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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Hanley B, Naresh K N, Roufosse C, et al. Histopathological findings and viral tropism in UK patients with severe fatal COVID-19: a post-mortem study. *Lancet Microbe* 2020; published online August 20. https://doi.org/10.1016/S2666-5247(20)30115-4.

Appendix: Histopathological findings and viral tropism in UK patients with severe fatal COVID-19: a post-mortem study

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Contents

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Clinical Case Vignettes and Major Post-mortem findings for COVID-19 autopsies:

Post-mortem 1 (PM1): A 61-year-old male was brought in by ambulance with acute shortness of breath and cyanosis, but no chest pain. He had a background history of chronic obstructive pulmonary disease and ischaemic heart disease with prior coronary artery bypass grafting and percutaneous coronary intervention. He went into respiratory arrest with ambulance service and subsequently into cardiac arrest. He underwent several rounds of cardiopulmonary resuscitation with return of spontaneous circulation but returned to asystole. He had a recent history of difficulty in breathing, temperature and cough and had attended a separate emergency department one week previously where he had tested positive for COVID-19 by upper respiratory tract swab. Neither blood tests nor chest x-ray were undertaken prior to death. He died approximately ten days after the onset of symptoms. A full post-mortem was performed in this case.

Peripheral blood tests were not undertaken in this case as the patient was in cardiac arrest upon presentation to the emergency department.

Body mass index was 33.1kg/m^2.

The most significant findings in this case were florid diffuse alveolar damage in the exudative phase and an acute thrombus in the stented right coronary artery with an early neutrophil infiltrate in the posterior left ventricle consistent early myocardial infarction (12-24 hours). The kidney showed an intraluminal fibrin thrombus in one artery and severe intimal thickening of renal arteries. Acute tubular injury is noted. Brain examination revealed evidence of early ischaemia, mild perivascular T cell infiltrations and microglial activation. The liver showed established micronodular cirrhosis. The splenic periarteriolar T cells were mostly CD4 positive and the hilar lymph nodes showed a complete lack of CD8 positive T cells.

The cause of death given by the clinical team was:
1a COVID-19 pneumonia
2 Chronic obstructive pulmonary disease, ischaemic heart disease

The cause of death after autopsy was given as:
1a Diffuse alveolar damage and myocardial infarction
1b SARS-CoV-2 infection and coronary artery atherosclerosis (stented)
2 Ischaemic heart disease, liver, elevated BMI

Post-mortem 2 (PM2): A 64-year-old man was admitted to the Intensive Care Unit from an external hospital after three days of intubation and ventilation for COVID-19 pneumonitis. He symptoms (cough, dyspnoea and fever) had begun nine days previously. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR He had high oxygen requirements and required inotropic support and became oliguric. His inflammatory markers continued rise. He had a background history of obstructive sleep apnoea (on home CPAP), previous exercise tolerance of 5 miles per day, migraine with aura, benign prostatic hyperplasia and a previous umbilical hernia repair. Serial chest x-rays showed extensive bilateral airspace shadowing worsening over time, typical for COVID-19. He continued to be haemodynamically unstable. His last blood tests prior to death are summarised below. He died 13 days after the onset of symptoms and six days after admission to the intensive care unit. A full post-mortem was performed in this case.

Peripheral blood results: white cell count (WCC) 21.7x10^9/L, Lymphocyte 0.7x10^9/L, Haemoglobin 119g/L, Platelets 249x10^9/L, Fibrinogen 7.87g/L, prothrombin time (PT) 15.2s, activated partial thromboplastin time (APTT) 32.3s, C-reactive peptide (CRP) 416.9mg/L, High sensitivity troponin 11pg/mL, Amylase 49g/L, Ferritin 1369ug/L, D-dimer 8346ng/mL, Procalcitonin 5.64ug/L.

Body mass index was 35.86.

At post-mortem, the major finding was diffuse alveolar damage predominantly in the exudative phase with a few focal regions showing acute fibrinous and organizing pneumonia. Occasional micro-thrombi were noted in the

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

pulmonary vasculature. The heart had a mottled appearance and subendocardial contraction band necrosis was noted on histology. No coronary thromboses were noted. It was uncertain whether this related to ischaemia or inotropes received in the intensive care unit. The adrenal gland showed focal areas of infarction in the cortex. The brain showed vascular congestion, perivascular T lymphocytes and moderate to intense activation of microglial cells. No phagocytosis was noted in bone marrow, spleen or lymph node samples.

The cause of death given by the clinical team was:

1a COVID-19 pneumonitis

2 Obstructive sleep apnoea

The cause of death after post-mortem was given as:

1a Diffuse alveolar damage

1b SARS-CoV-2 infection

2 Obstructive Sleep Apnoea

Post-mortem 3 (PM3): A 69-year-old female presented with a five-day history of productive cough, shortness of breath, central chest pain, diarrhoea and fever. She had a past medical history of COPD, Obstructive sleep apnoea, Cor Pulmonale on O2 (housebound), Ischaemic Heart Disease, Hypertension, Type 2 Diabetes mellitus and peripheral neuropathy. She had a 10-15 pack year smoking history. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR. A chest x-ray showed peripheral consolidation and pulmonary congestion. She developed acute kidney injury and deteriorated with tachypnoea, accessory muscles of respiration use and tiring. Her last blood tests prior to death are summarised below. She was referred for palliative care input and treatment was not escalated above ward-level. She died 8 days after the onset of symptoms. A full post-mortem was performed in this case.

Peripheral blood results: WCC 9.9x10^9/L, Lymphocyte 0.6x10^9/L, Haemoglobin 143g/L, Platelets 132x10^9/L, Fibrinogen 5.35g/L, PT 14.6s, APTT 26.8s, CRP 118.8mg/L, High sensitivity troponin 102pg/mL, LDH 313U/L, Amylase g/L, Ferritin 289ug/L, D-dimer 850ng/mL, Procalcitonin 0.42ug/L.

Body mass index was 44.1

At post-mortem examination, the most significant finding was exudative phase diffuse alveolar damage with widespread pulmonary oedema. Multiple platelet-rich thrombi were noted in the pulmonary circulation. A benign adrenocortical adenoma was noted. The liver showed mild large droplet fatty change, but no ballooning or nuclear vacuolation. There was evidence of acute tubular injury in the kidney and moderate arterial intimal thickening. Some splenic sinus-lining macrophages showed phagocytic activity. The heart showed patchy early interstitial fibrosis consistent with old ischaemic damage.

The cause of death given by the clinical team was:

1a COVID-19 Pneumonitis

2 Chronic obstructive pulmonary disease, obstructive sleep apnoea, ischaemic heart disease, hypertension, obesity, smoker, type two diabetes mellitus

The cause of death after autopsy was given as:

1a Pulmonary oedema and diffuse alveolar damage

1b SARS-CoV-2 infection

2 Obesity, hypertension, type II diabetes mellitus, smoker, ischaemic heart disease, obstructive sleep apnoea

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Post-mortem 4 (PM4): A 78-year-old male presented with a four-day history of non-productive cough, fever and worsening shortness of breath. He had increasing confusion and dysphagia. He had a past medical history of advanced dementia (bed bound), hypertension, type 2 diabetes mellitus and osteoarthritis. A chest x-ray showed bilateral airspace opacification. He was desaturating on room air and given oxygen supplementation. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR. He continued to deteriorate clinically. He was referred for palliative care input and treatment was not escalated above ward-level. His last blood tests prior to death are summarised below. A full post-mortem was performed in this case. He died 12 days after the onset of symptoms.

Peripheral blood results: WCC 9x10^9/L, Lymphocyte 1.5x10^9/L, Haemoglobin 135g/L, Platelets 143x10^9/L.

Body mass index was 24.7

Post-mortem examination showed diffuse alveolar damage in organising and exudative phases with a superimposed bronchopneumonia. Very focally, there appeared to be an area of lymphocytic vasculitis. A very occasional micro-thrombus was noted in the lung. The spleen showed prominent haemophagocytosis. The bone marrow and spleen showed prominent haemophagocytosis. The hilar lymph nodes showed a CD4:CD8 ratio of ~3:1. There was evidence of acute tubular injury and multiple arterial fibrin thrombi in the kidney. The heart was 428g (body weight 65kg) and there was moderate arterial intimal thickening in the kidney. There was peripheral muscle wasting on external examination. This liver was markedly autolytic but appeared normal.

Cause of death given by clinical team:

1a COVID-19 Pneumonia

2 Dementia, frailty, hypertension

Cause of death after post-mortem examination:

1a Diffuse alveolar damage and haemophagocytosis

1b SARS-CoV-2 infection

2 Dementia, frailty, hypertension.

Post-mortem 5 (PM5): A 22-year-old male was admitted to the Intensive Care Unit from an external hospital with suspected COVID-19 pneumonia and a subacute right middle cerebral artery infarct. He had and reduced oxygen saturations. He had a background history of obesity and hypothyroidism. Serial chest x-rays showed bilateral airspace consolidation consistent with COVID-19. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR. He was intubated and ventilated. His inflammatory markers worsened over time. A CT-pulmonary angiogram identified multiple sub-segmental pulmonary emboli. He was treated with argotroban, caspofungin, linezolid, meropenam and tigecycline. He became hypotensive and developed acute kidney injury and rhabdomyolysis. A CT head showed a haemorrhagic transformation into the right MCA infarct. Subsequently an ECG and transthoracic echocardiograph demonstrated pericarditis and a pericardial effusion which was drained. A had increasing requirement of vasopressors, noradrenaline and vasopressin and became acidotic with an elevated lactate. His last blood tests prior to death are summarised below. He died after 22 days on a ventilator and 27 days after symptom onset. A full post-mortem was performed in this case.

