

COVID-19 autopsy in people who died in community settings: the first series

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ABSTRACT

Here, we report the pathological findings of nine complete autopsies of individuals who died in community settings in the UK, three of which were positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), three tested negative for SARS-CoV-2 but are likely false negatives, and three died of other respiratory infections. Autopsy revealed firm, consolidated lungs or lobar pneumonia. Histology of the lungs showed changes of diffuse alveolar damage with fibrin membrane formation, thickened alveolar walls and interstitium with lymphocytic infiltrate, and type 2 pneumocyte hyperplasia with shedding into the alveolar space. This series is the first in the world to describe autopsy findings in individuals dying suddenly in the community, not previously known to have COVID-19 infection, and the first autopsy series in the UK. During a time when testing in the UK is currently primarily offered to patients in hospital or symptomatic key workers, with limited testing available in community settings, it highlights the importance of testing for COVID-19 at autopsy. Two deaths occurred in care homes where a diagnosis of COVID-19 allowed the health protection team to provide support in that 'closed setting' to reduce the risks of onward transmission. This work highlights the need for frequent COVID-19 testing in the management of patients in community settings. Comprehensive virology and microbiology assessment is pivotal to correctly identify the cause of death, including those due to COVID-19 infection, and to derive accurate death statistics.

INTRODUCTION

As of Saturday, 18 April 2020, there were 114 217 cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the UK, with 15 464 deaths.¹ To date, testing for SARS-CoV-2 in the UK has been limited to patients in hospital and certain key workers with limited testing in community settings.² This has meant that there is a lack of knowledge about the true scale of community infection and deaths that may be related to COVID-19.^{3 4}

For centuries, autopsy has been an important tool in understanding disease processes and their effects on different organ systems. It can help inform clinical practice and management, particularly in new diseases, such as COVID-19. To the best of our knowledge, this is the first autopsy case series of COVID-19 deaths in community settings in the world and the first autopsy series of such deaths in the UK.

METHODS

Postmortem examination

Autopsies were performed at the Royal Glamorgan Hospital, Llantrisant, at the request of the coroner. These cases were all unexpected deaths of unknown cause, so the purpose of the autopsy was to establish the cause of death. The deceased were not being treated for acute illness and had not been tested for COVID-19 prior to death.

Comprehensive postmortem external and internal examinations were performed by a consultant histopathologist in a mortuary equipped with suitable ventilation and equipment, with personal protective equipment including full gown, plastic apron, gloves (including cut-proof under gloves), face visor, boots and filtering facepieces protect (FFP)3 mask. Postmortem examinations were performed in line with the recently published guidelines for suspected COVID-19 cases.^{5 6}

Diagnostic testing for COVID-19

To test for COVID-19, swabs were taken from any of the following: trachea, lung parenchyma, pericardium and pleural cavity. Collected specimens were sent to the laboratory for a real-time reverse transcriptase PCR as previously described.⁷

If COVID-19 was not detected, 'reflex' testing of other respiratory viruses was undertaken by the laboratory, including influenza A and B, respiratory syncytial virus, rhinovirus, human metapneumovirus, enterovirus, adenovirus, mycoplasma and other coronaviruses.

In addition, in selected cases, microbiology culture for bacteria was performed.

Histology

Representative samples were obtained from the lung and heart and submitted in standard tissue cassettes. These were fixed in formalin for 72 hours as per the guidance from the Centers for Disease Control and Prevention.⁸ Formalin renders the virus inactive.⁸ Samples were processed, embedded in paraffin, sectioned, mounted onto glass slides and stained with H&E. All slides were examined by two histopathologists.

RESULTS

Clinical summary

This series includes nine deaths in community settings, most of whom had various respiratory symptoms immediately prior to death, but were not tested for or diagnosed with COVID-19 (table 1). Two deaths occurred in care homes and the local health protection team was informed.



