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Case Series

Safety with Green Zones in Hospital Medicine Practice Post Covid-19: A Case Series Report -

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ABSTRACT

We describe four complex cases of patients who had presented to hospital with a diagnostic dilemma wherein they came with signs and symptoms suggestive of COVID-19 infection with clinical, biochemical and radiological evidence of the infection but they had recurrent negative tests with nasopharyngeal RT-PCR swabs. Differential diagnoses were entertained in all patients and COVID-19 was not the only possibility in this group. We however feel that patients like these pose a challenge especially in the respiratory wards with aerosol generating procedures and a vulnerable patient cohort. Hence early identification and isolation of the suspected COVID-19 infections should take priority to ensure appropriate patient care is being delivered.

BACKGROUND

The novel coronavirus SARS-CoV2 has caused significant global morbidity and mortality. The clinical course of the virus can range from a mild respiratory tract illness to full-blown acute respiratory distress syndrome (ARDS) in severe cases. Currently, the infection is confirmed using RT-PCR techniques which have shown a 30% false negative [1].

We describe four cases where standard oxygen therapy & Continuous Positive Airway Pressure (CPAP) was used in the treatment similar to COVID-19 patients despite having serial negative swabs to highlight the importance of looking at a holistic picture to make a diagnosis rather than relying on negative RT-PCR swabs alone to rule out the infection. This we feel will lead to appropriate clinical care being delivered when infection control measures are being followed.

CASE DESCRIPTION

Case 1

A 71-year-old female non-smoker with no co-morbidities was admitted with shortness of breath, pyrexia and a non-productive cough. She had been reviewed in the community and had completed a course of oral Amoxicillin. She developed tachycardia, tachypnoea and hypoxia with a type one respiratory failure ultimately requiring hospital admission.

Given the concern raised by her clinical picture, inflammatory markers (Table 1) and a suspicious chest x-ray (Figure 1), she was initially treated as community acquired pneumonia but the high oxygen requirement and biochemical markers had prompted us to do a CT pulmonary angiogram (CTPA) which showed extensive bilateral ground glass changes felt to be consistent with COVID-19 (Figure 2). Due to persistent hypoxia despite standard oxygen therapy, she was commenced on CPAP.

During her admission, she had three serial negative RT-PCR COVID-19 swabs. However, the progression of her illness alongside high clinical suspicion led to a differential diagnosis of pneumonitis secondary to COVID-19 which ultimately prompted the use of steroids in addition to CPAP.

The patient ultimately improved after seven days of CPAP, a second course of antibiotics and a steroid wean. She was subsequently discharged home after making a full recovery.

Case 2

A 55-year-old male was admitted with pyrexia, cough and shortness of breath. He had a raised BMI (35) but was otherwise a fit, non-smoker. On admission, he was hypoxic and tachypnoeic;

Table 1: Blood results according to day of admission for Case 1.

	Admission (Day 0)	Day 3	Day 7	Day 14
LDH	681	-	-	-
Ferritin	134	-	-	-
CRP	110	91	159	3
D-dimer	452	581	-	-
Troponin	-	-	-	-
WCC	10.26	11.49	10.95	10.68
Neutrophils	8.78	9.49	9.20	9.73
Lymphocytes	0.88	0.78	0.67	0.63



Figure 1: Case 1 admission radiograph.

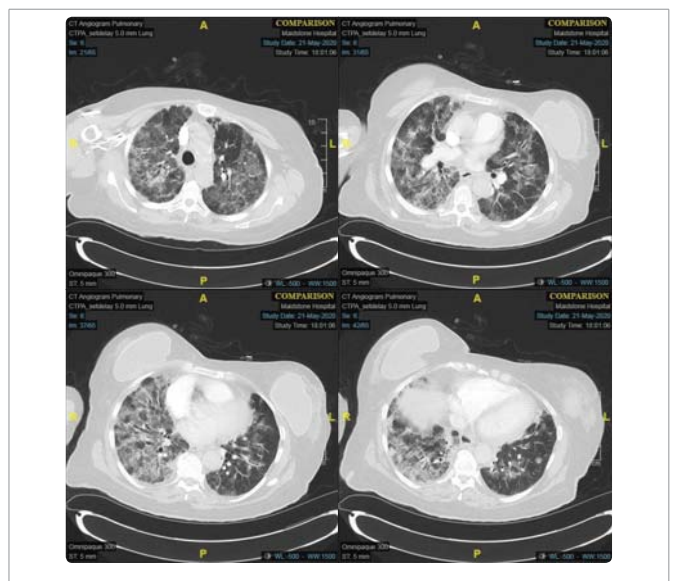


Figure 2: Cross-sectional CT images for Case 1.

his chest x-ray (Figure 3) showed evidence of bilateral peripheral infiltrates and his inflammatory markers were elevated (Table 2).