Peripheral blood results: WCC 22.5x10^9/L, Haemoglobin 78g/L, Platelets 133x10^9/L, Fibrinogen 4.8g/L, PT 31.5s, APTT 51.3s, CRP 395mg/L, High sensitivity troponin 631pg/mL, LDH 2840U/L, Ferritin 1401ug/L, D-dimer 14441ng/mL, Procalcitonin 100ug/L.

Body mass index was 48.8.

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

The major findings at post-mortem were disseminated mucormycosis involving the lungs, hilar lymph nodes, brain and kidney. A severe acute haemorrhagic, necrotic pancreatitis was noted and no fungal hyphae were noted in the pancreas on Grocott Silver, H&E and PAS stains. The lungs showed severe marked pulmonary oedema and haemorrhage with focal frank necrosis in the right lung. Diffuse alveolar damage was focal and a mixture of exudative/organising in the lung. The liver showed bridging fibrosis, moderate large droplet fatty change and mild ballooning. The thyroid showed atrophic thyroid epithelium, fibrosis, chronic inflammation and lymphoid follicles and IgG4 staining showed only occasional positive cells. The kidney showed acute tubular injury and myoglobin casts. The brain showed recent haemorrhagic infarction in the right cerebral hemisphere with infiltration by mucor. Multi-organ thrombo-emboli were present. The heart showed fibrinous pericarditis with fungal hyphae present in the pericardial space.

Cause of death given by clinical team was:

1a COVID-19 pneumonia

2 Cerebral infarct, hypothyroidism

Cause of death after post-mortem examination was:

1a Multi-organ failure

1b Disseminated Mucormycosis

1c SARS-CoV-2 Infection

2 Elevated body mass index, hypothyroidism, steatohepatitis

Post-mortem 6 (PM6): A 24-year-old man had been self-isolating at home with symptoms indicative of COVID-19 (cough, fever and shortness of breath). These symptoms became progressively worse and he underwent an out of hospital cardiac arrest. He was brought into hospital by ambulance, resuscitated and transferred to the Intensive Care Unit for intubation and ventilation. He had a background history of non-alcoholic steatohepatitis (Biopsy proven, Activity Score 5/8, Fibrosis 3/4), lichen planus and Gonadotrophin releasing hormone deficiency (testosterone replacement every three months). Chest x-ray showed widespread airspace opacification and whiteout of the right hemithorax. It was thought that the x-ray findings may have been impacted by the out of hospital arrest. His last blood tests prior to death are summarised below. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR. He died eight days after the onset of symptoms. A full post-mortem was performed in this case.

Peripheral blood results: WCC 9x10^9/L, Lymphocyte 0.6x10^9/L, Haemoglobin 88g/L, Platelets 53x10^9/L, Fibrinogen 0.41g/L, PT 43.7s, APTT 118.9s, CRP 13.1mg/L, High sensitivity troponin 4142pg/mL, LDH 5464U/L, Amylase 399g/L, Ferritin 44487ug/L, D-dimer 20000ng/mL.

Body mass index was 25.2

The most significant finding at post-mortem was florid diffuse alveolar damage in the exudative phase with platelet rich thrombi in the lungs. Brain examination revealed evidence of recent ischaemia, moderate to intense microglial activation and occasional perivascular T cells. A portion of splenic and nodal sinus-lining histiocytes showed phagocytosis. The kidney showed acute tubular injury and moderate arterial intimal thickening out of proportion with his young age. The showed mild large droplet fatty change but no ballooning.

The cause of death given by the clinical team was:

1a Multi-organ failure

1b Pneumonia – COVID-19

2 Non-alcoholic steatohepatitis

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

The cause of death after autopsy was given as:

1a Diffuse Alveolar Damage

1b SARS-CoV-2 infection

Post-mortem 7 (PM7): A 77-year-old female had a two-week history of malaise with severe shortness of breath, productive cough, pleuritic chest pain, abdominal pain and diarrhoea. She had a background history of hypertension, left ventricular hypertrophy, osteoporosis, osteoarthritis, chronic kidney disease, vasculitis, hypercholesterolaemia, hiatus hernia, vitamin B12 deficiency, Vitamin D deficiency and gallstone pancreatitis. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR. The tachypnoea and hypoxia became worse. She was referred for palliative care input and treatment was not escalated above ward-level. She died on the second day of her admission and 15 days after the onset of symptoms. A limited post-mortem was performed in this case.

A limited biopsy consisting of core biopsies of the lung, heart, liver, kidney and bone marrow was performed in this case. The major findings were diffuse alveolar damage in exudative and organising phases, myeloid hyperplasia, acute tubular injury in the kidney, moderate arterial intimal thickening, and mild large droplet fatty change in the liver without ballooning. There was no evidence of vasculitis in any biopsies.

The cause of death given by the clinical team was:

1a COVID-19 Pneumonia

2 ANCA-associated vasculitis, pulmonary fibrosis, hypertension, chronic kidney disease

The case of death after autopsy was given as:

1a Diffuse alveolar damage

Post-mortem 7 (PM7): A 79-year-old male admitted with fever, with low oxygen saturation and a raised respiratory rate. He had a one-week history of sore throat and left shoulder pain prior to this. His background medical history included hypercholesterolaemia and trigeminal neuralgia. He was a non-smoker. During his admission he had ongoing fevers, drowsiness and worsening hypoxia and he was admitted to the intensive care unit. He was intubated and ventilated. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR. Serial chest x-rays showed worsening bilateral lung consolidation and widespread ground-glass change consistent with COVID-19. He had escalating ionotropic requirements, worsening acute kidney injury, coagulopathy and rising inflammatory markers. His last blood tests prior to death are summarised below. He died after 13 days in ICU and after 23 days since the onset of symptoms. A full post-mortem was performed in this case.

Peripheral Blood results: WCC 13.4x10^9/L, Lymphocytes 0.4x10^9/L, Haemoglobin 94g/L, Platelets 283x10^9/L, Fibrinogen 6.62g/L, PT 39.3s, APTT 43.4s, CRP 353.2mg/L, High sensitivity troponin 192pg/mL, Amylase 58g/L, Ferritin 3471ug/L, D-dimer 5027ng/mL, ALT 90U/L, Alk Phos 148 U/L, Bilirubin 57umol/L.

The Body Mass Index was 31.2kg/m^2.

At post-mortem examination, lung sections showed florid diffuse alveolar damage in both organising and exudative phases. Microthrombi were noted in the heart and lung. Acute inflammation was noted in the epidcardial fat. Marked autolysis hampered the interpretation of the liver histology. The kidney showed evidence of acute tubular injury. The brain showed mild chronic inflammation and focal hypoxic changes of cortical neurones. Focal haemophagocytosis was noted in the bone marrow. Significant phagocytic activity was noted in the histocytes of the hilar lymph nodes and a proportion of bone marrow histiocytes showed phagocytosis. Both spleen and lymph nodes showed a reduction in T-cell with a marked depletion of CD8 positive T cells.

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

The cause of death give by the clinical team was:

1a SARS-COVID-19

The case of death after autopsy was given as:

1a Diffuse Alveolar Damage

1b SARS-CoV-2 Infection

2 Hypertension, chronic kidney disease

2 Left ventricular hypertrophy, coronary atherosclerosis.

Post-mortem 8 (PM8): A 97-year-old man presented with general malaise. He had a background history of recurrent urinary tract infections, dementia, bladder cancer (treat with radiotherapy 2000), anaemia, hypothyroidism, glaucoma, alcohol-related liver disease and a pacemaker in-situ. His General Practitioner had treated him for a urinary tract infection (UTI) but he had not improved. He was initially treated as a UTI. During his admission, he developed fever/rigors, lethargy, decreased mobility and a cough. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR. He had no abdominal pain recorded in his medical notes. He began to require supplemental oxygen and his CRP began to rise. He was referred for palliative care input and treatment was not escalated above ward-level. Serial chest x-rays showed worsening bilateral airspace consolidation consistent with COVID-19. He began to clinically deteriorate with cyanosis, dyspnoea and tachypnoea. His last blood tests prior to death are summarised below. He died 23 days after onset of symptoms. A full post-mortem was performed in this case.

Peripheral blood results: WCC 5.4x10^9/L, Lymphocyte 0.6x10^9/L, Haemoglobin 135g/L, Platelets 78x10^9/L, CRP 143mg/L.

Body mass index was 18.3kg/m^2.