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Table 1 Summary of the meta-data

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Age	88	86	73	67	33	70	87	77	68
Sex	Female	Male	Female	Female	Female	Male	Female	Male	Male
BMI	29	24	32	30	38	29	27	26	13
Race	White Caucasian	White Caucasian	White Caucasian	White Caucasian	White Caucasian	White Caucasian	White Caucasian	White Caucasian	White Caucasian
Diabetes			✓ (type 1)		✓ (type 1)	✓ (type 1)	✓ (type 2)		
Hypertension		✓		✓	✓	✓			
COPD		✓					✓	✓	✓
Asthma			✓						
Heart disease		✓	✓			✓		✓	
Other comorbidities	Dementia	Dementia		DVT, alcoholism		Parkinson's disease	Stroke		HIV
Symptoms prior to death	None	Cough, fever, unsteadiness	Shortness of breath	Chronic cough, non- specifically unwell, collapse, sudden cardiac arrest	Cough, pleuritic chest pain	Sudden asystolic cardiac arrest	Sudden-onset shortness of breath	Sudden asystolic cardiac arrest	Chronic cough and shortness of breath (no new symptoms)
Place of death	Care home	Care home	Home	A&E	Home	A&E	Home	A&E	Home
PMI	5 days	8 days	10 days	10 days	5 days	7 days	8 days	7 days	10 days

A&E, accident and emergency; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DVT, deep vein thrombosis; PMI, postmortem interval.

All but one case had significant underlying disease, with chronic obstructive pulmonary disease and type 1 diabetes mellitus being the most common. In one case, the only medical condition of note was dementia (case 1, [table 1](#)).

Macroscopic findings

In the COVID-19-positive cases (cases 1–3), the main pathological findings were seen in the chest ([table 2](#)). The lungs were heavy, with the left ranging from 448 g to 693 g (normal 325–480 g⁹) and the right ranging from 581 g to 802 g (normal 360–570 g⁹). There was consolidation or features to suggest lobar pneumonia. No macroscopic thromboemboli or areas of infarction were seen. The heart was enlarged in two of three individuals, weighing from 582 g to 592 g (heavier than predicted weight for body mass). There was no pericarditis or myocardial mottling to suggest myocarditis macroscopically. In one of the patients (case 2), the spleen was markedly enlarged with macroscopic appearances suggesting splenic lymphoma (not previously diagnosed).

In the cases with negative COVID-19 swabs (but likely falsely negative) (cases 4–6), the macroscopic findings were similar to the above-described three individuals who were found to be COVID-19-positive. Specifically, the lungs were heavy, with the left ranging from 622 g to 815 g and the right ranging from 782 g to 1082 g. Consolidation or bronchopneumonia and associated pulmonary oedema were also observed. In addition, purulent sputum, pleural effusion with turbid fluid in the cavity and fibrinous exudate over the visceral pleura were identified in one individual (case 5) ([figure 1](#)).

In the cases with other proven infections (cases 7–9), macroscopic examination of the lungs showed features of bronchopneumonia/lobar pneumonia, with associated pulmonary oedema and pleurisy, and a background of emphysema. Right ventricular hypertrophy, consistent with the presence of chronic lung disease, was found in one individual (case 9) ([table 2](#)).

Microscopic findings

Lungs

All COVID-19-positive cases showed diffuse alveolar damage (DAD) with fibrin membrane formation, clumps of fibrin

within alveoli, type 2 pneumocyte hyperplasia and shedding, and widening of alveolar walls and interstitium with lymphocytic infiltrate ([table 3](#) and [figure 2A–F](#)). No microthrombi were identified in the examined tissue blocks. The same microscopic features of DAD and viral pneumonia were seen in cases 4, 5 and 6, with superimposed bronchopneumonia in cases 5 and 6 ([table 3](#) and [figure 2G–I](#)). The same features of DAD and viral pneumonia were seen in case 7 (rhinovirus infection) with superimposed bronchopneumonia ([figure 2J–L](#)).

In cases 8 and 9 typical changes of bronchopneumonia/lobar pneumonia were seen, with neutrophils filling the alveolar spaces. There were no features of viral pneumonia or DAD ([table 3](#)).

