JOURNAL OF CLINICAL AND HEALTH SCIENCES

CASE REPORT

Histopathological Findings in COVID-19 with Concurrent Septicaemia: An Autopsy Case Report

Razuin Rahimi[1,2,3], Nur Ilyani Nor Azmal[2], Noor Kaslina Mohd Kornain[4], Mardiana Abdul Aziz[3]

1 Department of Forensic Pathology, Faculty of Medicine, Universiti Teknologi MARA, Selangor, Malaysia
2 Department of Forensic Medicine, Hospital Sungai Buloh, Ministry of Health Malaysia
3 Institute of Pathology, Laboratory & Forensic Medicine (I-PPerForM), Faculty of Medicine, Universiti Teknologi MARA, Selangor, Malaysia
4 Department of Pathology, Faculty of Medicine, Universiti Teknologi MARA, Selangor, Malaysia

Received
3rd February 2022
Received in final revised form
17th May 2022
Accepted
14th July 2022
Published
1st September 2024

Corresponding author:
Assoc. Prof. Dr. Razuin Rahimi,
Department of Forensic Pathology, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh Campus, Jalan Hospital, 47000 Sungai Buloh, Selangor, Malaysia.
Telephone: +6012-9652145
Fax: +603 61401632
Email: dr_razuin@uitm.edu.my
razuin@gmail.com

ABSTRACT

COVID-19 infection results in a disease ranging from asymptomatic to severe pneumonia and death. This case report aimed to describe the autopsy findings of a COVID-19 positive patient with concurrent septicaemia associated with gastrointestinal tract perforation. We report a case of a 29-year-old prison detainee who collapsed and died at a hospital prior to a surgical procedure. The diagnosis of COVID-19 was confirmed by RT-PCR testing on postmortem nasopharyngeal swabs. Apart from fever, there was no COVID-19 symptoms reported by the patient. The autopsy revealed massive suppurative ascites with evidence of septicaemia and large bowel perforations. The lungs' macroscopy did not show distinct pneumonic changes, however, microscopically, organizing pneumonia, perivascular lymphocytic infiltrates and increased number of megakyocytes were present. Vascular pathology such as endothelialitis and thrombosis were also seen in other organs. We affirmed the spectrum of pathological changes associated with COVID-19 infection from the previous studies. This case report highlighted that the detrimental microscopic changes could be present irrespective of the degree of severity of the clinical symptoms.

KEYWORDS: COVID-19; Autopsy; Histopathology; Acute respiratory distress syndrome; Pneumonia

INTRODUCTION

In December 2019, a novel coronavirus SARS-CoV-2 was identified in Wuhan, China, causing an outbreak of deadly pneumonia within the country. Soon, in March 2020 the World Health Organization (WHO) declared the virus as pandemic as it began to spread worldwide at an alarming rate. The emerging disease was termed Coronavirus disease 2019 (COVID-19) [1,2]. Coronaviruses are single stranded, enveloped, RNA viruses that may cause respiratory illness to humans or animals. The viruses may result in common cold to severe acute respiratory syndrome [1,3]. The COVID-19 infection causes disease ranging from asymptomatic or minimal symptoms to severe pneumonia and death. It is associated with higher morbidity and mortality as it causes significant release of pro-inflammatory cytokines which results in interstitial pneumonia and acute respiratory distress syndrome [2]. Thrombosis is another feature of COVID-19 which is linked with poor prognosis of the disease [2,3]. By December 2021, WHO recorded nearly 300 million of confirmed number of infections and approximately 5.4 million fatalities worldwide [4]. Malaysia has reported around 2.7 million cases and over 30,000 fatalities, bringing the COVID-19 deaths to 1.1% of the total number of infection [5].

We present a case of man who was brought from a detention centre to a hospital for a surgical

follow-up appointment due to prolonged diarrhoea and abdominal pain. Unfortunately, he collapsed and departed at the waiting room. A medico-legal autopsy was performed after confirming his COVID-19 status. The diagnosis of COVID-19 was confirmed by real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing on postmortem nasopharyngeal swabs. The autopsy examination revealed massive suppurative ascites with evidence of septicaemia. The lungs' macroscopic findings were in keeping with COVID-19 pneumonia. The aim of this case report is to describe the postmortem findings in a COVID-19 positive patient with concurrent septicaemia originating from the gastrointestinal tract infection.

