

Case Report

An Unusual Presentation of Pleural Effusion in an Elderly Woman Post-COVID-19 Infection: A Case ReportLucy Keers ¹, Claudia Lee ², Samara White ¹, Tammie Lee Demler ^{1, 2, 3, *}

1. University at Buffalo School of Pharmacy and Pharmaceutical Sciences, 160 Hayes Rd, Buffalo, NY, USA; E-Mails: lucykeer@buffalo.edu; samarajwhite@gmail.com; tammielee.demler@omh.ny.gov
2. The Buffalo Psychiatric Center, Office of Mental Health, 400 Forest Ave, Buffalo, NY, USA; E-Mail: Claudia.Lee@omh.ny.gov
3. University at Buffalo School of Medicine, Department of Psychiatry, 955 Main St, Buffalo, NY, USA

* **Correspondence:** Tammie Lee Demler; E-Mail: tammielee.demler@omh.ny.gov**Academic Editor:** Pedro Morouco*OBM Geriatrics*

2025, volume 9, issue 2

doi:10.21926/obm.geriatr.2502313

Received: February 18, 2025**Accepted:** May 22, 2025**Published:** May 29, 2025**Abstract**

Pleural effusions are defined as accumulations of fluid in the pleural cavity surrounding the lungs. They are often secondary outcomes of underlying conditions, such as congestive heart failure, malignancy, or pneumonia. Acute cases of COVID-19 pneumonia have been linked to episodes of pleural effusion, but these cases are often rare. In this report, we analyze a case of pleural effusion in a 71-year-old female patient who had been declining after a recent COVID-19 infection and later died in the hospital. It is not certain whether the cause of this effusion was due to post-COVID-19 complications, but we aim to examine the possibility.

Keywords

Drug-induced pleural effusion; adverse drug reaction; COVID-19; elderly; pneumonia



© 2025 by the author. This is an open access article distributed under the conditions of the [Creative Commons by Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium or format, provided the original work is correctly cited.

1. Introduction

Pleural effusions are often not a stand-alone disease, but a clinical finding secondary to another condition. Therefore, analysis of the pleural fluid is necessary to properly confirm the diagnosis [1, 2]. Further, to identify what precipitated the effusion, it is important to first characterize the fluid as either exudate or transudate. Transudate and exudate differ by the mechanism in which they were produced. Transudate occurs when hydrostatic pressure increases and oncotic pressure decreases, causing fluid to build up in the extravascular space, which commonly occurs in congestive heart failure, cirrhosis, and nephrotic syndrome, among others [1, 2]. Exudate occurs when there is an increase in capillary permeability, which allows fluid to leak into the extravascular space and is typically due to a previous pulmonary infection, malignancy, or inflammatory disorder [1, 2]. Since observation alone is insufficient to determine whether the effusion is a transudate or an exudate, clinical tests are required. The most common clinical tests to differentiate the fluid are complete blood cell count (CBC), serum lactate dehydrogenase (LDH), pleural LDH, pleural pH, pleural fluid culture, and pleural fluid cytology [3].

SARS-CoV-2 infects type II alveolar (ATII) cells that are responsible for surfactant production across the alveoli and alveolar macrophages that express human ACE2 receptors (hACE2-R) [4, 5]. The hACE2-R allow SARS-CoV-2 to spread across tissues, and when infected, the levels of hACE2-R are increased through a positive feedback loop causing an increase in angiotensin II (Ang II), subsequent vasoconstriction, and associated inflammatory reactions [4, 5]. These inflammatory reactions are caused by initiation of fibrinogenesis, death of alveolar cells, and increased alveolar permeability that allows fluid to occupy the air space [4, 5]. Thereby, this is the mechanism seen in rare cases of COVID-19-induced pleural effusions.

