Postmortem lung biopsy for COVID-19 patients in Iraq.

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Research Article

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Abstract

Background: The entire world was affected by the outbreak of novel coronavirus 2 (SARS-CoV-2), which influenced daily life worldwide and affected the medical, social, and economic prospects of all nations. This virus occurs clinically in four variants: Asymptomatic; mild upper respiratory tract infection (URTI); anosmia and/or ageusia as the only symptoms; and severe systemic disease, such as bilateral interstitial pneumonia. Approximately 20% of the population develops the severe course associated with cytokine release syndrome (CRS). Those who develop lung injury and dyspnea have a higher mortality. An autopsy can reveal the pathogenesis and determine the cause of death.

Objectives: to understand the pathophysiological changes that occur in lung tissue in COVID-19 affected individuals and specify the cause of death.

Patients and methods: This is a case series of post-mortem lung histopathology examinations of deceased COVID-19 positive patients. Samples were collected from postmortem models were acquired from six diseased individuals who tested positive for SARS-CoV-2 by reverse transcriptase polymerase chain (PCR) reaction and subsequently passed away in the tertiary hospital between July and September 2020 as a result of COVID-19. Their slides and paraffin embedded blocks regarding lung biopsies, together with their reports, were obtained and submitted for assessment by two pathologists (specialist and consultant) for further assessment of lung changes caused by COVID-19.

Results: Only 2 of the 6 patients confirmed features of diffuse alveolar injury with hyaline layer and fibrin thrombi in pulmonary arteries, small vessel congestion, and pulmonary infarction. Two patients demonstrated diffuse alveolar fibrosis (organizing pneumonia), severe inflammation, and foci of squamous metaplasia, in addition to the deposition of carbon particles. One case had diffuse pulmonary fibrosis with pulmonary artery thrombosis without an inflammatory background. One case showed intra-alveolar atypical large cells, ischemic necrosis, and severe inflammation with intra-alveolar macrophages and pneumocyte hyperplasia.

Introduction

The entire world was affected by the outbreak of novel coronavirus 2 (SARS-CoV-2), which influenced daily life worldwide and affected the medical, social, and economic prospects of all nations. This pandemic is the most severe, but not the first in this millennium, as it was preceded by two other outbreaks in China the SARS-COV pandemic in 2002 and the MERS-COV pandemic in Saudi Arabia in 2012, but the first two pandemics had less impact on the world, although together they caused 10556 cases and 1622 deaths.(1)

This virus occurs clinically in four variants: 1)) asymptomatic, 2)) mild upper respiratory tract infection (URTI), 3)) Anosmia and/or ageusia as the only symptoms, and 4)) severe systemic disease such as bilateral interstitial pneumonia.(2) Approximately 20% of the population develops the severe course associated with cytokine release syndrome (CRS). Those who develop lung injury and dyspnea have a higher mortality.(3-4) Autopsy can reveal the pathogenesis and determine the cause of death. To our knowledge, there are limited data on autopsy of Iraqi COVID-19 patients. In this study, we investigate the histopathological changes in the lungs of Iraqi patients who died from SARS-CoV-2.

Patients And Methods

This is a retrospective study through collecting Postmortem models were acquired from 6 mature diseased individuals who tested positive for SARS-CoV-2 by reverse transcriptase polymerase chain (PCR) reaction and subsequently pass away in the IMAMEIN KADHIMEIN MEDICAL CITY in Baghdad / Iraq between July and September 2020 as a result of COVID-19. Their slides and paraffin embedded blocks regarding lung biopsies were obtained form and submitted for assessment by two pathologists (specialist and consultant) for further assessment of lung changes caused by COVID-19. The samples and their previous report were obtained from the department of legal medicine in Baghdad / ministry of health.

Medical facts such as oldness, sexual category, associated diseases, period of sickness were caught from the hospital documentation. Ethical support for this study was offered by Ibn Sina university for medical and pharmaceutical sciences / Research Ethics Committee.

All the patients received antimicrobial agents, anticoagulant drugs and corticosteroids as scheduled for COVID-19 management in addition to treatment of the co-existing diaseases.