CASE PRESENTATION

A 29-year-old male prison detainee was brought to a hospital for a surgical follow-up appointment. He had been complaining of prolonged diarrhoea and abdominal pain for about four months. He had been hospitalized, diagnosed, and treated for septicaemia due to gastrointestinal tract infection prior to the current episode. While his condition improved and he was able to be discharged, he continued to have on and off recurrent diarrhoea of more than ten times per day at the prison. A colonoscopy examination was performed approximately six weeks prior to his demise. During the procedure, the patient was noted to be having poor bowel preparation, thus preventing the surgeon from getting a conclusive finding. Nonetheless, bowel mucosa biopsy specimens were obtained. The detainee was arranged for a repeat colonoscopy procedure at five weeks interval. On the day of the surgical appointment, he appeared weak as he continued to have loose stool diarrhoea over ten times per day for about a week. He also complained of abdominal pain and fever. However, there was no history of cough or shortness of breath recorded. As he had collapsed at the waiting room, he was immediately brought to the Emergency Department (ED) and resuscitated, to no avail. The body was sent to the Forensic Department for medico-legal autopsy examination. Prior to autopsy, postmortem nasopharyngeal swabs were obtained and tested for COVID-19 using RT-PCR method. The result was positive. A postmortem computed tomography (PMCT) which was performed prior to autopsy revealed pneumoperitoneum with complicated ascites possibly in keeping with viscus perforation, generalized mesenteric fat stranding with suspicion of bacterial peritonitis and subcutaneous fat stranding at the lower thorax, abdomen and lower limbs likely in keeping with severe sepsis. The lungs findings revealed near symmetrical ground glass changes at the upper and lower lobes of the lungs. Within the ground glass opacities, asymmetric dense central and peripheral consolidations were seen along the bronchovascular vessels at the upper and lower lobes of the left lung. These features were in keeping with COVID-19 pneumonic changes in the background of pulmonary oedema and gravitational hypostasis.

Autopsy findings

An autopsy was performed at 48 hours postmortem. The deceased was a thin adult male, measuring 177 cm in length and 60 kg in weight, with body mass index (BMI) of 19.2 kg/m^2. The cheekbone was prominent, and the eyes were sunken, indicating severe dehydration. There was no injury or congenital deformity noted. Postmortem changes such as lividity was present at the posterior aspect of the body and rigor mortis was generalized. Upon internal examination, there were blood-stained bilateral pleural effusions amounting to 10 ml and 50 ml on the right and left sides respectively. Blood-stained pericardial effusion was also observed, measuring 10 ml. The lower lobes of both lungs were markedly congested (Fig. 1a & 1b). Pulmonary embolism was not detected upon examination of the pulmonary trunk and main branches of the pulmonary arteries. The abdominal cavity contained approximately 500 ml of suppurative ascites with markedly inflamed peritoneum and the small intestine (Fig. 1c). The lower segment of the large intestine was thickened and inflamed, with formation of a solid mass with adhesions to the surrounding structures. The section was obtained and fixed in formalin for further histopathology examination. Detailed examination of the specimen revealed 4 foci of perforations in the sigmoid colon, measuring 3 mm to 4 mm each. There was also a flattened and elongated polypoidal structure arising from the mucosal surface of the colon, which was later confirmed to be a benign polyp (Fig 1d).

Vol 9(2) (2024) 75-81 | jchs-medicine.uitm.edu.my | eISSN 0127-984X
https://doi.org/10.24191/jchs.v9i2.17070