2. Case Report

A 71-year-old Caucasian female was admitted to the hospital with hypoxia at an oxygen saturation of 78-81% and shortness of breath for 2 to 3 days. Her past medical history included schizoaffective disorder, irritable bowel syndrome (IBS), hyperlipidemia, poor nutritional intake, vitamin B12 deficiency, chronic obstructive pulmonary disease (COPD), gastroesophageal reflux disease (GERD), anemia, substance use disorder, and history of clozapine-induced dysphagia and resulting aspiration pneumonia. She resided at a long-term psychiatric hospital where her medications included aspirin, atorvastatin, cyanocobalamin, lubiprostone, mirtazapine, albuterol as needed and olanzapine. Just prior to admission to the acute hospital, the nursing staff reported consistent dyspnea when eating but not while talking despite decreased lung aeration. A chest x-ray revealed a right lower lobe infiltrate and right-sided pleural effusion; she was subsequently sent to the hospital. Of note, the patient contracted COVID-19 approximately 3 months prior to hospital admission.

Upon admission, a repeat chest x-ray revealed elevation of the right hemidiaphragm versus confluent opacification of the right lower lung. A new large loculated effusion was found along the lateral aspect of the right chest wall measuring up to about 5 cm in thickness. Her left lung was found to be clear with no evidence of pneumothorax. A coronary angiogram (CTA) was conducted and did not reveal pulmonary emboli within the main pulmonary arteries or the proximal right segmental pulmonary arteries. The CTA confirmed moderate to large loculated right pleural effusion with near complete atelectasis of the right middle lobe and moderate atelectasis of the right lower

lobe. A thoracentesis yielded approximately 1200 mL of cloudy, orange, serosanguinous fluid, which was sent for analysis, culture, and cytology. Analysis of the pleural fluid revealed elevated LDH (712 units/L) and total protein (3.8 g/dL), and a low pleural pH (7.45) (Table 1). Cytology was negative for malignant cells and no organisms were found in the gram-stain. Additional abnormal lab findings observed were an elevated D-dimer (0.9 mcg FEU/mL) and CBC with differential (Table 2). Nearly five days after thoracentesis, the patient was transferred to the MICU and intubated. She later developed a coagulopathy with an INR of 20 and a prothrombin time (PT) above 120 seconds, and eventually died.

Table 1 Characteristics of pleural fluid.

Parameter	Lab Finding	Reference Range
pH	7.45 (L)	7.6
Total protein (g/dL)	3.8 (H)	1-2
Fluid lactate dehydrogenase (LDH) (U/L)	712 (H)	135-214
Amylase (U/L)	43	30-110 U/L
Glucose (mg/dL)	75	~plasma level
WBC	No WBCs	<1,000 WBC/ μ L
Appearance	Cloudy	Clear
Color	Orange	Colorless
Gram stain	No organisms	
Cytology	Negative for malignant cells	

Table 2 Additional lab findings.

Parameter	Lab Finding	Reference Range
D-dimer (mcg FEU/mL)	0.9 (H)	0.27-0.49
WBC count ($\times 10^9$ /L)	6.4	4.8-10.8
Hemoglobin (g/dL)	11.8	12.0-16.0
Platelets	293	130-400
Eosinophils (%)	0.2 (L)	0.5-11.0
Neutrophils (%)	80.1 (H)	40.0-75.2
Lymphocytes (%)	5.6 (L)	16.0-51.0
Monocytes (%)	13.6 (H)	1.7-12.0
Sodium (mmol/L)	147 (H)	133-145
Chloride (mmol/L)	104 (H)	96-108
Creatinine (mg/dL)	0.6	0.5-1.0
HCO ₃ ⁻ (mmol/L)	33 (H)	19-30
Serum lactate dehydrogenase (LDH) (U/L)	703 (H)	140-280
Total Protein (g/dL)	6.4	6.6-8.7

2.1 Ethics Statement

The study was conducted following the Declaration of Helsinki and approved by the Research Monitoring Committee for Institutional Review Board Protocols of the Buffalo Psychiatric Center on

April 24th, 2024. Informed consent to publication was not applicable, as the patient is now deceased and has no consent for notification of next of kin.

