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COVID-19 post-mortem findings: how the departed can teach us

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Abstract

We present an asthmatic 39 year old female frontline healthcare worker in contact with COVID-19 patients, who suffered from respiratory problems for a few days, after which she was found dead by her spouse. Post-mortem (PM) examination showed lung consolidation and histological evidence of diffuse alveolar damage (DAD), in form of hyaline membrane disease, as well as atypical cells, thrombi and fibrin plugs inside pulmonary capillaries. Swab sample testing for SARS-CoV-2 confirmed the infection status. SARS-CoV-2 is a novel coronavirus which first emerged in Wuhan, China, and PM is contributing immensely to uncovering the pathophysiological mechanism of this disease. SARS-CoV-2 enters host cells via the angiotensin-converting enzyme 2 (ACE2), and can lead to a fatal pneumonia characterized histologically by DAD (the most consistent PM finding). This is due to invasion by the virus of type II pneumocytes, which leads to the death of both type I and II pneumocytes and increased capillary permeability. This compromises gas exchange which can lead eventually to cardiorespiratory failure and death.

Keywords ACE2; DAD; hyaline membrane; post-mortem; SARS-CoV-2

Case presentation

We present an asthmatic 39 years old female frontline healthcare worker in contact with COVID-19 patients. She suffered from respiratory problems for a few days after which she was found unconscious at home by her spouse, who called an ambulance. On arrival of ambulance staff, she was found to be in cardiac arrest. Due to the deceased's line of work and symptoms, a SARS-CoV-2 infection was suspected.

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This Short Case is brought to you in association with the Pathological Society of Great Britain and Ireland. Each month we feature a Short Case written by a member of the Trainees' Subcommittee of the Pathological Society of Great Britain and Ireland. This case, including its scanned slides, is published on the Pathological Society's website www.pathsoc.org/index.php/trainees/case-of-the-month (previous cases can be accessed by members via the education portal login). The Short Case includes a series of Test Yourself Questions at the end to check your understanding of the case. We hope you enjoy reading it.

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Post-mortem examination

The body was that of a young Asian female, in keeping with the stated age. On organ examination, the left lung weighed 531 grams and the right lung weighed 740 grams, and both lungs showed extensive consolidation, particularly in the lower lobes. There was widespread lymphadenopathy in the thoracic lymph nodes draining the lungs. There was no evidence of excess bronchial secretions or lung hyperexpansion and hence no macroscopic evidence of an asthma attack at the time of death. The other major internal organs showed no macroscopic abnormality.

Histology

Lung specimens were taken for histology, which showed evidence of diffuse alveolar damage, in form of hyaline membrane disease. Pulmonary oedema was noted, and atypical cells were seen in endothelial spaces. Furthermore, thrombi and fibrin plugs were seen inside pulmonary capillaries. Examination of a thoracic lymph node showed sinus expansion with blast-like lymphoid cells. [Figure 1](#) demonstrates the histology findings mentioned.

Ancillary testing

Swabs were taken from the nose, throat, trachea and bronchi for PCR testing, which proved positive for SARS-CoV-2. As such, the cause of death was recorded as pneumonia due to SARS-CoV-2 (COVID-19) infection.

Discussion and conclusion

SARS-CoV-2 is a novel coronavirus which first emerged in Wuhan, China where it caused an outbreak of unusual pneumonia in December 2019.¹ What is intriguing is how this disease can be fatal in a short span of time in otherwise relatively healthy and young individuals, as described in our case report.

SARS-CoV-2 enters host cells via the angiotensin-converting enzyme 2 (ACE2), which leads to an initial localized infection where patients are asymptomatic and infective.² This progresses, in some individuals, to upper and lower respiratory tract infections, where the virus invades type II pneumocytes. This stimulates a cascade of inflammatory cytokines resulting in both type I and II pneumocyte apoptosis and increased capillary permeability.³

While in the majority of cases (80%) the acute immune host response is sufficient to clear infection,¹ a group of patients develop severe to fatal disease in the form of diffuse alveolar damage (DAD)