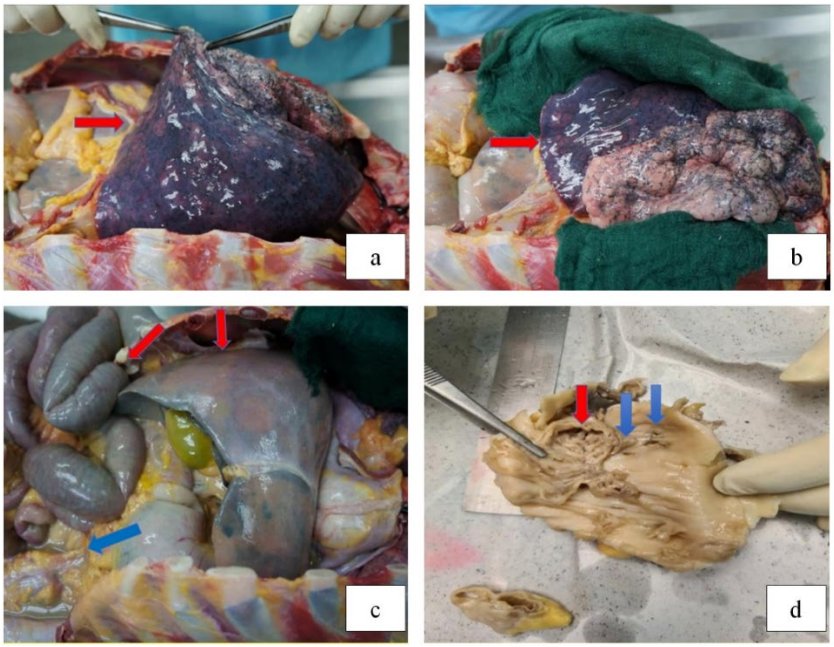

Figure 1 (a & b) The lower lobes of both lungs were markedly congested (red arrows). **(c)** The abdominal cavity showed yellowish discolouration of the liver with markedly distended and ischaemic small intestines (red arrows). Yellowish exudative fluid was also visible at the left lower corner of the photograph (blue arrow). **(d)** The cut-open sigmoid colon showed presence of a flattened benign polyp (red arrow) and perforations (blue arrows).

Histopathological findings

Representative tissue samples from the heart, lungs, liver, kidneys, spleen and the sigmoid colon were obtained for histology examination. Microscopically, the lungs showed markedly congested capillaries with neutrophil margination. Perivascular and interstitial lymphocytic infiltrate was also present (Fig. 2a). There were patchy areas of organizing pneumonia (Fig. 2b). Scattered megakaryocytes (MKs) were identified (Fig. 2c). Sections from the heart showed markedly congested blood vessels with foci of vascular and mural thrombosis (Fig. 2d) with fibrinoid necrosis. The cardiomyocytes were otherwise unremarkable. The kidneys demonstrated acute tubular necrosis, multiple foci of fibrinoid necrosis of the vessels (Fig. 2e) and vascular thrombosis. The glomeruli were unremarkable. Microscopic examination of the perforated colonic segment showed full thickness necrosis of the bowel wall with mucosal ischaemic changes in the adjacent mucosa. Foci of lymphocytic endothelialitis were demonstrable (Fig. 2f). A benign polyp with inflammatory changes was confirmed. The liver showed extensive macro and microvesicular steatosis and cholestasis with mild lymphocytic infiltrate in the portal tracts (Fig. 2g).

Laboratory investigations

Several specimens were obtained during autopsy for laboratory investigations. Microbiology specimens included blood, right and left lung tissues, and stool for culture. Both the blood and lung tissue cultures yielded significant pathogens; *Escherichia coli* and *Klebsiella pneumoniae*. The stool culture showed no enteric pathogens isolated.

In view of the case history, autopsy and microscopic findings, and laboratory investigations' results, the cause of death was concluded as 'Septicaemia secondary to suppurative peritonitis due to perforated bowel, with COVID-10 pneumonia'. In summary, the perforated bowel was the likely primary event which led to a cascade of reactions resulting in widespread bacterial infection and inflammation, leading to severe septicaemia. The concurrent COVID-19 infection which demonstrated primary viral infection changes and complications in the lungs, has compounded the severe inflammatory response, resulting in shock, leading to his demise.

Vol 9(2) (2024) 75-81 | jchs-medicine.uitm.edu.my | eISSN 0127-984X
https://doi.org/10.24191/jchs.v9i2.17070