Heart

Myocarditis was not seen in any of the COVID-19 positive or suspected cases. One case of bacterial bronchopneumonia showed an associated myocarditis. One case (case 2) showed contraction band necrosis. There were chronic ischaemic changes in several cases, consistent with the known medical history and macroscopic findings. One case showed cardiac amyloidosis.

Other findings

One COVID-19-positive case had a previously undiagnosed splenic B cell lymphoma, confirmed with histology and immunohistochemistry.

DISCUSSION

This case series illustrates the histological changes observed in COVID-19 infection. The three individuals were found to have different degrees of lung disease, but all showed changes of DAD and changes associated with viral pneumonia (lymphocytic infiltrate). Our findings are in line with clinical studies which describe adult respiratory distress syndrome in patients requiring Intensive Therapy Unit (ITU) support, although these cases are of people who did not attend hospital.¹⁰ The finding of type 2 pneumocyte hyperplasia and shedding was

Table 2 Summary of macroscopic findings at autopsy

System	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Central nervous system	Brain atrophy.	Normal.	Circle of Willis atheroma.	Old infarct and old head injury.	Normal.	Circle of Willis atheroma, neurostimulator present.	Circle of Willis atheroma.	Circle of Willis atheroma.	Normal.
Respiratory system	Right lung 654 g, left lung 448 g. Bilateral lobar pneumonia, inflamed trachea with mucus.	Right lung 802 g, left lung 693 g. Lung consolidation, inflamed trachea with mucus, pulmonary oedema, anthracosis.	Right lung 581 g, left lung 458 g. Lung consolidation, inflamed trachea with mucus, pulmonary oedema, pleural adhesions.	Right lung 85.4 g, left lung 622 g. Lung consolidation, pulmonary oedema.	Right lung 782 g, left lung 650 g. Lung consolidation, pulmonary oedema, fibrinous exudate right pleura, turbid right pleural effusion, inflamed trachea and purulent sputum.	Right lung 1082 g, left lung 815 g. Bilateral bronchopneumonia and consolidation.	Right lung 892 g, left lung 448 g. Right lung bronchopneumonia, pulmonary oedema, emphysema.	Right lung 2033 g, left lung 1146 g. Lobar pneumonia, pulmonary oedema, emphysema, pleural adhesions and fibrinous exudate.	Right lung 707 g, left lung 500 g. Bilateral bronchopneumonia, purulent sputum, marked emphysema, pulmonary oedema, pleural adhesions.
Cardiovascular system	Minimal coronary artery atheroma.	Enlarged heart (592 g), minimal coronary artery atheroma.	Enlarged heart (582 g), focal significant coronary artery stenosis by atheroma, old myocardial scarring.	Enlarged heart (669 g), fibrous pericarditis.	Enlarged heart (534 g), normal coronary arteries and myocardium.	Two-vessel significant coronary artery stenosis by atheroma.	Enlarged heart (502 g), moderate coronary artery atheroma (50% stenosis).	Triple-vessel significant stenosis by atheroma, old myocardial scarring.	Right ventricular hypertrophy.
Gastrointestinal system	Normal.	Normal.	Normal.	Normal.	Normal.	Normal.	Normal.	Normal.	PEG feeding tube.
Pancreatobiliary system	Normal.	Chronic venous congestion of the liver.	Chronic venous congestion of the liver.	Chronic venous congestion of the liver.	Fatty change of the liver.	Absent gall bladder.	Gallstones.	Normal.	Chronic venous congestion of the liver.
Genitourinary system	Scarred, shrunken kidneys.	Scarred kidneys.	Scarred kidneys, renal stones.	Normal.	Normal.	Scarred kidneys.	Scarred kidneys, hysterectomy.	Scarred kidneys.	Renal cysts.
Endocrine system	Normal.	Normal.	Normal.	Normal.	Normal.	Nodular goitre.	Nodular goitre.	Normal.	Normal.
Lymphoreticular system	Normal.	Enlarged (662 g) with pale nodules.	Normal.	Normal.	Normal.	Normal.	Soft, autolysed spleen.	Enlarged spleen (594 g).	Normal.
Musculoskeletal system	Lower thoracic spine deformity.	Rib fractures from resuscitation.	Normal.	Rib fractures from resuscitation.	Normal.	Rib fractures from resuscitation.	Rib fractures from resuscitation.	Rib fractures from resuscitation.	Normal.
SARS-CoV-2 test (PCR)	Positive (trachea and lung swabs).	Positive (trachea swab).	Positive (trachea swab).	Negative (pericardial swab).	Negative (trachea, right lung, pleural fluid).	Negative (trachea and lung swabs).	Negative (trachea and lung swabs).	Negative (lung swab).	Negative (lung and trachea swabs).
Other virology/microbiology			Negative virology panel, postmortem contaminants in bacteriology culture.			Rhinovirus detected (trachea and lung swabs).		<i>Streptococcus pneumoniae</i> cultured (lung).	<i>Streptococcus pneumoniae</i> cultured (lung).

