 was deemed to be most likely diagnosis; this was supported by the fact that she had rapid respiratory deterioration in the time frame of current COVID 19 pandemic.

Rapid identification of COVID-19 patients is essential for accurate triage and correct treatment. Currently, RT-PCR is used for diagnosis. Previous studies showed that almost all the patients who diagnosed with COVID-19 had characteristic changes on chest CT [2,3]. A recent study from China of 1014 cases confirmed this, and showed a sensitivity of chest CT of 97% based on positive RT-PCR scans [7]. Interestingly, in patients with negative swab RT-PCR, 75% patients had positive chest CT. This was able to identify a large proportion of patients who later on tested positive with RT-PCR [7].

In our patient, chest CT was positive but RT-PCR was negative twice. We suggest that in light of limited sensitivity for RT-PCR, clinical judgement and chest CT for patients presenting with symptoms highly suggestive of COVID-19 should be utilised for diagnosis. It also dictates a dire need to find new more highly sensitive ways to screen for COVID-19 infection; the emergence of new serological testing may serve this purpose.

Another learning point is the appearance of serial chest X-rays and their use in monitoring the progression of the disease. For our patient, the degree of patchy opacification in the CXR reflected the degree of severity of the disease itself. Additionally, CXR is a widely available and cost-effective technique, and could serve a very potent role in determining the progression and response to treatment of COVID-19.

5. Learning Points

1) There are limitations in the sensitivity of the RT-PCR COVID-19 swab test, hence other investigation modalities should be utilised to supplement the test, especially in cases with high clinical suspicion.

2) Computed tomography is very sensitive in finding the characteristic changes in lungs infected with COVID-19.

3) Early recognition and isolation are very important to prevent the spread both to other patients and to medical health professionals.

4) Serial Chest X-rays are a cost effective and reliable tool to check the progression of the disease.

5) Though so far, no established treatment method is identified for COVID-19 but supportive therapy and ventilatory support in selected patients could warrant effective outcome.

REFERENCES

1. Lythgoe MP, Middleton P. Ongoing Clinical Trials for the Management of the COVID-19 Pandemic. Trends Pharmacol Sci. 2020.

2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.

3. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020.

4. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13.

5. Sun P, Lu X, Xu C, et al. Understanding of COVID-19 based on current evidence. J Med Virol. 2020;92(6):1-4.

6. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368.

7. Ai T, Yang Z, Hou H, et al. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology. 2020:200642.

8. Caruso D, Zerunian M, Polici M, et al. Chest CT Features of COVID-19 in Rome, Italy. Radiology. 2020:201237.