The major findings at autopsy were florid diffuse alveolar damage in the exudative phase and widespread thromboemboemboli in the lungs. Haemophagocytosis was prominent in the bone marrow. The spleen showed focal phagocytic activity in splenic sinusoidal histiocytes. Microscopic acute inflammation was noted in the pancreas and fat necrosis was identified in the fat surrounding the left adrenal. Pancreatitis had not been appreciated macroscopically. and the spleen showed focal phagocytic activity in splenic sinusoidal histiocytes. Microscopic acute inflammation was noted in the pancreas and fat necrosis was identified in the fat surrounding the left adrenal. Pancreatitis had not been appreciated macroscopically. The hilar lymph node sampling revealed a single large fibrotic granuloma with central necrosis containing acid-fast bacilli. There was no evidence of re-activation of tuberculosis on any other sections and this man had no documented clinical history of tuberculosis. The kidney showed evidence of thrombotic microangiopathy, acute tubular injury and marked glomerular senescence along with hypertensive changes. The liver showed focal bridging fibrosis with steatosis and widespread zone 3 necrosis and haemorrhage. Cardiac amyloidosis was noted along with multiple micro-thrombi in the small cardiac vessels. The amyloidosis was considered to most likely represent wild-type transthyretin amyloid and was not pursued further. Peripheral muscle wasting was noted on external examination. No evidence of persistent bladder cancer was identified.

The cause of death given by the clinical team was:

1a Pneumonia – COVID-19

2 Advanced frailty, dementia, liver cirrhosis, bladder cancer (treated).

The cause of death after autopsy was given as:

1a Diffuse alveolar damage and widespread thrombosis

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

1b SARS-CoV-2 Infection

2 Early hepatic fibrosis, dementia, frailty and cardiac amyloidosis

Post-mortem 9 (PM9): A 79-year-old female was admitted with acute kidney injury and a one-week history of diarrhoea and intermittent vomiting while being unable to eat or drink. She had raised inflammatory markers (WCC18, CRP 220). A PCR test for clostridium difficile in the stool was positive and she was treated with antibiotics. She had a past medical history of chronic obstructive pulmonary disease, cutaneous systemic lupus erythematosus, hypertension, type 2 diabetes mellitus and vitamin B12 deficiency. During her admission she had ongoing elevated inflammatory markers and began to desaturate on room air. She developed a fever, cough, wheeze and worsening type two respiratory failure. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR. Her oxygen requirements increased. She was referred for palliative care input and treatment was not escalated above ward-level. Her last blood tests prior to death are summarised below. She died 24 days after the onset of symptoms. A full post-mortem was performed in this case.

Peripheral blood results: WCC 6.8x10^9/L, Lymphocyte 0.7x10^9/L, Haemoglobin 87g/L, Platelets 164x10^9/L, CRP 49.2mg/L.

Body mass index was 19.72.

The most significant finding at autopsy was focal diffuse alveolar damage with widespread vascular congestion and micro-thrombi in the pulmonary vasculature. Patchy fibrosis was noted in the heart consistent with old ischaemia. The spleen showed relative attenuation of the white pulp and a congested red pulp. Splenic CD3+ T cells were markedly reduced and CD20+ B cells were well preserved. Splenic sinus linking macrophages were prominent and some showed phagocytosis. The lymph node showed relative shrinking of paracortical areas and most T-cells were CD4+. Most brain regions showed moderate to intense activation of microglial cells and T lymphocyte excess. Microscopic infarction-type necrosis was noted in the adrenal glands with organising thrombi present.

The cause of death given by the clinical team was:

1a Pneumonia (COVID-19)

2 Hypertension, Diabetes Mellitus (type II), Chronic Obstructive Pulmonary Disease

The cause of death after autopsy was given as:

1a Diffuse alveolar damage

1b SARS-CoV-2 Infection

2 Hypertension, diabetes mellitus type II, chronic obstructive pulmonary disease.

The Body Mass Index was 31.2kg/m^2.

At post-mortem examination, lung sections showed florid diffuse alveolar damage in both organising and exudative phases. Microthrombi were noted in the heart and lung. Acute inflammation was noted in the epicardial fat. Marked autolysis hampered the interpretation of the liver histology. The kidney showed evidence of acute tubular injury. The brain showed mild chronic inflammation and focal hypoxic changes of cortical neurones. Focal haemophagocytosis was noted in the bone marrow. Significant phagocytic activity was noted in the histocytes of the hilar lymph nodes. Both spleen and lymph nodes showed a reduction in T-cell with a marked depletion of CD8 positive T cells.

Post-mortem 10 (PM10): A 77-year-old female had a two-week history of malaise with severe shortness of breath, productive cough, pleuritic chest pain, abdominal pain and diarrhoea. She had a background history of hypertension, left ventricular hypertrophy, osteoporosis, osteoarthritis, chronic kidney disease, vasculitis, hypercholesterolaemia, hiatus hernia, vitamin B12 deficiency, Vitamin D deficiency and gallstone pancreatitis. Swab of the upper respiratory tract identified SARS-CoV-2 infection by PCR. The tachypnoea and hypoxia

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

became worse. She was referred for palliative care input and treatment was not escalated above ward-level. She died on the second day of her admission and 15 days after the onset of symptoms. A limited post-mortem was performed in this case.

WCC 4.2x10^9/L, Lymphocyte 0.6x10^9/L, Haemoglobin 134g/L, Platelets 280x10^9/L, Fibrinogen 7.29g/L, PT 14.6s, APTT 40.7s, CRP 288mg/L, High sensitivity troponin 9pg/mL, LDH 798U/L, Ferritin 1909ug/L, D-dimer 4497ng/mL, Procalcitonin 65.53ug/L.

A limited biopsy consisting of core biopsies of the lung, heart, liver, kidney and bone marrow was performed in this case. The major findings were diffuse alveolar damage in exudative and organising phases, myeloid hyperplasia, acute tubular injury in the kidney, moderate arterial intimal thickening, and mild large droplet fatty change in the liver without ballooning. Very occasional bone marrow histiocytes showed phagocytic activity. There was no evidence of vasculitis in any biopsies.

The cause of death given by the clinical team was:

1a Diffuse Alveolar Damage

1a COVID-19 Pneumonia

2 ANCA-associated vasculitis, pulmonary fibrosis, hypertension, chronic kidney disease

The case of death after autopsy was given as:

1a Diffuse alveolar damage

1b SARS-CoV-2 Infection

2 Left ventricular hypertrophy, coronary atherosclerosis.

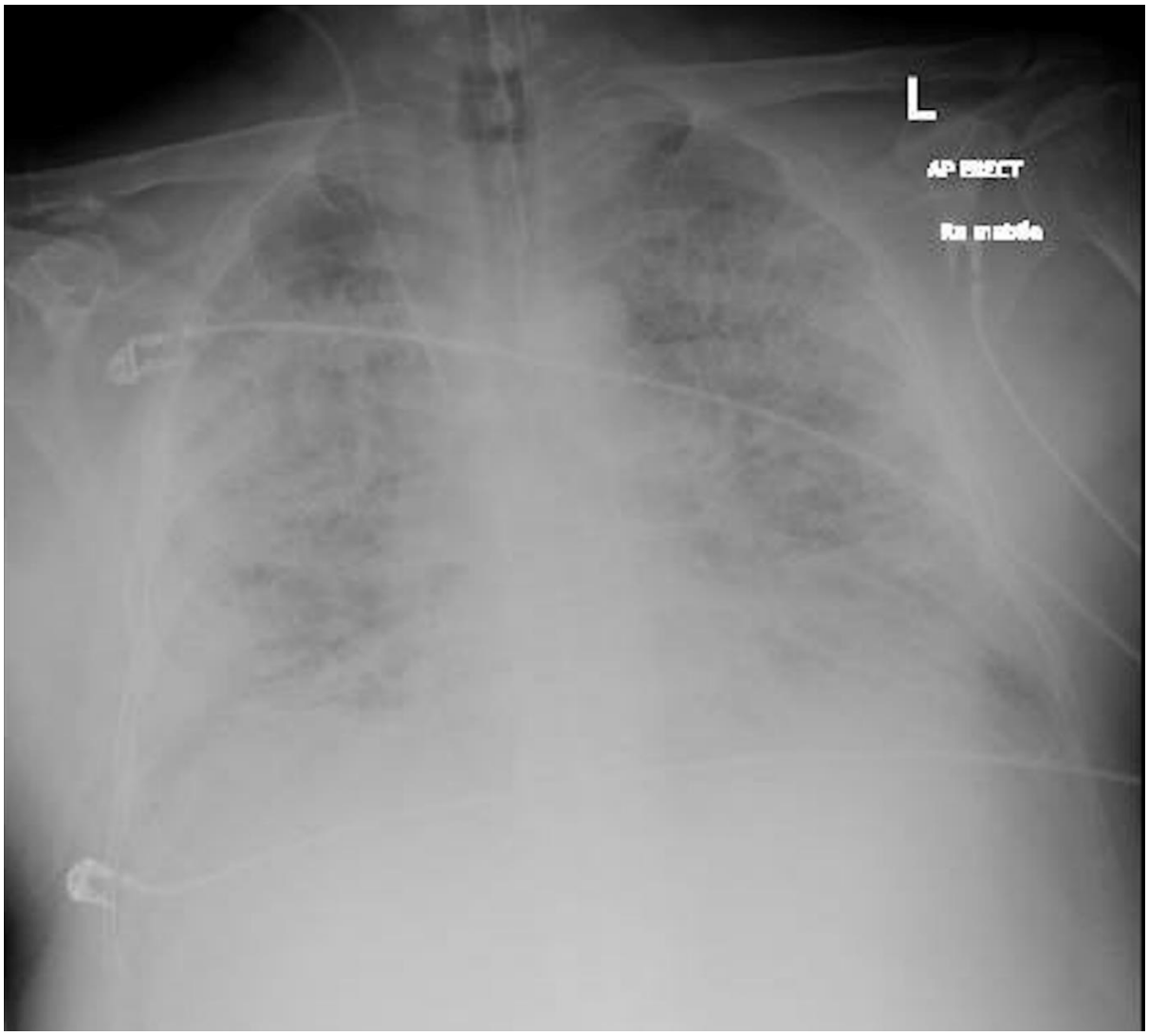
2 Hypertension, chronic kidney disease

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Radiological Imaging of COVID-19 Patients

