

Detection of SARS-CoV-2 in a transudative pleural fluid by Real-Time Reverse Transcriptase-Polymerase Chain Reaction Assay: A Case Report

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ABSTRACT: *COVID-19 infection is ubiquitous now, and it is not unusual to find various clinical presentations of this notorious infection; nevertheless, the common infection site is the respiratory epithelium or lung parenchyma; hence, SARS-CoV-2 is most commonly isolated from the respiratory tract by a real-time polymerase chain reaction (RT-PCR) assay, and is considered as a gold-standard test for COVID-19 diagnosis. We reported a case presented with a right-side pleural effusion and underlying consolidation, and aspirated transudative pleural fluid revealed a positive COVID-19 RT-PCR result. So far, only a few positive pleural fluid COVID-19 RT-PCR cases have been reported; however, our case was detected in mid-2020.*

KEYWORDS: SARS-CoV-2, COVID-19, pleural fluid, SARS-CoV-2, RT-PCR, pleural effusion, pneumonia, transudative fluid

INTRODUCTION

Since it was declared a pandemic on March 11, 2020, by the World Health Organization (WHO), knowledge about the clinical profile and management of COVID-19 is continuously evolving. COVID-19 patients are commonly present with fever, cough, dyspnea, fatigue, anorexia, myalgia, and diarrhoea. Some patients also experienced anosmia, ageusia and lower back pain. A severe case may reach a cascade of multiple organ failure secondary to a cytokine release syndrome characterized by high fevers, thrombocytopenia, hyperferritinemia, and elevation of other inflammatory markers.^[1] Along with clinical features and RT-PCR, chest radiography is the initial investigation for the diagnosis of COVID-19, and it commonly shows bilateral consolidations or ground-glass opacities (GGO).^[2] The pleural effusion in COVID-19 is not an initial common radiological presentation. In one study, pleural effusion was found in only 3% of confirmed COVID-19 cases.^[2] The detection of SARS-CoV-2 by RT-PCR in the pleural fluid has been reported in only a few cases, although nucleic acid detection by RT-PCR from the other body fluids has rarely been applied and validated in the early stage of the pandemic.

Case Report

An eighty-five-year-old, bed-bound female presented on May 14, 2020, with dyspnea, cough and increased pedal oedema for the past three days. She was a known case of hypertension, chronic heart failure and chronic atrial fibrillation. On examination, she was afebrile, her oxygen saturations were 96% on room air, and chest auscultation revealed left basal crackle sounds and decreased breath sounds at the right base. Her chest X-ray showed moderate to marked right-sided pleural effusion with features of underlying lung collapse and mild contralateral mediastinal shift, accentuated bronchovascular lung markings with prominent hilar vasculature (Fig. 1). Her blood initial investigations showed Hb 12.4 gm%, WBC $4.26 \times 10^3/\mu\text{L}$, platelet counts $185 \times 10^3/\mu\text{L}$, CRP 14.8 mg/L and procalcitonin 0.15 ng/mL. Her kidney function test showed raised urea (10.70 mmol/L) and creatinine (156.00 $\mu\text{mol/L}$). Her nasal swab for influenza A and B was negative. Her D-dimer level was 0.51 $\mu\text{gFEU/mL}$ (normal range: 0-0.5 $\mu\text{gFEU/mL}$), Trop T 0.022 $\mu\text{g/L}$, pro-BNP 1400 pmol/l, total protein 73.00 g/L, ferritin 52.09 $\mu\text{g/L}$ and serum LDH 260 U/L (upper reference limit: 214 U/L).



Figure 1. Chest X-ray showing right side moderate pleural effusion with an underlying collapsed lung

Figure 2. Chest X-ray showing resolving right pleural effusion, but the persistence of bilateral shadows

She was started on broad-spectrum antibiotics, and USG-guided 1000 ml serosanguinous pleural fluid was aspirated from the right side. The pleural fluid analysis showed it to be transudate in nature, with lymphocytes 72%, protein 27.1 g/L and LDH 138 U/L. In addition, her pleural fluid pro-BNP was high (1069 pmol/L), suggestive of cardiogenic origin. The pleural fluid cytology showed chronic inflammation composed of many histiocytes, scattered lymphocytes and

occasional plasma cells. Her echocardiography revealed severe PAH, severe TR, mild MR, minimal pericardial effusion and adequate left ventricular function.