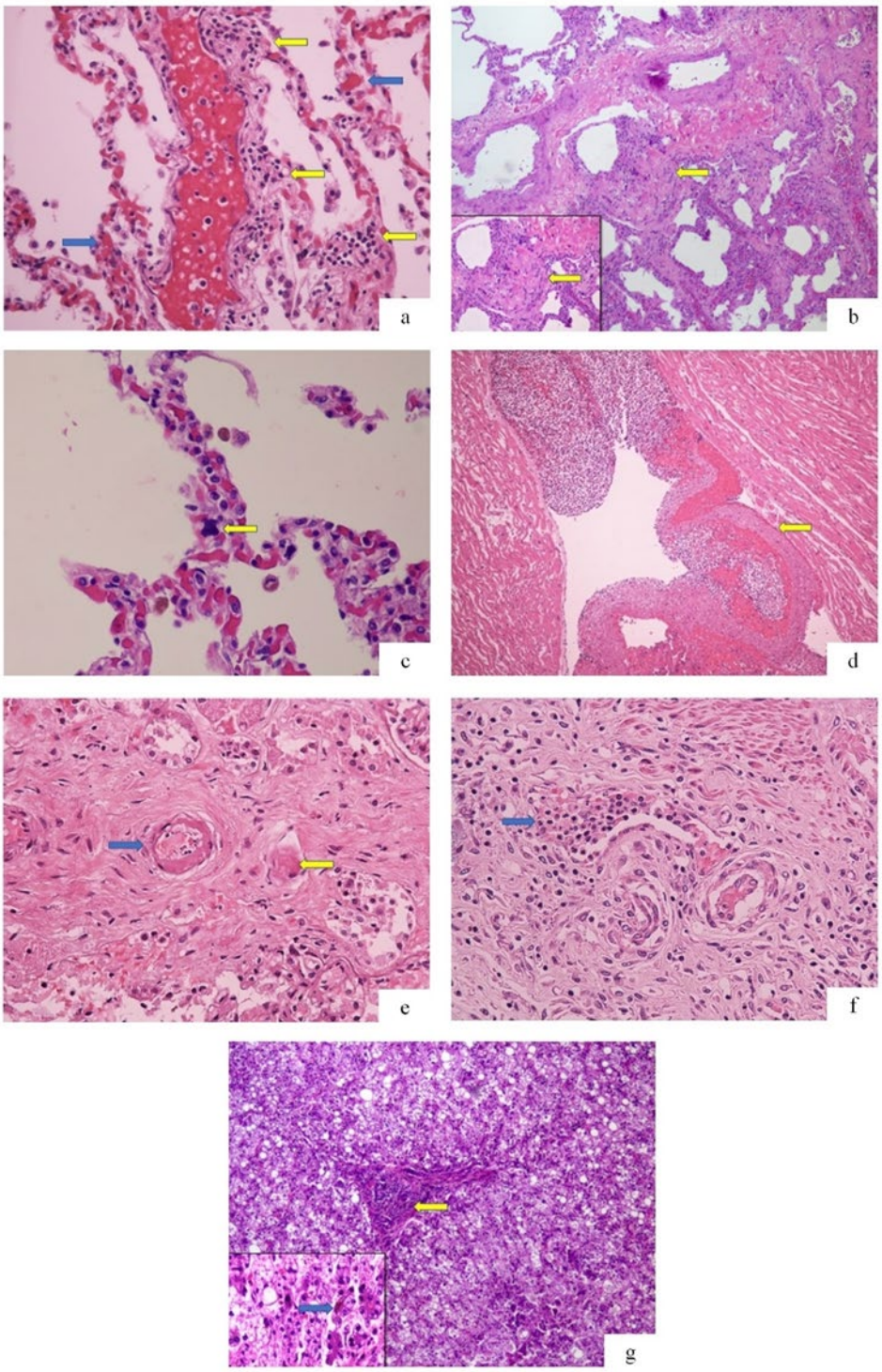

Figure 2. (a) The alveolar capillaries were markedly congested (blue arrows). Perivascular and interstitial lymphocytic infiltrate were focally conspicuous (yellow arrows); H&E 10x. (b) There was focal consolidation of lung parenchyma by loose plugs of connective tissue (yellow arrow). The alveolar walls in the background were thickened with scattered lymphocytic infiltrate; H&E 4x. This is further highlighted on higher power (inset); H&E 10x. (c) A pulmonary megakaryocyte is shown, with hyperchromatic convoluted nucleus; H&E 20x. (d) A cardiac mural thrombus was seen in the heart, characterised by laminated layers of fibrin, platelets and red blood cells (yellow arrow). The cardiac myocytes were unremarkable; H&E 4x. (e) Fibrinoid necrosis was seen in the wall of a small blood vessel in the kidney (blue arrow) with adjacent fibrin thrombus (yellow arrow); H&E 10x. (f) Lymphocytic endothelialitis was observed (blue arrow) in the tissue adjacent to the colonic perforation. (g) The liver showed marked steatosis. The portal tracts contained lymphocytic infiltrate (yellow arrow); H&E 4x. Cholestatic pigments were also evident (blue arrow) (inset); H&E 20x.