The patient had four negative serial PT-PCR COVID-19 swabs over a period of two weeks. He ultimately had a CTPA which showed bilateral peripheral consolidation with ground-glass opacification (Figure 4); this combined with his inflammatory response prompted a differential diagnosis of ARDS secondary to COVID-19.

The challenging issue was the location this patient was going to be treated due to his conflicting clinical picture.

He was managed actively with CPAP to maintain his oxygen requirement and his nutritional needs with an NG tube being placed with feeds. He required CPAP for 21 days & did not develop nosocomial infections during his stay. After extensive physiotherapy, he was discharged home with good recovery.

Case 3

A 79-year-old female presented with pyrexia, shortness of breath and a non-productive cough. She was known to suffer with frequent exacerbations of her COPD and bronchiectasis. Despite a history of heart failure, there was no evidence of decompensation preceding her admission. She was normally independent with a Rockwood clinical frailty score of 3.

Her chest radiograph showed extensive left upper lobe consolidation (Figure 5); this combined with her history and raised inflammatory markers (Table 3) led to an initial diagnosis of Community Acquired Pneumonia (CAP) on a background of emphysematous lung disease. She was treated with oral steroids,

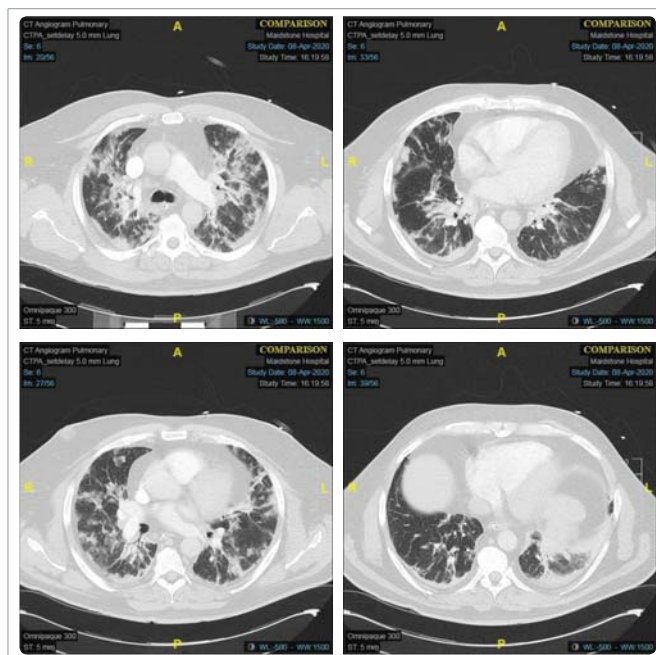


Figure 4: Cross-sectional CT images for Case 2.

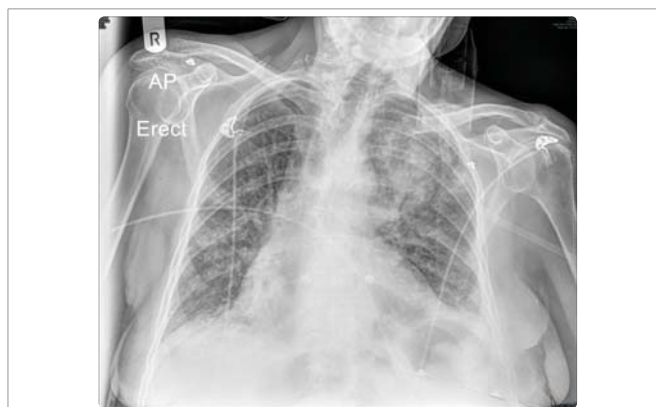


Figure 5: Case 3 admission radiograph.

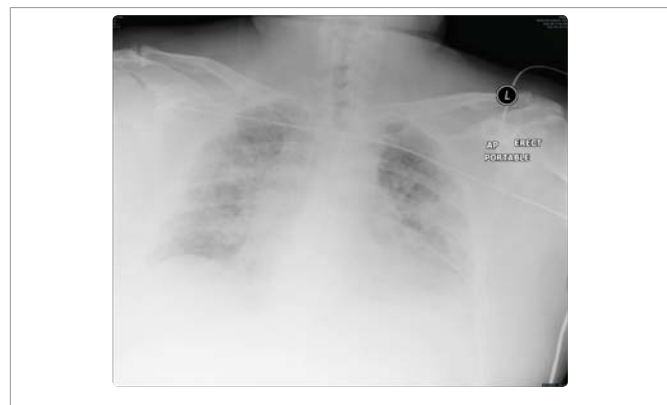


Figure 3: Case 2 admission radiograph.