3. Discussion

According to Light's criteria, only one of the following criteria must be met to classify the effusion as exudative [2, 6]:

1. Pleural fluid protein/serum protein ratio of more than 0.5.
2. Pleural fluid lactate dehydrogenase (LDH)/serum LDH ratio of more than 0.6.
3. Pleural fluid LDH is more than two-thirds of the upper limits of normal laboratory value for serum LDH.

Our patient's laboratory findings met all three criteria for exudative pleural effusion. Further, Light's criteria states that pleural fluid protein >35 g/L confirms exudative fluid; our patient's pleural fluid contained 3.8 g/dL (38 g/L) of total protein [6]. As previously stated, exudates are more commonly associated with infection or malignancy. Negative cytology indicated no presence of malignancy, and negative Gram stain indicated no sign of bacterial infection. She had negative PCR tests for SARS-CoV-2 and influenza A & B. She had no signs or symptoms of tuberculosis or any rheumatologic disease. In addition, she was not hypothyroid and was not on medications likely to cause a pleural effusion. Therefore, it is possible that the damaging inflammatory processes of COVID-19, specifically increased permeability in the alveolar space, may have provided an opportunity for pleural fluid to occupy the pleural space with great capacity. The patient had been diagnosed with COPD, but it was very well-controlled. She only had albuterol prescribed for as needed use but rarely needed it. She also had aspiration pneumonia when she was on clozapine, but she was off clozapine for years without further aspiration. She had no evidence of heart failure. Also, none of the medications she was on are commonly associated with pleural effusions. Olanzapine-induced pleural effusion is rare and causes eosinophilic pleural effusion. Our patient pleural effusion differential was neutrophils 9%, lymphocytes 75%, mesothelial cell 6%, macrophage 10%. During this episode, markers of aspiration that were done included highly sensitive CRP, which was 137.12 mg/L (0.2-10.00), and procalcitonin, which was 0.04 (low). It may be argued that the development of pleural effusion occurred three months after the initial infection with SARS-CoV-2, which complicates the establishment of a direct causal relationship. However, we propose that the development of the pleural effusion may have started after the COVID infection and worsened gradually to the point that the patient became very hypoxic at three months.

When examining why this patient, compared to most COVID-19 survivors, developed this complication, we propose that the patient may have been more susceptible to developing the pleural effusion post-COVID because of her age, history of COPD, and very petite frame with prealbumin of 7.2 (20-40). The pH abnormalities are still consistent with an exudate (Table 1) and the low levels of prealbumin can be attributed to malnutrition, but inflammation is still in the differential. It is also worth noting that despite the D dimer elevation, the patient had no evidence of edema, warmth, tenderness, or color changes on physical exam of her lower extremities. Although no signs of DVT were noted on physical examination, lower extremity Doppler ultrasound was not performed to definitively rule out deep vein thrombosis.

In support of our hypothesis of direct viral involvement or delayed immune response in the pleural space, Keskin et al. provide additional insight based on their research which has

demonstrated direct viral involvement in the pleural space, with detection of SARS-CoV-2 RNA in pleural fluid via rRT-PCR. This would suggest that delayed immune response, viral persistence or both factors may contribute to post-COVID pleural effusions [7, 8].

Although the medical community is now well-versed in managing the acute phase of COVID-19, the collective understanding of the clinical impacts and sequelae continue to develop. Of the sequelae, some of the most common are pulmonary involvement [9, 10]. Although there have been some valuable cases that have documented post-COVID-19 pleural effusions, due to the relative scarcity, the significance of this complication is not currently well understood and therefore warrants further investigation [11-14]. A study that examined acute-care rehospitalizations within four months of discharge found that elderly patients with diabetes mellitus or COPD were more likely to be readmitted post-COVID-19. Amongst these patients, about 20% were readmitted due to pulmonary complications, some of which included pulmonary effusion [14]. In the documented incidences of COVID-19-induced pleural effusions, all of the pleural drainage have been found to be exudate [6, 14]. Similarly, in this present case, an elderly patient with a history of COPD who was three months post-COVID-19 infection presented with a substantial amount of exudative pleural fluid.