Her pleural fluid COVID-19 RT-PCR (Roche)/KingFisher Flex 96 (Thermofisher)/Chemagic 360 (Perkin Elmer) was found to be positive (low viral load), so she was started on hydroxychloroquine and lopinavir-ritonavir. Her two consecutive nasal swabs for COVID-19 RT-CPR were also found positive. However, her follow-up chest X-ray (Fig. 2) on May 23, 2020, showed the persistence of prominent interstitial and vascular markings on both sites and persistent haziness in the right upper and mid zone and the left mid and lower zone. Subsequently, the patient became COVID-19 negative in nasal swab RT-PCR, but she succumbed to her illness and died after a cardiac arrest.

DISCUSSION

The respiratory system is the most common site for the entry and clinical manifestations of SARS-CoV-2. Because of a non-specific clinical presentation, the radiological evaluation and RT-PCR assay of the nasopharyngeal swab are the basic investigations for diagnosing and triaging a patient with COVID-19. A chest X-ray is not as characteristic as a CT scan in COVID-19. Therefore, combined with radiology and RT-PCR, the latter has greater accuracy in diagnosing COVID-19. As per WHO, several molecular assays based on reverse transcription-polymerase chain reaction (RT-PCR) for detecting SARS-CoV-2 genes are recommended to confirm COVID-19.^[3]

A chest X-ray can be normal in up to 30% of cases; in an abnormal chest X-ray, the most common radiological findings are a patchy bilateral consolidation and ground-glass opacities. However, a chest CT scan is more sensitive to detecting the ground glass opacities. The radiological severity of COVID-19 pneumonia is classified based on Warren et al.'s scoring system of lung oedema in ARDS cases. A score of 0–4 is assigned to each lung depending on the extent of involvement by consolidation or ground-glass opacities (score 0: no involvement, score 1: <25% involvement, score 2: 25%–50% involvement, score 3: 50%–75% involvement, and score 4: >75% involvement).^[4]

The characteristic chest X-ray findings of COVID-19 are bilateral involvement, patchy opacities, and peripheral and lower-zone distribution. Pleural effusion as initial presentation is a rare radiological finding of COVID-19; however, pleural effusion and pneumothorax are occasionally seen during severe COVID-19 pneumonia. Three retrospective studies showed pleural effusion prevalence at 5%-10% in COVID-19 patients.^[5,6,7] Unilateral pleural effusion presentation is more common than bilateral effusion,^[5] and the risk of pleural effusion is higher in severe cases of COVID-19 pneumonia. One study also revealed that the prognosis of COVID-19 pneumonia is worse in cases where pleural effusion is present.^[8]

Although lymphopenia is common in SARS-CoV-2 infection, pleural effusion was lymphocytic in our case and transudative as per Light's criteria.^[9] RT-PCR of the nasopharyngeal swab is the

gold standard for diagnosing COVID-19; however, RT-PCR assay was also used to detect COVID-19 from the BAL fluid and stool.^[10]

The detection of SARS-CoV-2 by RT-PCR of the pleural fluid was a unique experience for us, as only a few instances are cited in the literature. The first case of RT-PCR detection of SARS-CoV-2 in pleural fluid was described by Federico Mei et al.^[11] The initial radiological presentation of unilateral and moderate pleural effusion, rather than consolidation and bilateral pleural effusion, could mislead the diagnosis of COVID-19. The incidence of pleural effusions in acute viral infection was reported to be 8%, which has increased to 18% on application of lateral decubitus chest X-rays,^[12] and pleural effusion secondary to viral infections are typically exudative.^[13] In our case, pleural effusion was unilateral and lymphocytic, but it was transudative, which is unusual in infection; this can be explained by some components of heart failure, as the patient was a known case of chronic heart failure, and pleural fluid pro-BNP was also raised.

CONCLUSION

Pleural effusion in COVID-19 pneumonia is not a common radiological presentation, and detection of the SARS-CoV-2 by RT-PCR in the pleural fluid is reported only in a few case reports, but none of them has transudative effusion. Early presentation of moderate, unilateral transudative effusion while positive for COVID-19 was unique in our case. In the current pandemic, we should keep COVID-19 in consideration as an important differential in patients presenting with large unilateral pleural effusion with underlying chronic disease.

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