Table 2: Blood results according to day of admission for Case 2.

	Admission (Day 0)	Day 3	Day 7	Day 10	Day 14
LDH	670	-	-	-	-
Ferritin	1210	-	713	590	874
CRP	271	183	65	31	148
D-dimer	-	-	-	-	506
Troponin	16	-	-	-	9
WCC	8.86	7.29	9.92	9.70	13.24
Neutrophils	7.80	5.87	7.69	7.24	10.4
Lymphocytes	0.58	0.56	0.84	1.23	1.17

Table 3: Blood results according to day of admission for Case 3.

	Admission (Day 0)	Day 3	Day 6
LDH	-	-	-
Ferritin	-	-	-
CRP	123	176	56
D-dimer	2038	-	-
Troponin	-	-	-
WCC	21.97	8.35	7.08
Neutrophils	19.58	6.94	4.75
Lymphocytes	1.52	1.08	1.78

nebulisers and intravenous antibiotics. Alternative diagnoses such as atypical pneumonia or thromboembolic disease were considered to be a possible cause of her deterioration. During her admission, she had two RT-PCR COVID-19 swabs completed 48 hours apart both of which were negative.



The patient failed to improve and ultimately had a CTPA which showed extensive ground-glass opacity most confluent in the left upper lobe with focal consolidation (Figure 6). This imaging, alongside her biochemical and clinical picture, favoured a diagnosis of COVID-19 with secondary bacterial infection. The patient required a seven-day course of CPAP but ultimately made a good clinical recovery before discharge home.

Case 4

A 54-year female non-smoker presented with shortness of breath, pyrexia and a non-productive cough. On admission, she was hypoxic, tachycardic and pyrexial with raised inflammatory markers (Table 4). Her first RT-PCR swab was negative however her chest radiograph demonstrated bilateral infiltrates (Figure 7).

She developed type one respiratory failure which necessitated supplemental oxygen therapy with a maximum requirement of 40% FiO₂. She also had a CTPA due to worsening hypoxia, which showed extensive areas of ground-glass changes (Figure 8). Given this in combination with her laboratory findings, she too was treated as a suspected COVID-19 case.

The patient was initially treated with antibiotics which were



Figure 7: Case 4 admission radiograph.

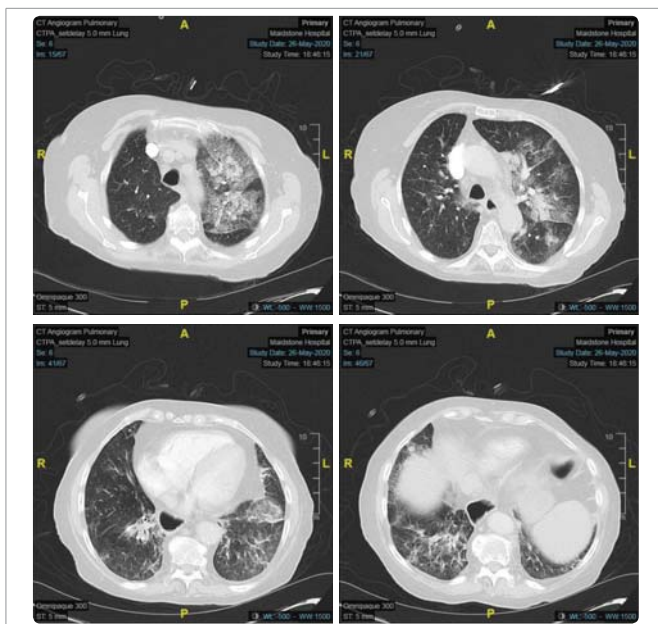


Figure 6: Cross-sectional CT images for Case 3.