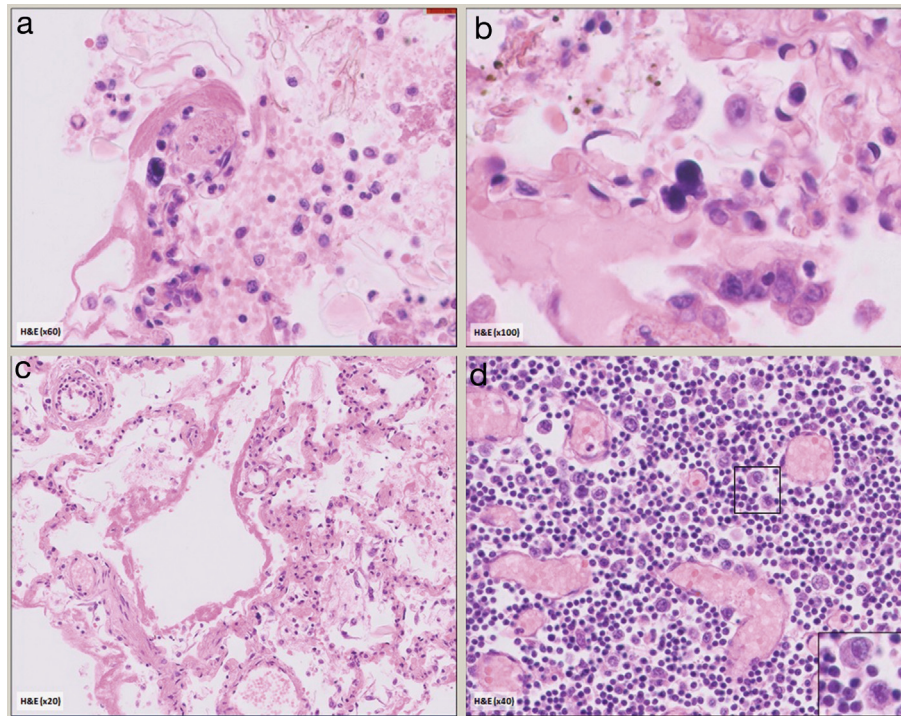


Figure 1 Haematoxylin and eosin images of different magnifications demonstrating (a) Alveolar atypical cell, fibrin and thrombosed capillary (x60), (b) a cytopathic cell on a damaged alveolar wall (x100), (c) hyaline membrane formation (x20), (d) blast-like cells in a lymph node sinus (x40) with an inset showing a magnified image of these cells.

resulting clinically in acute respiratory distress syndrome (ARDS).⁴ One study highlighted DAD as the most consistent lung finding in all deceased COVID-19 patients, accurately detailing the hallmark characteristics of DAD seen histologically.⁴

DAD caused by SARS-CoV viruses occurs in two phases which can occur simultaneously in different areas of the lung parenchyma; this depends on whether the lung tissue is exhibiting an immune response to the virus (acute phase) or if its organizing to a reparative end (organizing phase).³ The acute phase is caused either by a direct effect of viral life cycle (resulting in apoptosis of infected cells) or via ‘cytokine storm’.¹ It is characterized by the formation of hyaline membranes from fibrin polymerization of the excess fluid within the alveoli and interstitium, as seen in our case. Intra-alveolar oedema and interstitial widening is also visualized, in addition to thrombin formation.⁴ The organizing phase is discerned by acute fibrinous organizing pneumonia due to fibroblast proliferation. This is an attempt to repair the parenchyma in response to alveolar damage. The extensive tissue damage and remodelling can compromise gas exchange, and the deoxygenation can occur rapidly enough to lead to cardio-respiratory failure and death,^{2,5} as seen in our case.

To conclude, infection with SARS-CoV-2 can manifest on a clinical scale from asymptomatic to fatal disease. Post-mortem studies have been integral in determining the pathophysiological process of COVID-19 and the classical histopathological features of DAD are seen consistently in COVID-19 positive patients. ◆

REFERENCES

- 1 Parasher A. COVID-19: current understanding of its pathophysiology, clinical presentation and treatment. *Postgrad Med* 2021; **97**: 312–20.
- 2 Osuchowski MF, Winkler MS, Skirecki T, et al. The COVID-19 puzzle: deciphering pathophysiology and phenotypes of a new disease entity. *Lancet Resp Med* 2021; **9**: 622–42.
- 3 Batah SS, Fabro AT. Pulmonary pathology of ARDS in COVID-19: a pathological review for clinicians. *Respir Med*, 2020; 106239.
- 4 Montero-Fernández MA, Pardo-García R. Histopathology features of the lung in COVID-19 patients. *Diagn Histopathol* 2020; **27**: 123–7.
- 5 Guan W-j, Ni Z-y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; **382**: 1708–20.

Practice points

- Infection with SARS-CoV-2 can be fatal even in young and healthy individuals.
- Post-mortem histological evidence of DAD is the most consistent finding in COVID-19 patients.
- Post-mortem examination is playing an important role in uncovering the pathophysiological mechanisms of the disease.

Self-assessment

1. What is the most consistent finding during post-mortem histological examination of COVID-19 patient samples?:

- A. Lung collapse**
- B. Pulmonary embolism**
- C. Diffuse alveolar damage**
- D. Peri-vascular inflammatory infiltrate**
- E. Lung cavitation**

Correct answer: C

2. What percentage of SARS-CoV-2 infected patients are unable to eliminate the initial infection?:

- A. 10%**
- B. 20%**
- C. 50%**
- D. 60%**
- E. 80%**

Correct answer: B