Results

Clinical findings:

This case series includes six patients, four males and two females, aged between 26 and 45 years. Regarding comorbidities, two patients out of six (2/6) had hypertension & diabetes mellitus, one out of six patients (1/6) had IHD & HT, one out of six patients (1/6) had HT only, and two out of six (2/6) had no comorbidities. All patients have received full treatment since their admission to the hospital, including oxygen. The acute-phase reactants and D-dimers were elevated in all six patients. All patients received the COVID-19 protocol for management as shown in (Table-1).

Clinical facts	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	45	43	27	45	42	26
Sex	Male	female	female	male	Male	male
Comorbidity	IHD + HT	DM + HT	HT	HT + DM	-	-
Duration of illness	21 days	29 days	43 days	45 days	28	45
Treatment	Antimicrobial Anticoagulant Corticosteroid	Antimicrobial Anticoagulant Corticosteroid	Antimicrobial Anticoagulant Corticosteroid	Antimicrobial Anticoagulant Corticosteroid	Antimicrobial Anticoagulant Corticosteroid	Antimicrobial Anticoagulant Corticosteroid
Acute phase reactant D-dimers	Both elevated	Both elevated	Both elevated	Both elevated	Both elevated	Both elevated
Method of ventilation	CPAP	CPAP	CPAP	CPAP	CPAP	CPAP

Histology:

The histopathological findings include: only two of the six patients confirmed features of diffuse alveolar injury with alveolar hyaline layer and pulmonary artery fibrin thrombi, small vessel congestion, and pulmonary infarction (Fig. 1 & 2). Two patients demonstrated diffuse alveolar fibrosis (organizing pneumonia), severe inflammation, and foci of squamous metaplasia, in addition to the deposition of carbon particales (fig. 3, 4 & 5). One case had diffuse pulmonary fibrosis with pulmonary artery thrombosis without an inflammatory background. One case showed intra-alveolar atypical large cells, ischemic necrosis, and severe inflammation with intra-alveolar macrophages and pneumocyte hyperplasia (fig. 6 & 7). No microbial or fungoid organisms were cultured in any of our samples.

Table -2-: the histopathological findings in COVID -19 lung samples

No .	Slide review
Patient 1	• Intra-alveolar hyaline membrane formation • Heavy mixed inflammation (mainly lymphocytes & plasma cells) • Capillary congestion and ischemic necrosis • Alveolar collapse
Patient 2	• Diffuse alveolar fibrosis (organizing pneumonia) • Inflammation • Squamous metaplasia • Carbon particles depostion
Patient 3	• Diffuse alveolar fibrosis • Squamous metaplasia • Carbon particles deposition • Inflammation
Patient 4	• Diffuse alveolar fibrosis (organizing pneumonia) • Thrombosis
Patient 5	• Intra-alveolar hyaline membrane formation • Alveolar collapse • Diffuse alveolar fibrosis • Thrombosis • Capillary congestion and ischemic necrosis
Patient 6	• Atypical large pneumocytes • Ischemic necrosis and thrombosis • Severe inflammation

Discussion

Our research demonstrated the respiratory histopathological outcome in 6 patients with COVID-19 from autopsy of lung material. This verified various pathologies, including diffuse alveolar damage with hyaline membranes and fibrin thrombosis with pulmonary vascular congestion and lung tissue infarction, diffuse alveolar fibrosis (organizing pneumonia), severe inflammation, foci of squamous metaplasia and reactive atypia, in addition to deposition of carbon particules, intra-alveolar atypical large cells, ischemic necrosis with intra-alveolar macrophages, and pneumocyte hyperplasia. The medical factors of these patients are considered, including comorbidities and older age. The histopathological examination revealed alterations sufficient to be the reason for the death. These included diffuse lung injury, widespread fibrin thrombi, capillary congestion, and intra-alveolar hyaline membrane formation.

AlNameerr et al. (2019) describe similar pulmonary changes in an autopsy of 21 patients dyed from COVID-19. (5)

Other findings, such as squamous metaplasia within alveoli, were demonstrated to result from inflammatory stress on tissue caused by COVID and other viral infections such as SARS. A similar finding was seen in the Northern Italy series (6).

Hyaline membrane formation and alveolar collapse were noted in two cases and diffuse alveolar fibrosis was seen in four cases, suggesting that COVID-19 causes severe inflammatory reactions leading to increased levels of cytokines that play a major role in lung tissue damage.

Carbone particle deposition is either related to the environment or habit of the patient "smoking", and this may play a role in exacerbation of the lung injury caused by the COVID virus as it enhances cytokine production, fibrosis, and further lung damage.