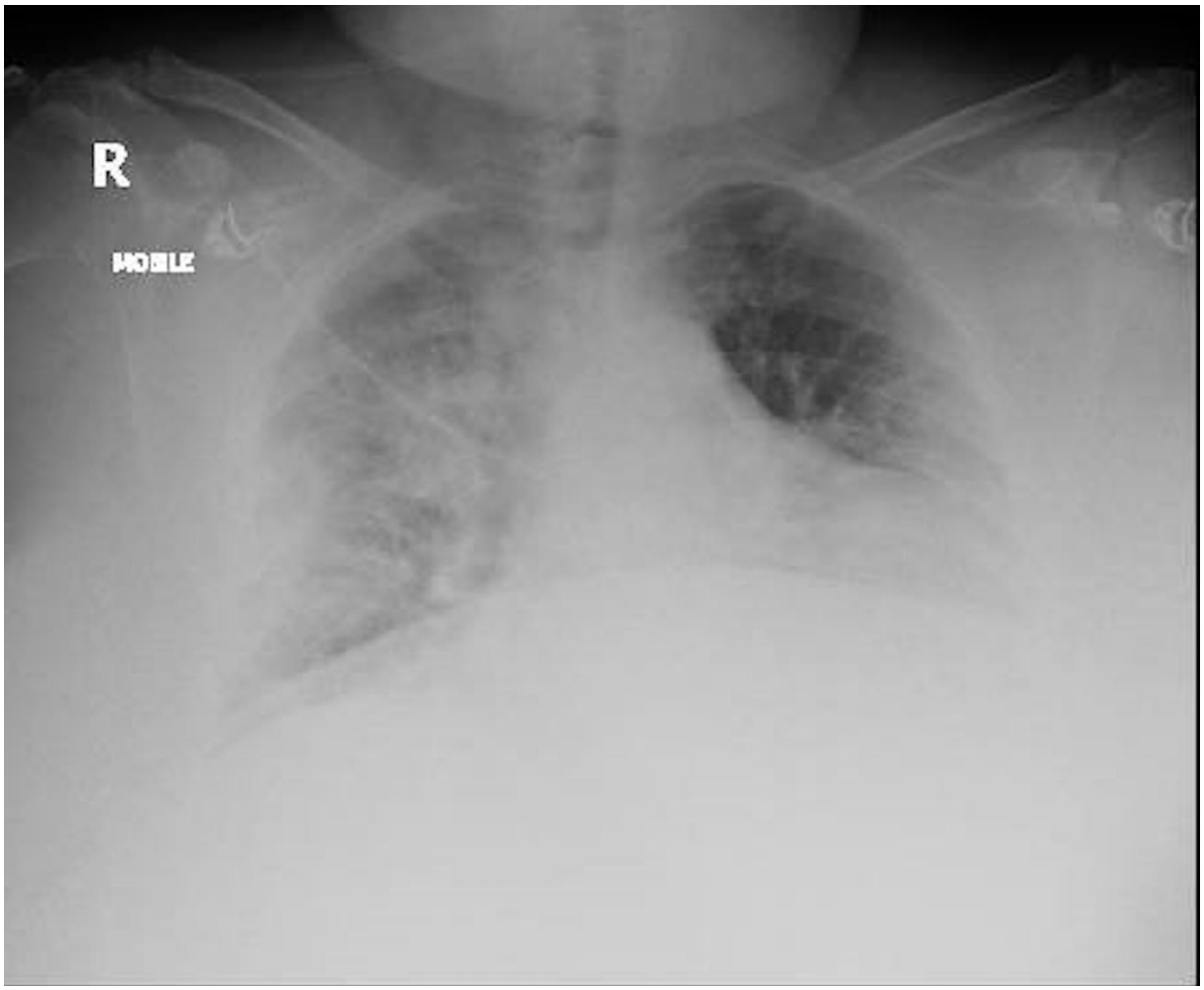
PM1: No Radiology Available

PM2: Chest X-Ray



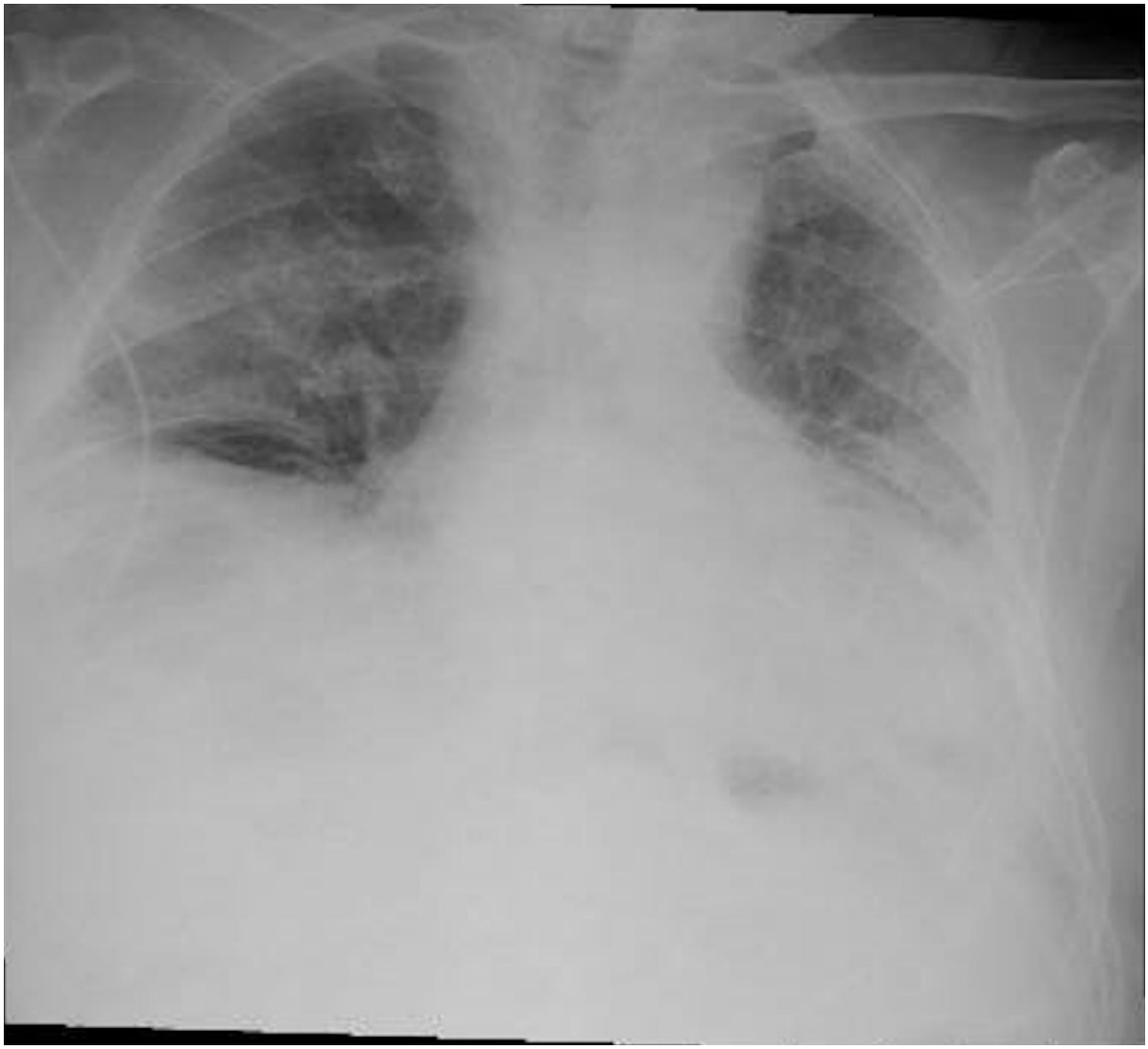
Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