Vol 9(2) (2024) 75-81 | jchs-medicine.uitm.edu.my | eISSN 0127-984X
https://doi.org/10.24191/jchs.v9i2.17070

DISCUSSION

Coronavirus disease 2019 (COVID-19) is a result of novel coronavirus SARS-CoV-2 infection. It has similar disease spectrum produced by two other coronaviruses namely Severe Acute Respiratory Syndrome (SARS-CoV-1) and the Middle East Respiratory Syndrome (MERS-CoV) [6,7,8]. Autopsy is crucial in providing invaluable information regarding the pathology of COVID-19 worldwide. Initially, information was gleamed by minimally invasive autopsies, which were mostly limited to sampling of the lungs. Complete autopsies are more common now, especially in regions with more advanced facilities.

A uniform histopathological finding in almost all autopsies is diffuse alveolar damage (DAD) in the lungs, either exudative or proliferative, which has been reported in many case reports and case series and as summarised in several literature reviews [1,2,6,7,8,9,10]. Other additional lung pathological findings previously reported included interstitial lymphocytic infiltrate pulmonary microthrombi, organizing fibrosis and viral cytopathic effects [1,7,6,10]. In cases of asymptomatic COVID-19 infection, variable histopathologic changes ranging from absence of histologic abnormalities to focal oedema with proteinaceous exudate, patchy chronic inflammation, multinucleated pneumocytes as well as scant intra-alveolar fibrin were reported [7]. However, there has been limited data regarding histopathological findings in those who suffered from mild or moderate COVID-19 infection, as the autopsy case reports, and case series were performed on patients who succumbed to the disease.

In our case report, minimal and subtle pulmonary histopathological changes were present, corresponded to the absence of respiratory manifestations. The lungs histology revealed perivascular and interstitial lymphocytic infiltrate, as well as foci of organizing pneumonia. Scattered capillary MKs were also identified; an increase in their number has been reported in the setting of COVID-19 as well as other pulmonary diseases [11]. The increase in the number of pulmonary MKs may be related to a compensatory production of MKs due to platelet consumption, a response to inflammatory cytokines and a result of increased expression of thrombopoietin in the setting of COVID-19 [11]. Interestingly, an antiviral role of pulmonary MKs has also been postulated [11]. In essence, all these features seen in our case were in keeping with the findings previously reported in the literature, albeit much less severe. In combination with the COVID-19 specific pneumonic changes on PMCT, we concluded that COVID-19 pneumonia was present in this case. While the lung culture yielded growth of *Escherichia coli* and *Klebsiella pneumoniae,* the absence of bacterial colonies and acute inflammatory cell infiltrates perhaps gave an indication that the superimposed bacterial infection was at the early stage, therefore, it was not visible on PMCT, gross autopsy, as well as microscopic examination.

Extrapulmonary pathology related to COVID-19 has been described, but many of these features were not unequivocal or specific enough to be attributed fully to COVID-19. Microthrombi in extrapulmonary sites have been almost consistently described involving the kidneys, heart, and lymph nodes, among others [1,6,10]. A series of 6 cases of COVID-19 infected young adults suggested that this cohort may be more prone to develop thromboembolic events and ischaemic organ damage, however this remains to be proven [12]. In our case, fibrin thrombi were demonstrable in the kidneys, but not elsewhere. Cardiac mural thrombosis was present in our case; however, this could not be unequivocally linked to the COVID-19 infection. Liver steatosis was also a feature seen in a number of cases [1,6,13]. However, due to the presence of severe septicaemia in this case, the possibility of COVID-19 infection causing steatosis in this case was somewhat unlikely. Other changes in the liver included lymphocytic infiltrate in the portal tracts and parenchyma with spotty hepatocyte necrosis and biliary plugs, as seen in the previous cases and in this case report. However, these findings were also not unequivocally related to COVID-19 [1,6,13]. In the kidneys, COVID-19-related changes included acute tubular injury, epithelial cell sloughing with luminal debris, cytoplasmic vacuolization with occasional necrosis and glomerular and arteriolar fibrin thrombi [6,13]. Our case also demonstrated acute tubular injury, fibrinoid necrosis and foci of fibrin thrombi. However, in the background of concurrent septicaemia, these thrombotic events could not be established as part of the

Vol 9(2) (2024) 75-81 | jchs-medicine.uitm.edu.my | eISSN 0127-984X
https://doi.org/10.24191/jchs.v9i2.17070

spectrum of COVID-19 infection with full certainty. Gastrointestinal mucosal ischaemia and endothelialitis have been described in some COVID-19 autopsies, however most cases lacked significant intestinal abnormalities [6]. Interestingly, histopathological examination of the perforated colonic segment in our case also showed bowel wall necrosis with mucosal ischaemic changes and lymphocytic endothelialitis in the adjacent mucosa. As the pathology was seen in the vicinity of the perforation, its significance could not be ascertained.