PEG, percutaneous endoscopic gastrostomy; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.



Figure 1 Macroscopic findings. Gross examination of the heart in case 5 showed features of fibrinous pericarditis.

prominent in these cases and is similar to recent work on SARS-CoV-1^{11 12} and SARS-CoV-2.¹³

Myocarditis has been postulated to account for rising troponin measurements in people deteriorating with COVID-19 and associated with adverse outcome.^{14 15} In this autopsy series myocarditis was not observed. Myocardial injury could be due to other reasons including cytokine storm, hypoxia, microthrombi or direct vascular injury¹⁶; in one case contraction band necrosis was observed, in someone who did not have acute infarction and was not treated with inotropes or epinephrine. Similarly, pulmonary thrombotic disease and associated ventilation/perfusion mismatch has been described in patients undergoing ITU treatment,¹³ but this was not observed in this case series. This may reflect different pathological manifestations of infection

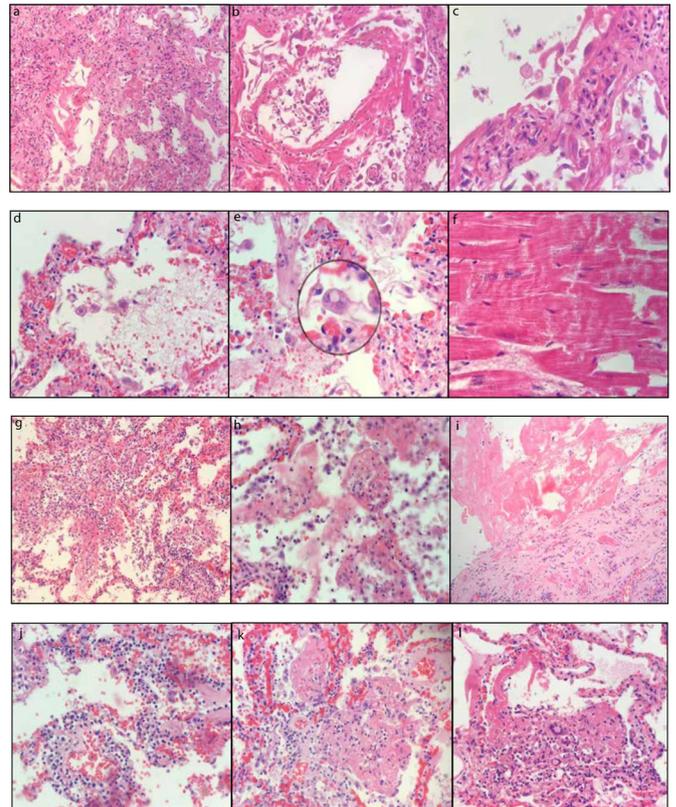


Figure 2 Microscopic findings on histology (H&E stained slides). (A–C) Lung histology in case 1 showing changes of diffuse alveolar damage, hyaline membrane formation (A, B), type 2 pneumocyte hyperplasia and shedding (C), and lymphocytic infiltration (A–C). (D–F) Lung and heart histology in case 2 showing changes of diffuse alveolar damage, lymphocytic infiltrate (D, E), type 2 pneumocyte hyperplasia (E), possible cytopathic features in pneumocytes (E) and contraction band necrosis (F) in cardiac myocytes. (G–I) Lung and heart histology in case 4 showing diffuse alveolar damage, fibrin clumps within alveoli, thickened alveolar walls with lymphocytic infiltrate (G, H) and fibrinous pericarditis (I). (J–L) Lung histology in case 7 showing thickened alveolar septae with lymphocytic infiltrate (J–L), diffuse alveolar damage (K, L) and lack of type 2 pneumocyte hyperplasia (L).

consequences in those treated on ITU versus those dying suddenly in the community.