PM3: Chest x-ray



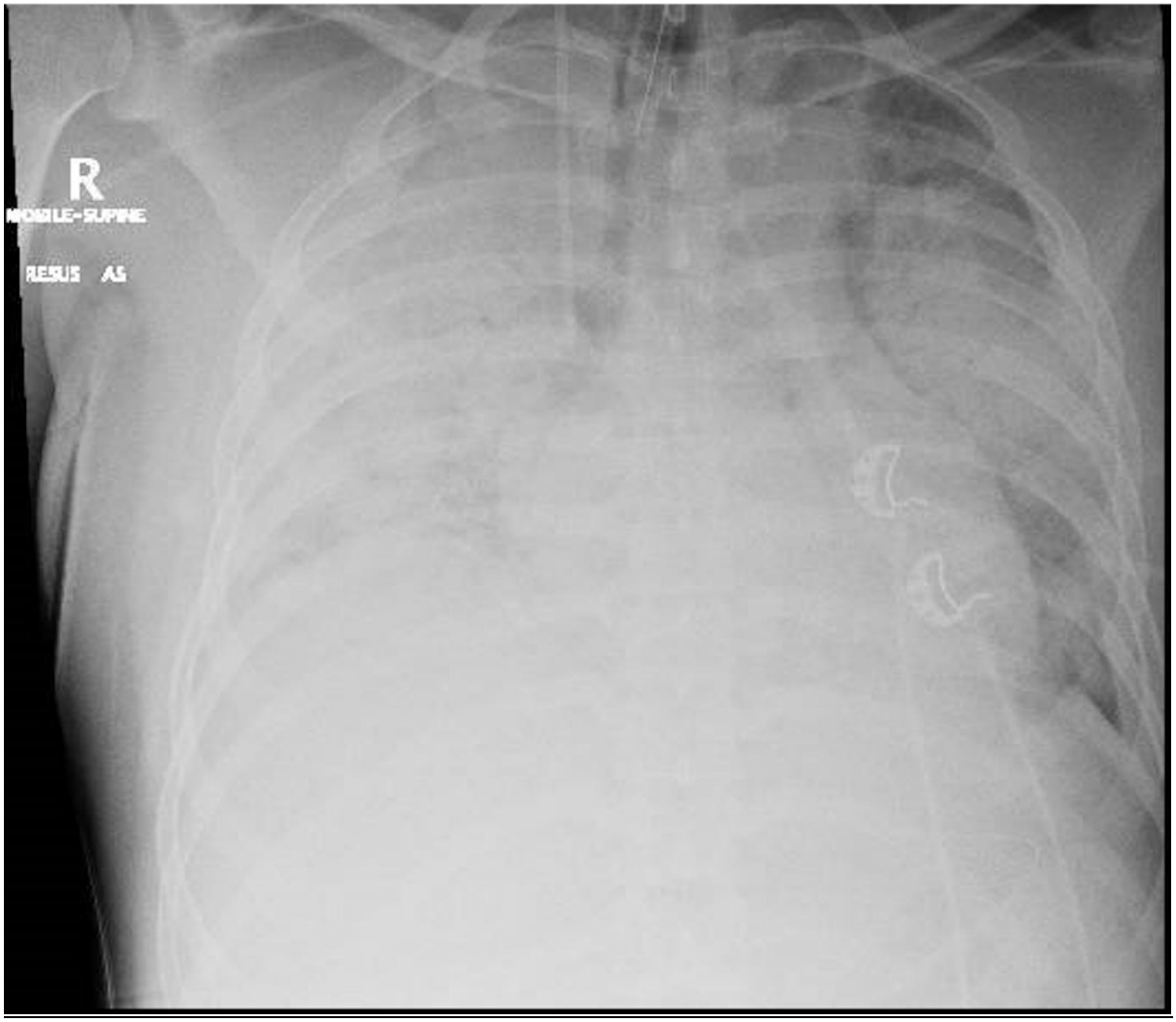
Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

PM4: Chest x-ray



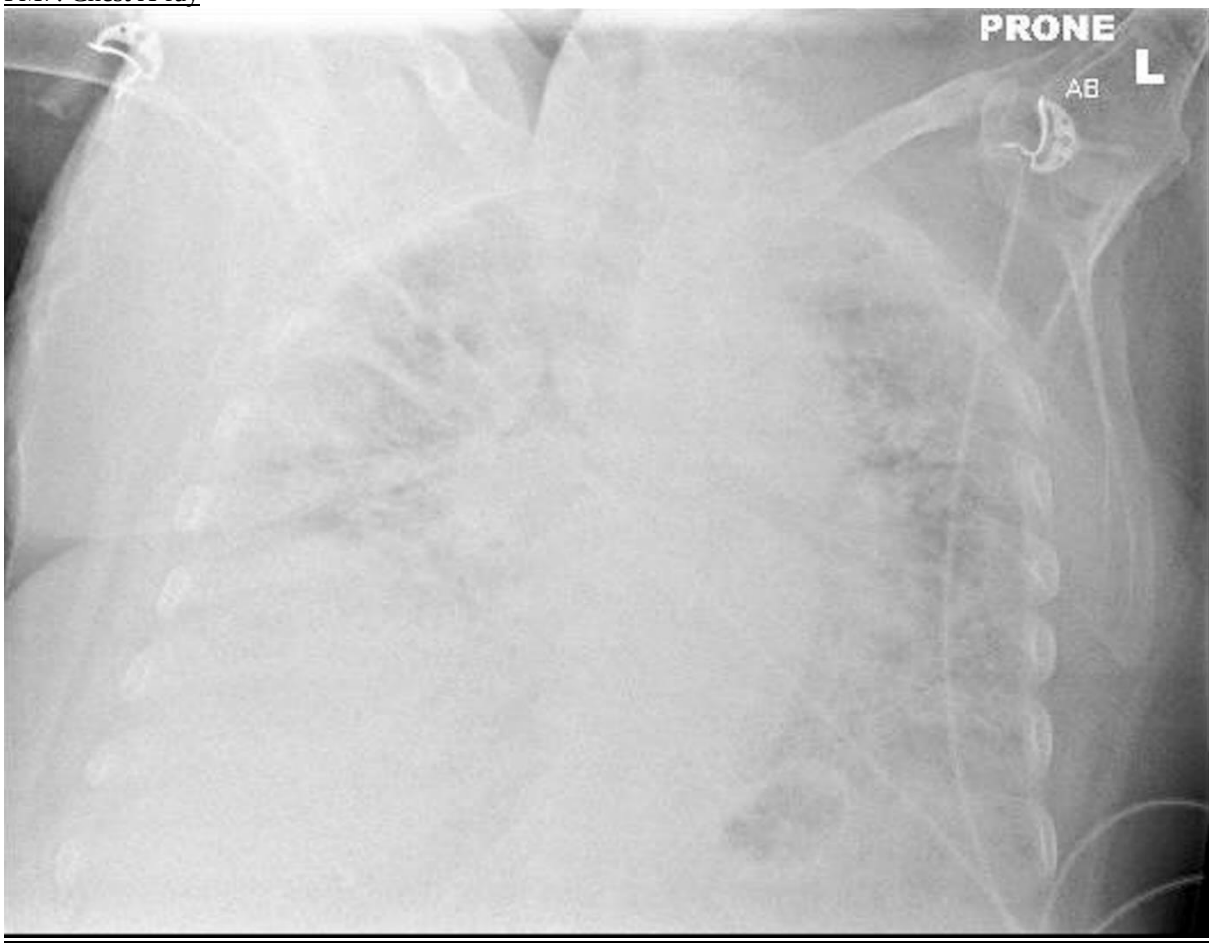
Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

PM6: Chest x-ray



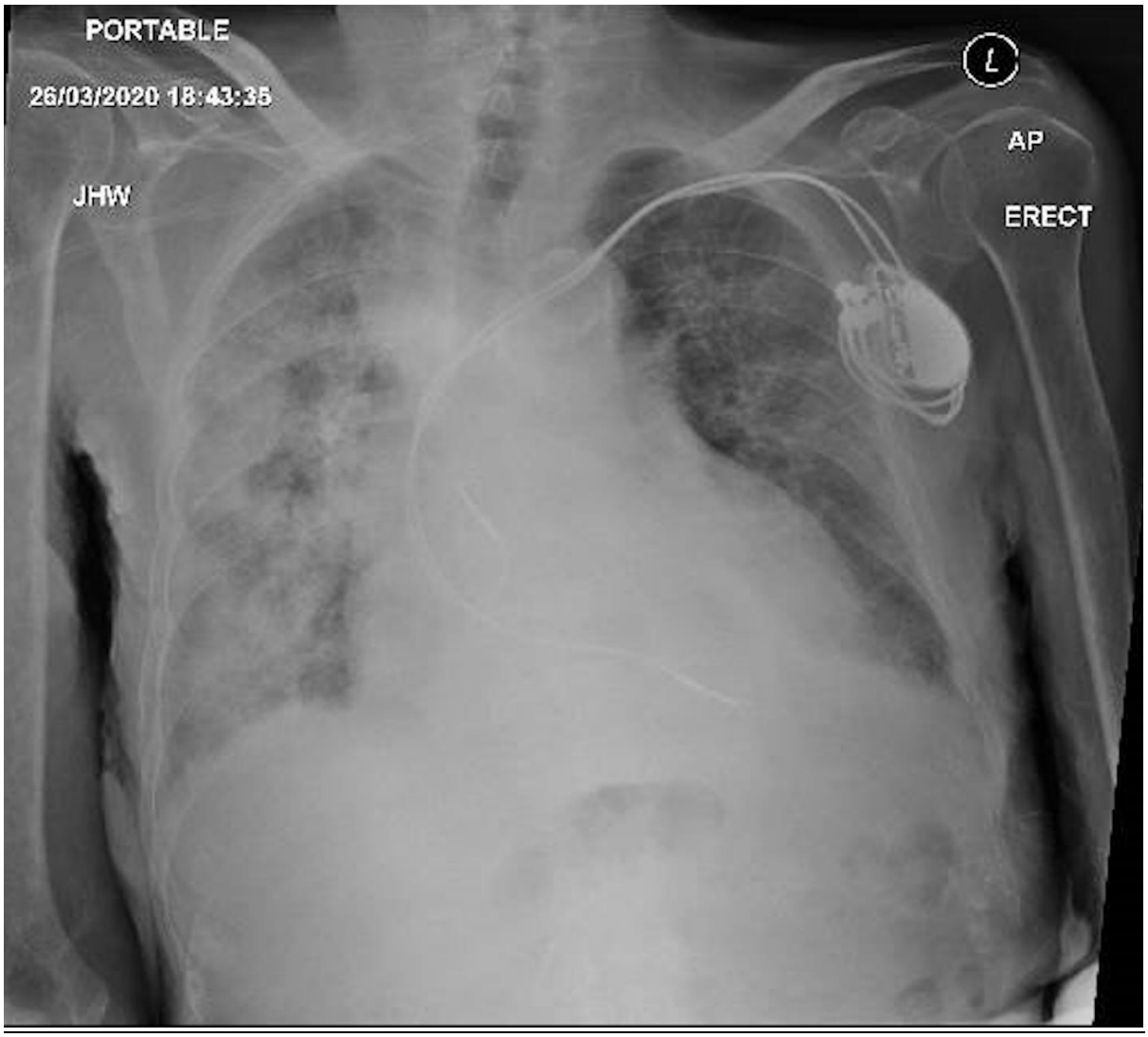
Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