Our case provides an insight into the histopathological changes that can be seen in mild COVID-19 infection, as a case of death *with* COVID-19, rather than *due to* COVID-19. While the concurrent septicaemia might have contributed to some of the pathological changes, the findings that we have demonstrated are in keeping with the previous reports. Despite the features of organizing pneumonia and increased number of megakaryocytes might not be specific for COVID-19, we speculate that the lung pathological changes in this case are due to the COVID-19 infection as the presence of perivascular and interstitial lymphocytic infiltrate was a pointer towards viral-induced inflammation.

CONCLUSION

We affirmed the spectrum of pathological changes that may be seen associated with COVID-19 infection from the previous studies. Despite the absence of respiratory symptoms in this case, including the grossly normal lungs on macroscopic examination, the pulmonary histology changes unmasked the true nature of the disease. This case report highlighted that the detrimental pathology could be present irrespective of the degree of severity of the clinical symptoms.

Conflict of Interest

Authors declare none.

Ethical approval

We seek for waiver of ethical review and approval since the data were not directly indicative of the individual subject, observatory in nature and the research involved no risk to the deceased subject.

Acknowledgement

The authors would like to thank the Director General, Ministry of Health Malaysia for the permission to publish this manuscript.

Authors' contribution

RR and NINA performed the autopsy examination. NKMK and MMA performed the histological examination and wrote the relevant part in the microscopy findings. RR and MAA were involved in the conceptual design of the study and major contributor in writing the manuscript. All authors read and approved the final manuscript.

REFERENCES

1. Elsoukkary SS, Motyska M, Dillard A et al. Autopsy Findings in 32 Patients with COVID-19: A Single-Institution Experience. Pathobiol 2021; 88: 56–68.
2. Maiese A, Manetti AC, La Russa R et al. Autopsy findings in COVID-19-related deaths: a literature review. Forensic Science, Medicine and Pathol 2021; 17: 279-296
3. Caramaschi S, Kapp ME, Miller SE et al. Histopathological findings and clinicopathologic correlation in COVID-19: a systematic review. Modern Pathol 2021. Available from: https://doi.org/10.1038/s41379-021-00814-w
4. World Health Organization, WHO Coronavirus (COVID-19) Dahsboard. Available from: https://covid19.who.int
5. Ministry of Health of Malaysia. COVID-19 update. Available from: https://covid-19.moh.gov.my/terkini
6. Hariri LP, North CM, Shih AR et al. Lung Histology in Coronavirus Disease 2019 as Compared With Severe Acute Respiratory Syndrome and H1N1 Influenza. A Systematic Review. Chest Infections 2021. Available from: https://doi.org/10.10106/j.chest.2020.09.259
7. Geramizdeh B, Marzban M. Histopahtologic Findings of Coronavirus in Lung: A Mini-Review. Clinical Pathol 2020; 13: 1-4

8. Roden AC, Bois MC, Johnson TF et al. The Spectrum of Histopathologic Findings in Lungs of Patients with Fatal Coronavirus Disease 2019 (COVID-19) Infection. Arch Pathol Lab Med 2021; 145: 11-21
9. Montero-Fernandez MA, Pardo-Garcia R. Histopathology features of the lung in COVID-19 patients. Diagn Histopathol (Oxf.) 2021 Mar; 27(3): 123-127. doi: https://dx.doi.org/10.1016%2Fj.mpdhp.2020.11.009
10. Deshmukh V, Motwani R, Kumar A, et al. Histopathological observations in COVID-19: a systematic review. J Clin Pathol 2021; 74: 76-83.
11. Huang D-Y, Wang G-M, Ke Z-R et al. Megakaryocytes in pulmonary diseases. Life Sciences July 2022; Available from: https://doi.org/10.1016/j.lfs.2022.120602
12. Greuel S, Ihlow J, Dragomir MP et al. COVID-19: Autopsy findings in 6 patients between 26 and 46 years of age. Int J Infect Dis 2021;108:274-281
13. Zarrilli G, Angerilli V, Businello G et al. The Immunopathological and Histological Landscape of COVID-19-Mediated Lung Injury. Int J Mol Sci 2021. Available from: https://doi.org/10.3390/ijms22020974

Vol 9(2) (2024) 75-81 | jchs-medicine.uitm.edu.my | eISSN 0127-984X
https://doi.org/10.24191/jchs.v9i2.17070