Limitations of this case include a comorbidity of COPD and a history of smoking and aspiration pneumonia. These confounding factors may have contributed highly to the patient's susceptibility to pleural effusion. Additionally, when exactly after COVID the pleural effusion started is not clear, but she did not have it when she first was diagnosed with COVID three months prior. Regardless, reports show that development of pulmonary conditions continue up to 12 months after COVID-19 infection [9].

In conclusion, this case report highlights the importance of following up with patients post-COVID-19 infection, in particular high-risk patients such as patients residing in long-term care facilities and those who present with multiple comorbidities. Providers should be aware of the risks associated with this patient population and should continue to monitor them closely for months after initial diagnosis.

Author Contributions

We declare an equal contribution of the authors to the writing of this case report. All listed authors concur in the submission and are responsible for its content; they have agreed to its publication and have given the corresponding author the authority to act on their behalf in all matters pertaining to publication.

Competing Interests

The authors have no conflict of interests to disclose.

References

1. Link T. Guidelines in practice: Hypothermia prevention. *AORN J.* 2020; 111: 653-666.
2. Turk EE. Hypothermia. *Forensic Sci Med Pathol.* 2010; 6: 106-115.

3. Szota AM, Araszkiewicz AS. The risk factors, frequency and diagnosis of atypical antipsychotic drug-induced hypothermia: Practical advice for doctors. *Int Clin Psychopharmacol*. 2019; 34: 1-8.
4. Zonnenberg C, Bueno-de-Mesquita JM, Ramlal D, Blom JD. Hypothermia due to antipsychotic medication: A systematic review. *Front Psychiatry*. 2017; 8: 165.
5. Lilly USA. Olanzapine [package insert]. Indianapolis, IN: Lilly USA; 2009.
6. Ortho-McNeil-Janssen Pharmaceutical. Risperidone [package insert]. Little Island, County Cork, Ireland: Ortho-McNeil-Janssen Pharmaceutical; 2009.
7. Keskin Z. Can diffusion-weighted imaging be used in the examination of peritoneal fluids? *Pol J Radiol*. 2023; 88: e149-e154.
8. Keskin Z, Yeşildağ M, Alkan E, Kayhan A, Tolu L, Keskin S. Differentiation between transudative and exudative pleural effusions by diffusion weighted magnetic resonance imaging. *Iran J Radiol*. 2019; 16: e78775.
9. Otsuka Pharmaceutical Co. Aripiprazole [package insert]. Tokyo, Japan: Otsuka Pharmaceutical Co.; 2014.
10. Ferreira V, Folgueira C, Guillén M, Zubiaur P, Navares M, Sarsenbayeva A, et al. Modulation of hypothalamic AMPK phosphorylation by olanzapine controls energy balance and body weight. *Metabolism*. 2022; 137: 155335.
11. Van Marum RJ, Wegewijs MA, Loonen AJ, Beers E. Hypothermia following antipsychotic drug use. *Eur J Clin Pharmacol*. 2007; 63: 627-631.
12. Kansagra A, Patel S, Wilcox SR. Prolonged hypothermia due to olanzapine in the setting of renal failure: A case report and review of the literature. *Ther Adv Psychopharmacol*. 2013; 3: 335-339.
13. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981; 30: 239-245.
14. Ajayi OO, Holroyd S. Severe recurrent hypothermia in an elderly patient with refractory mania associated with atypical antipsychotic, valproic acid and oxcarbazepine therapy. *BMJ Case Rep*. 2017. doi: 10.1136/bcr-2017-222462.