PM7: Chest X-ray



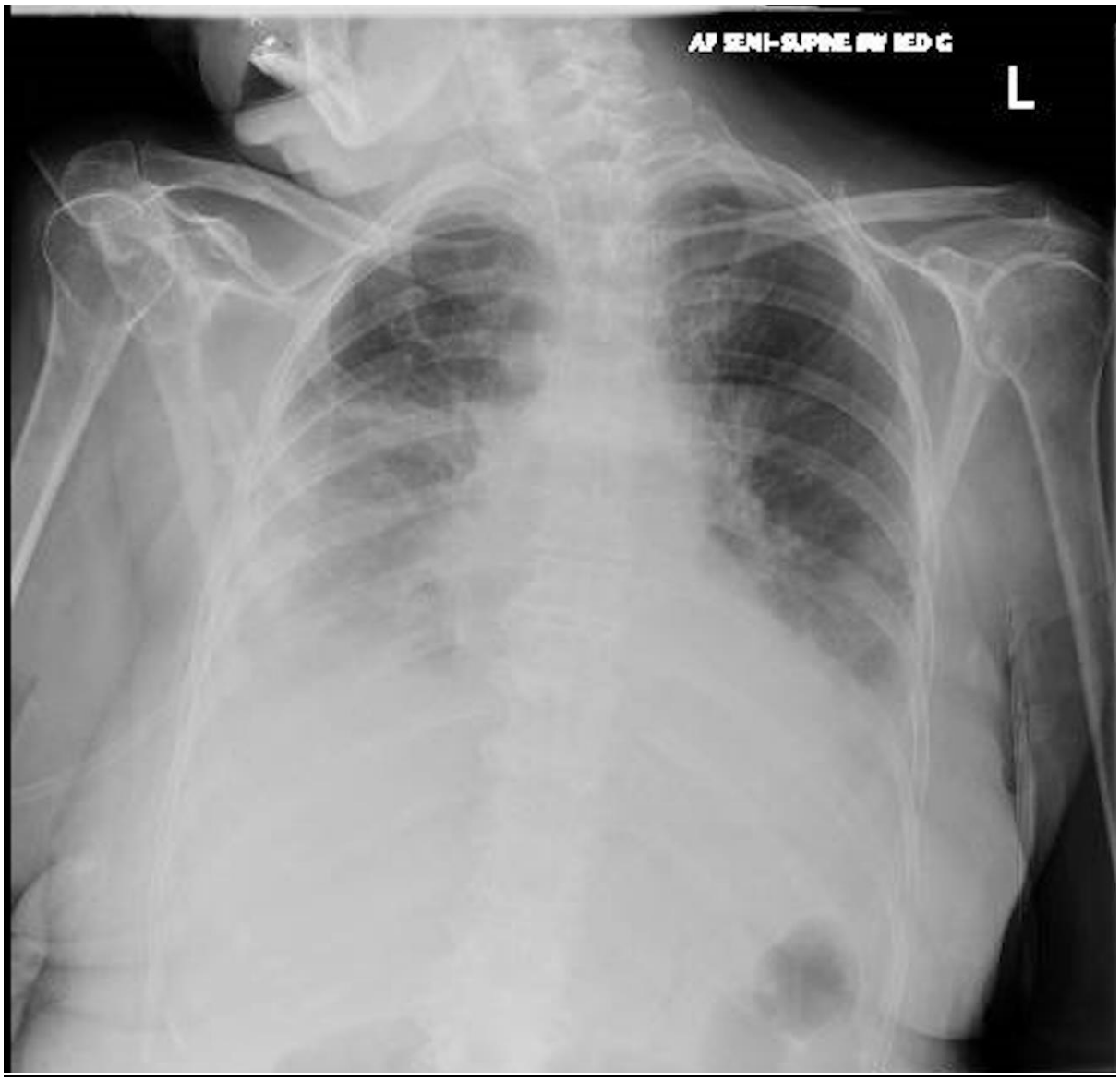
Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

PM8: Chest x-ray



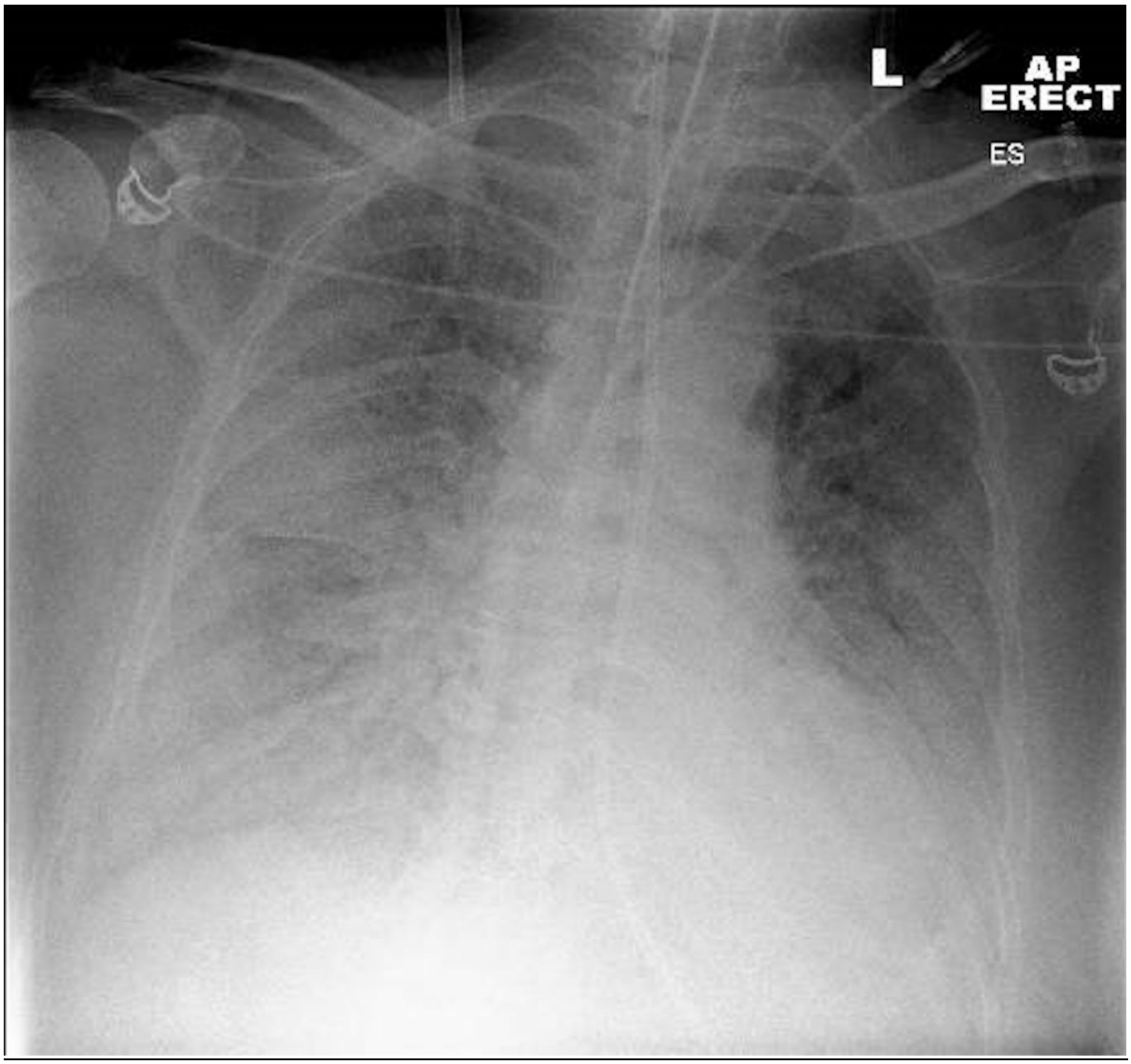
Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