Obesity is recognised to increase the risk of developing serious respiratory disease in COVID-19 infection.^{17–19} In this series a

Table 3 Summary of microscopic findings at autopsy

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Lungs									
Diffuse alveolar damage	✓	✓	✓	✓	✓	✓	✓	x	x
Bronchopneumonia	x	x	x	x	✓	✓	✓	✓	✓
Microthrombi	x	x	x	x	x	x	x	x	x
Other changes		Bone marrow embolism				Bone marrow embolism			
Heart									
Myocarditis	x	x	x	x	x	x	x	✓	x
Ischaemic changes	x	✓ (chronic)	✓ (chronic)	x	x	✓ (chronic)	✓ (chronic)	✓ (chronic)	x
Other changes		Contraction band necrosis		Fibrinous pericarditis			Amyloidosis		
Other organs		Splenic B cell lymphoma							

body mass index in the obese range (defined as greater than 30) was observed in three of six positive or likely COVID-19 cases.

Diabetes has been noted to be a significant comorbidity in patients with COVID-19 infection.¹⁸ In this series type 1 diabetes mellitus was known in three of six positive or likely COVID-19 cases.

It is well recognised that older age increases the risk of severe disease or fatality, with 95% of deaths in those aged over 60 years.²⁰ In this series all but one person was elderly (age >65 years). However, severe respiratory disease was noted in the one younger adult, reflecting that this disease is not only limited to the elderly.

The same changes of DAD and viral pneumonia were seen in cases 4, 5 and 6, despite a negative COVID-19 swab. In the context of this pandemic, and given the clinical information, macroscopic findings and histological features, in our view these likely represent false negative test results and these deaths are highly likely to be due to COVID-19 infection. This illustrates that pathologists must use all available information to come to a determination about the likely aetiology in any given case. The sensitivity of PCR testing at autopsy is not known, although this case series illustrates that the virus RNA can be detected at least 10 days after death. Possible reasons why a swab test might be falsely negative include sampling technique, test sensitivity and tissue degradation in the postmortem interval.

Superimposed bronchopneumonia (likely bacterial infection) was seen in two of the six cases of confirmed or likely COVID-19 infection, and in the case of rhinovirus infection. This accords with clinical experience²¹ and is useful knowledge for clinicians treating patients that bacterial infections do occur in the setting of COVID-19 and require appropriate therapy.

Similar histological changes were seen in case 7 (rhinovirus-positive), which illustrates that the histological tissue reaction in the lungs is not necessarily specific to the aetiology. Testing for a wider group of potential causative organisms can ensure identification of the correct aetiological agent. Cases 7, 8 and 9 illustrate that not all respiratory infections are due to COVID-19 infection. There is the potential to overestimate the impact of a pandemic such as COVID-19 and to assume that all respiratory distress or gross lung pathology is due to COVID-19. This has the potential to markedly distort the statistics on COVID-19 fatalities and would be a worrying trend. Recent changes to death certification in the UK under the Coronavirus Act 2020²² aim to smooth the process of death certification but could add to this false estimation of COVID-19 deaths. Virology and microbiology testing at autopsy is essential in correctly determining the aetiology of these infections rather than wrongly assuming they are due to COVID-19.

Finally, it is important that pathologists test for COVID-19 at autopsy to contribute to the wider public health. Deaths due to COVID-19 should be notified to the local public health body. The identification of two deaths in care homes was vital to ensure the health protection team were able to support the care workers and residents in what is known as a 'closed setting' and to support infection control measures to reduce the risks of onward transmission.

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