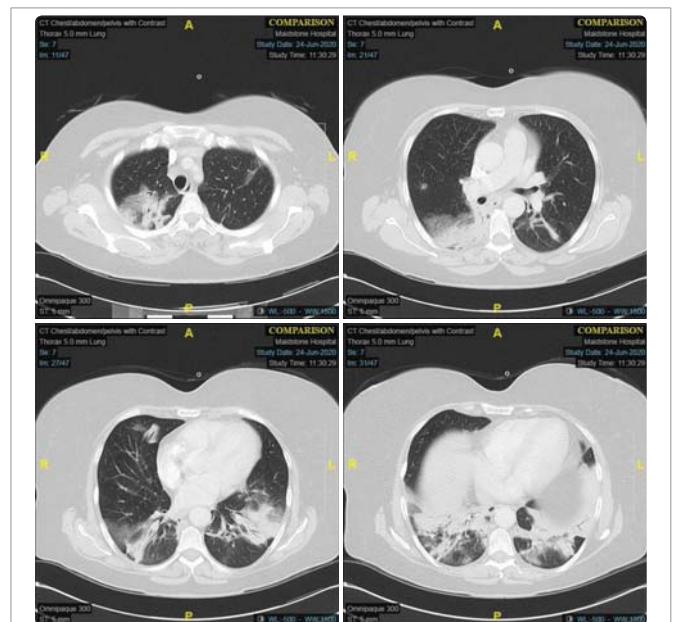


Figure 8: Cross-sectional CT images for Case 4.

subsequently stopped due to a negative atypical screen, sputum and blood cultures. She was started on steroids for suspected pneumonitis from COVID-19 and ultimately made a rapid recovery with reduction in her oxygen requirements without the need for CPAP and was discharged home after making a good recovery.

Table 4: Blood results according to day of admission for Case 4.

	Admission (Day 0)	Day 3	Day 7
LDH	-	-	-
Ferritin	1137	-	-
CRP	177	74	4
D-dimer	-	-	-
Troponin	3	-	-
WCC	13.5	11.3	13.8
Neutrophils	10.0	8.4	10.3
Lymphocytes	1.53	1.1	3.6

DISCUSSION

The cases described above show us that the universally accepted RT-PCR diagnosis is not entirely reliable on its own to exclude COVID-19 infection. If we were to rely on this alone, this would present a significant infection risk to both staff and other vulnerable patient groups due to the diagnostic dilemma. Existing reports suggest that there is only a 70% sensitivity of obtaining a definitive diagnosis from an RT-PCR swab versus a 98% diagnostic yield with CT scanning [1].

We believe this to be in line with other authors due to the diagnostic yield from the swab and its dependence on the following factors [2,3];



- Immature development of nucleic acid detection technology
- Variation in detection rate from different manufacturers
- Low patient viral load
- Improper clinical sampling: The reasons for the relatively lower RT-PCR detection rate in our sample compared to a prior report are unknown
- intrinsic limitations (i.e. collection and transportation of samples and diagnostic kit performance)

In view of the significant infectivity caused by COVID-19, a single or even multiple negative swabs does not necessarily dismiss the diagnosis especially in the presence of clinical, biochemical and radiological suspicion as demonstrated by the cases described above. Given the extensive and rapid spread of disease, more so when the R-value exceeds 1 [4], as well as the potential long term effects of the disease and associated therapies, we recommend that these aspects could supersede negative RT-PCR swabs in patients with high clinical suspicion.

As stated by other authors, if the pre-test probability is high, a CT scan would be useful to appropriately triage patients, ensure strict isolation protocols are maintained and treatment guided appropriately [5].

Several authors have already described that swab negative status does not rule out the possibility of COVID-19 infections; this has been described extensively and some have even recommended the use of bronchoalveolar lavage to aid in obtaining a diagnosis [6].

One of the factors that needs to be looked into and which would be extremely useful during the winter months which traditionally carry a high respiratory disease load would be to triage these patients appropriately and isolate away from other vulnerable groups of respiratory patients who have significantly impaired respiratory function and would do poorly in the event of a COVID-19 co-infection.

We also feel there is huge benefit in isolating these “Grey” cases away from the green zones dedicated for non-COVID infections, where people with advanced age, metabolic conditions and poor physiological reserve might succumb to the infection either due to the respiratory status or from the complications.

Learning Points

- Adopting Biochemical parameters at the front door for patients with respiratory symptoms: we recommend a COVID-19 blood test bundle including but not limited to: Full blood count, Urea, Electrolytes, Renal function, Liver function, Troponin, D-Dimer, Ferritin, Lactate Dehydrogenase, Pro-calcitonin, C-Reactive Protein
- CT is an important diagnostic aid in patients with diagnostic ambiguity and could supersede RT-PCR swabs [1,2,7].

Ideally, isolation in a negative pressure side room and the use of full respiratory precautions in these patients would be important not only to prevent them from infecting vulnerable cohorts but also to minimise the risk of them developing secondary infections themselves. This would also help protect healthcare workers and minimise any potential cross contamination between other patients.

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