PM9: Chest x-ray



Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

PM10: Chest x-ray



Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Supplementary Tables

Supplementary Table 1: (Immuno)histochemical stains used to interpret the histological findings in COVID-19 autopsies**.**

Antigen	Antibody Supplier	Clone	Section thickness	Product Code
CD20	Dako	L25	1um	M0755
CD3	Leica	LN10	1um	NCL-L-CD3-565
CD34	Dako	QBEnd-10	3um	M7165
CD4	Leica	4B12	1um	NCL-L-CD4-368
CD56	Leica	CD564	1um	PA0191
CD57	Leica	NK-1	1um	PA0443
CD61	Dako	Y2/51	3um	M0753
CD68/PGM1	Leica	514H12	1um	PA0273
CD8	Leica	1A5	1um	NCL-CD8-297
Cam5.2	BD		3um	345770
CD10	Leica	56C6	1um	NCL-L-CD10-270
CD138	Dako	MI15	1um	M7228
CMV	Dako	CCH2 and DDG9	1um	M0854
EBER	Leica		1um	PB0589
FOXP3	ThermoFisher	236A/E7	1um	14-4777-82
Glycophorin C	Dako	Ret40f	1um	M0820
Granzyme B	Leica	11F1	1um	NCL-L-Gran-B
IgD	Leica	DRN1C	1um	PA0061
IgG	Dako		1um	A0423
IgM	Dako		1um	A0425
Kappa	Dako		1um	A0191
Ki67	Leica	K2	1um	PA0230
Lambda	Dako		1um	A0193

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Supplementary Table 2. Clinical features, blood results and imaging findings in our series**.** Data presented as median and IQR (interquartile range) or % (N). OSA, Obstructive sleep apnoea, CABG, coronary artery bypass graft, COPD, Chronic Obstructive Pulmonary Disease, NASH, non-alcoholic steatohepatitis, ANCA antineutrophil cytoplasmic antibody, IHD, Ischaemic Heart Disease. T2DM, type 2 diabetes mellitus, ACEi angiotensin converting enzyme inhibitor, ARB, angiotensin receptor blocker. Blood results were those taken closest to death. taken as the last test prior to death. *co-morbidities taken to contribute to death if listed under Part 2 of the MCCD by the ONS format.

	Median (IQR) or % (n/N)	**Reference Range**	**N**
Age (years)	73 (51.8-79)		10
Race	Asian: 50% (5/10) White: 40% (4/10) Black: 10% (1/10)		10
Sex	Male 70% (7/10) Female 30% (3/10)		10
Co-morbidities contributing to death clinically*	Hypertension 40% (4/10) COPD 30% (3/10) OSA 20% (2/10) T2DM 20% (2/10) IHD 20% (2/10) Dementia 20% (2/10) Frailty 20% (2/10) Pulmonary Fibrosis 10% (1/10) Obesity 10% (1/10) Smoker 10% (1/10) CKD 10% (1/10) ANCA vasculitis 10% (1/10) NASH 10% (1/10) Liver cirrhosis 10% (1/10) Hypothyroidism 10% (1/10) Cerebral Infarct 10% (1/10)		10
Symptom onset to death, days	14 (9.5-23.3)		10
Time on Ventilator, days	0 (0-7.5)		
Smoker	Current Smoker 20% (1/5) Ex-smoker 20% (1/5) Non-smoker 60% (3/5)		5

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Prescribed ACEi/ARB	Yes 33.3% (3/9) No 66.7% (6/9)		9
Body mass index, kg/m^2	31.2 (22.3-40)	20-25	9
White blood cell count, x10^9/L	9 (6.1-17.6)	4.2-10.6	9
Neutrophil count, × 10^9/L	6.15 (4.7-11.3)	2-7.5	8
Lymphocyte count, × 10^{9}L	0.6 (0.6-0.7)	1.5-4.5	8
Haemoglobin, g/L	119 (87.5-135)	130-180 (male) 115-165 (female)	9
Platelet count, × 10^9/L	143 (105-264.5)	130-370	9
Fibrinogen, g/L	6 (3.7-7.4)	1.9-4.3	6
Prothrombin time, s	23.4 (14.6-40.4)	12.8-17.4	6
Activated partial thromboplastin time, s	42.1 (30.9-68.2)	25-35	6
D-dimer, ng/mL	6686.5 (3585-15,831)	<500	6
Ferritin, ug/L	1655 (1099-13,725)	20-300	6
C-reactive peptide, mg/L	215.5 (66.6-384.5)	0-5	8
Amylase	58 (49-58)	0-100	3
Albumin, g/L	23 (16-32.25)	35-50	6
Alanine aminotransferase, U/L	75.5 (35-543.5)	0-45	6
Total bilirubin, mmol/L	155 (7.5-82)	1.71-20.5	6
Potassium, mmol/L	3.9 (3.6-5.7)	3.5-5.5	7
Sodium, mmol/L	142 (133-148)	135-148	7
Creatinine, μmol/L	126.5 (84.5-222.5)	60-125	8
Creatine kinase, U/L	533 (121-4195.5)	22-198	5
Lactate dehydrogenase, U/L	1819 (434.3-4808)	140-280	4
Hypersensitive troponin I, pg/mL	147 (10.5-1508.8)	0-34	6
Procalcitonin, ug/L	35.6 (1.7-91.4)	0.1-0.49	4

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Chest-Xray	Bilateral Infiltrates: 77.8% (7/9) Unilateral Infiltrates: 22.2% (2/9)		9
Death to Autopsy, days	6 (4.8-7)		10

Supplementary Table 3. Pulmonary and cardiovascular pathology identified at autopsy in COVID-19 patients. Data presented as median and interquartile range (IQR) or number of cases showing pathology (n) over total number of cases examined (N) and percentage (%). *Indicative reference ranges given for organ weights. ** This corresponds to the patient documented in Figure 2a. Another patient had evidence of contraction band necrosis, however no coronary thrombus was identified. It is impossible to say whether this patient has contraction band necrosis related to ischaemia, inotropic medication or another cause and so it is not included. For precise reference ranges, correlation with body weight or surface area is required, Reference range taken from Autopsy Pathology: A Manual and Atlas, Third Edition (2016) by Andrew J. Connolly et. al.

	Median (IQR) or % (n/N)	Reference Range*	N
Pulmonary Pathology			
Right lung weight, g	1056 (740-1252)	360-570	9
Left Lung weight, g	732 (544-954)	325-480	9
Histological Diagnosis			
Diffuse Alveolar Damage	Exudative Phase 60% (6/10) Exudative/Organising Phase 40% (4/10)		10
Interstitium			
Acute Inflammation	Interstitial Neutrophils 30% (3/10)		10
Lymphocyte Inflammation	Mild 70% (7/10) Moderate 30% (3/10)		10
Multinucleated Giant Cells	Prominent 50% (5/10) Occasional 40% (4/10)		10
Pneumocyte Hyperplasia	Prominent 30% (3/10) Moderate 70% (7/10)		10
Viral Inclusions	Absent 100% (0/10)		9
Vessels			
Microthrombi	Prominent 88.8% (8/9)		9
Lymphocytic cuffing of small blood vessels	Focal 66.6% (6/9)		9
Lymphocytic Vasculitis	Focal 1/10 (10%)		9
Airway			
Chronic Bronchiolitis	100% (9/10)		10
Acute Bronchopneumonia	22.2% (3/9)		9

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Fungal lung infection	11.1%, (1/9)		9
Cardiac Pathology			
Heart weight, g	450 (312-535)	Male 270-360 Female 200-280	9
Myocardium			
Left ventricular wall thickness >15mm	44.4% (4/9)		9
Myocardial acute ischaemic damage	10% (1/10)**		10
Myocarditis	0% (0/10)		10
Amyloidosis	10% (1/10)		10
Vessels			
Coronary Artery Disease	Negligible 33.3% (3/9) Mild 44.4%(4/9) Moderate 22.2% (2/9)		9
Acute coronary thrombosis	11.1% (1/9)		9
Aortic dissection (contained)	11.1% (1/9)		9
Microthrombi	55.6.7% (5/9)		9
Endocardium			
Marantic Endocarditis	11.1% (1/9)		9
Pericardium			
Pericarditis	22.2% (2/9)		9
Pericardial Effusion	33.3% (3/9)		9

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Supplementary Table 4. Haematological and Endocrine Pathology in COVID-19 autopsies. Data presented as median and interquartile range (IQR) or number of cases showing pathology (n) over total number of cases examined (N) and percentage (%). $^{\$}$spleen is given as the average weight for a 20-65year old. For precise reference ranges, correlation with body weight or surface area is required. Reference range taken from Autopsy Pathology: A manual and Atlas, Third Edition (2016) by Andrew J. Connolly et. al.

	Median (IQR) or % (n/N)	Reference Range	N
Splenic Pathology			
Spleen weight, g	232 (130-498)	155$^{\$}$	9
Gross Splenic Infarction	11.1% (1/9)		9
Gross Peri-splenitis	11.1% (1/9)		9
Phagocytosis	57.1% (4/7)		6
Periarteriolar T-cell reduction	57.1% (4/7)		6
$CD8^{+}$ T-cell depletion	71.4% (5/7)		6
FoxP3 T^{reg} depletion	100% (2/2)		2
Hilar Lymph Node Pathology			
Phagocytosis	50% (3/6)		5
Necrotizing Granuloma	14.3% (1/7)*		7
T cell depletion	50% (4/8)		7
$CD8^{+}$ T-cell depletion	85.7%% (7/8)		6
FoxP3 T^{reg} depletion	100% (2/2)		2
Bone Marrow Pathology			
Phagocytosis	50% (4/8)		7
Endocrine Organs			
Pancreatitis	22.2% (2/9)		9
Adrenal Necrosis	33.3% (3/9)		9
Adrenalitis	0% (0/9)		9
Thyroid chronic inflammation	22.2% (2/9)		9

Reference Ranges: WCC 4.2-10.6x10^{9}/L, Lymphocyte count 1.5-4.5x10^{9}/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^{9}/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Supplementary Table 5. Renal, Hepatobiliary, gastro-intestinal and neuropathology in COVID-19 autopsies**.** Data presented as median and interquartile range (IQR) or number of cases showing pathology (n) over total number of cases examined (N) and percentage (%). *Indicative reference ranges given for organ weights. For precise reference ranges, correlation with body weight or surface area is required, Reference range taken from Autopsy Pathology: A manual and Atlas, Third Edition (2016) by Andrew J. Connolly et. al. ** autolysis hampered interpretation of gastro-intestinal organs, particularly on the mucosal aspect of the hollow viscera.

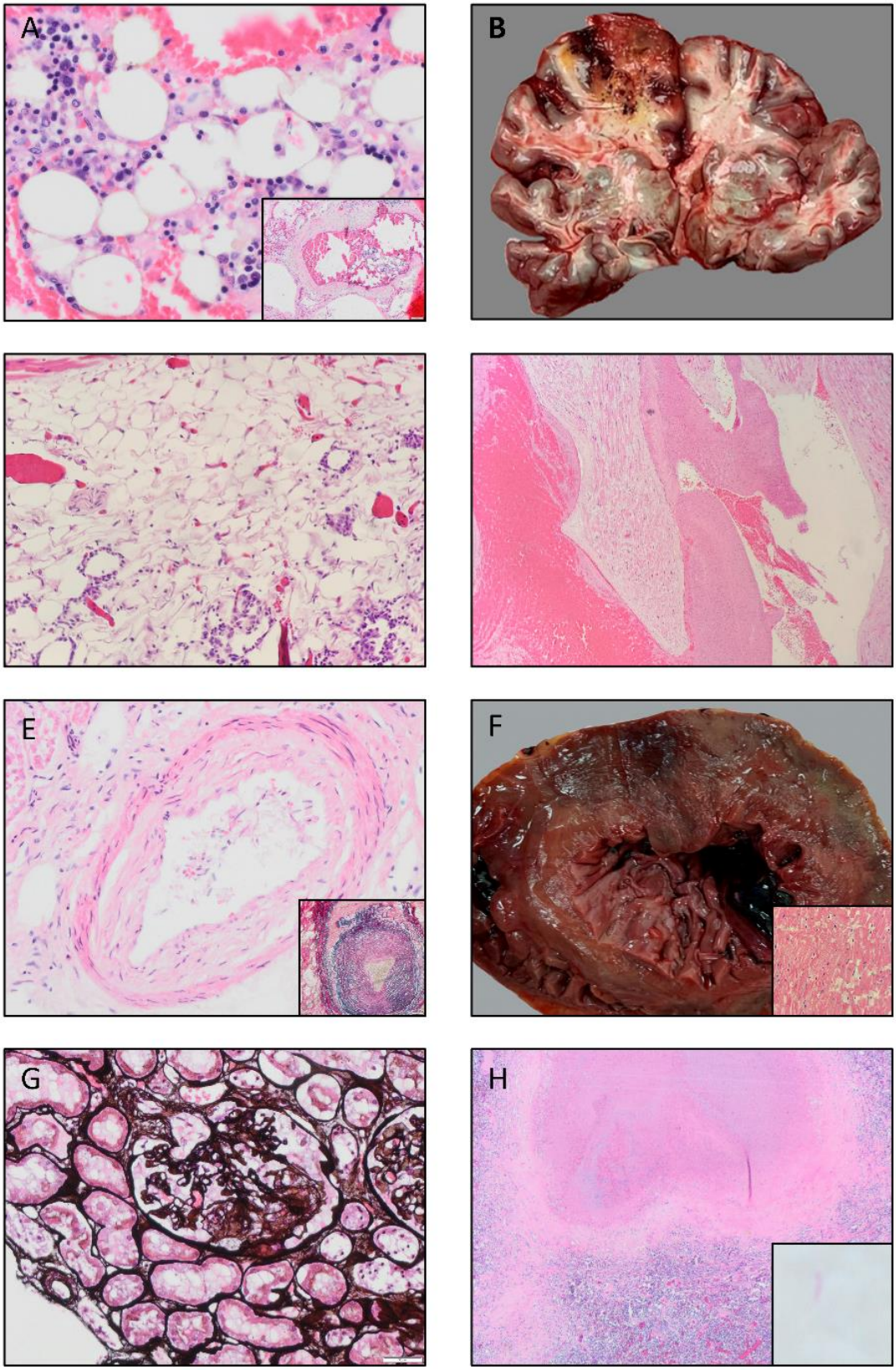
	Median (IQR) or % (n/N)	Reference Range*	N
Renal Pathology			
Combined Kidney Weight, g	264 (187-356)	230-440	9
Fibro-intimal thickening of renal vessels	Severe 50% (4/9) Moderate 33.3% (4/9) Mild 16.7% (1/9)		6
Acute Tubular Injury	100% (9/9)		6
Tubulo-interstitial Nephritis	0% (0/9)		6
Obsolete Glomeruli,%	5 (1.5-5)		9
Thrombi within Glomerular capillary loops	16.7% (1/9)		9
Glomerular Microaneuryms	16.7% (1/9)		9
Mild tubulo-interstitial fibrosis	16.7% (2/9)		9
Vasculitis/endothelialitis	0% (0/9)		9
Renal arterial microthrombi	44.4% (4/9)		9
Hepatobiliary Pathology			
Liver	1432 (1012-2466)	1500-1800	9
Macroscopic Hepatic Infarction	11.1% (1/9)		9
Large Droplet Fatty change	87.5% (7/8)		8
Cirrhosis or Bridging Fibrosis	37.5% (3/8)		8
Portal lymphocytic inflammation	Mild 25% (2/8)		8
Lobular lymphocytic inflammation	Mild 25% (2/8)		8
Microthrombi	0% (0/8)		8
Neuropathology			
Brain	1324g (1151-1434)	Male: 1400 Female: 1275	8
Macroscopic Infarction	11.1% (1/9)		9
Microglial Activation	100% (5/5)		5
Mild T-cell infiltrate	100% (5/5)		5

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Gastro-intestinal Tract			
No significant macro or microscopic pathology**	100% (9/9)		9

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Supplementary Figure



Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.

Supplementary Figure 1. Additional unexpected pathology at autopsy: A, Bone marrow embolism on H&E staining considered to be likely related to cardiopulmonary resuscitation on clinicopathological correlations. B, Macroscopic cerebral infarction in a 22-year-old man. C, Mild microscopic acute pericarditis in a 79-year-old man demonstrated on H&E. D, Right atrial thrombus in a 97-year-old man shown on H&E stain. E, Moderate fibro-intimal thickening of a medium sized renal artery, out of context with age in a 24-year-old man. Lower right insert includes severe fibro-intimal thickening in a 97-year old man demonstrated on H&E. F, Myocardium showing a mottled appearance with evidence of subendocardial contraction band necrosis on histology (lower right insert) in a 64-year-old man. Notably, this man was given inotropic medication in the intensive care unit. G, Glomerular segmental scar in a 97-year-old man on Jones silver stain. H, necrotizing granulomatous lymphadenitis in the hilar node of a 97-year-old man with the presence of acid fast bacilli on Ziehl-Neelsen staining (lower right insert).

Reference Ranges: WCC 4.2-10.6x10^9/L, Lymphocyte count 1.5-4.5x10^9/L, Haemoglobin 130-180g/L (male) and 115-165g/L (female), Platelet count 130-370x10^9/L, Fibrinogen 1.9-4.3g/L, PTT 12.8-17.5s, APTT 25-35s, D-dimer <500ng/mL, Ferritin, 20-300ug/L, CRP 0-5mg/L, Amylase 0-100U/L, LDH 140-280U/L, high sensitivity troponin 0-34pg/mL, Procalcitonin 0.1-0.49ug/mL.