We noticed massive hypercoagulability, which showed up as thrombosis and ischemic necrosis. This may be the cause of death in patients with high circulatory risk.

Coagulative disorders are associated with an increased frequency of thrombotic episodes and may be the cause of increased mortality in patients with circulatory hazard and evidence of myocardial injury.Llitjos et al. and Connors and Levy demonstrate similar findings. (7,8)

The finding of pulmonary infarction has also been described in "SARS_CoV" (severe acute respiratory syndrome coronavirus) (9).

In spite of receiving antibiotic therapy and negative cultures, four cases revealed bronchopneumonia in which interleukins, especially IL-6, play a major role.

Atypical enlarged pneumocytes were demonstrated in one case characterized by pleomorphic enlarged nuclei, amphiphilic granulated cytoplasm and conspicuous nucleoli with viral- related cytopathic changes in the intra-alveolar areas., which may be reactive changes due to severe inflammatory process or may be already existing before COVID-19 infection. Similar findings were demonstrated by Tian et al. (10).

Conclusion

The high rate of occurrence of thromboembolic episodes suggests an important role for COVID-19-induced coagulopathy. The molecular mechanisms should be studied, and the overall clinical incidence of COVID-19 should be thought about.

Atypical changes should be more investigated to confirm whether they're a result of COVID infection or not.

Declarations

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Competing interests: The authors declare no competing interests.

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Figures

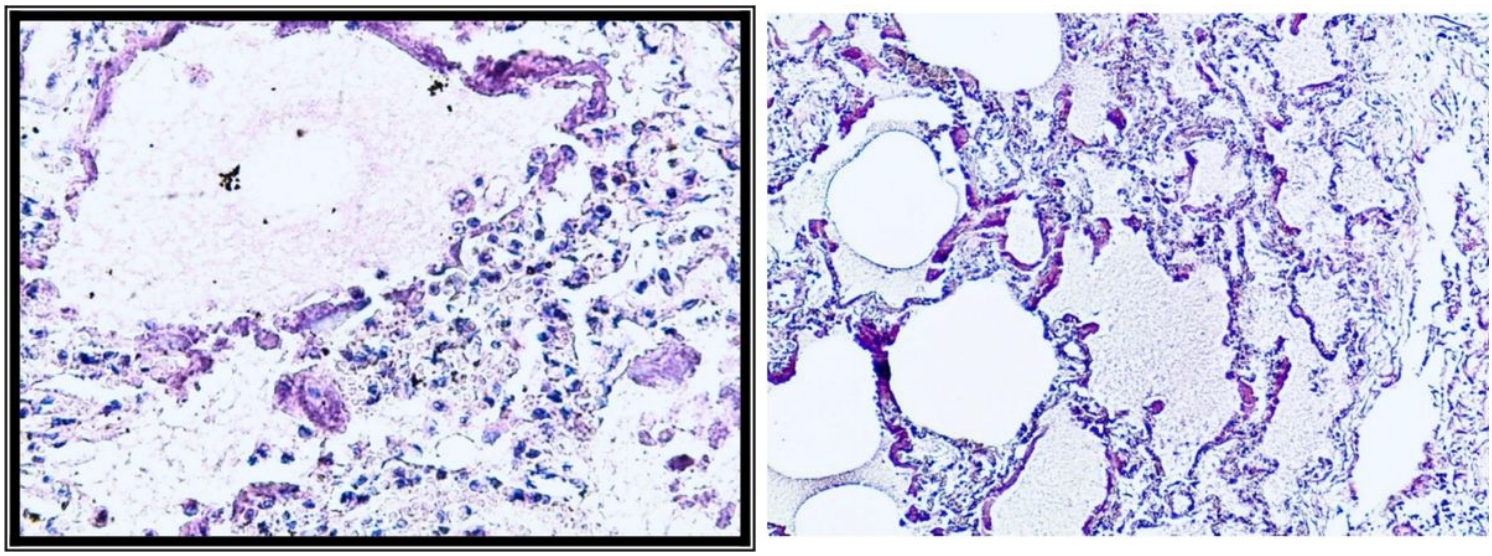

Figure 1

intra-alveolar hyaline with inflammatory cells infiltration (mainly lymphocytes and plasma cells), X40.

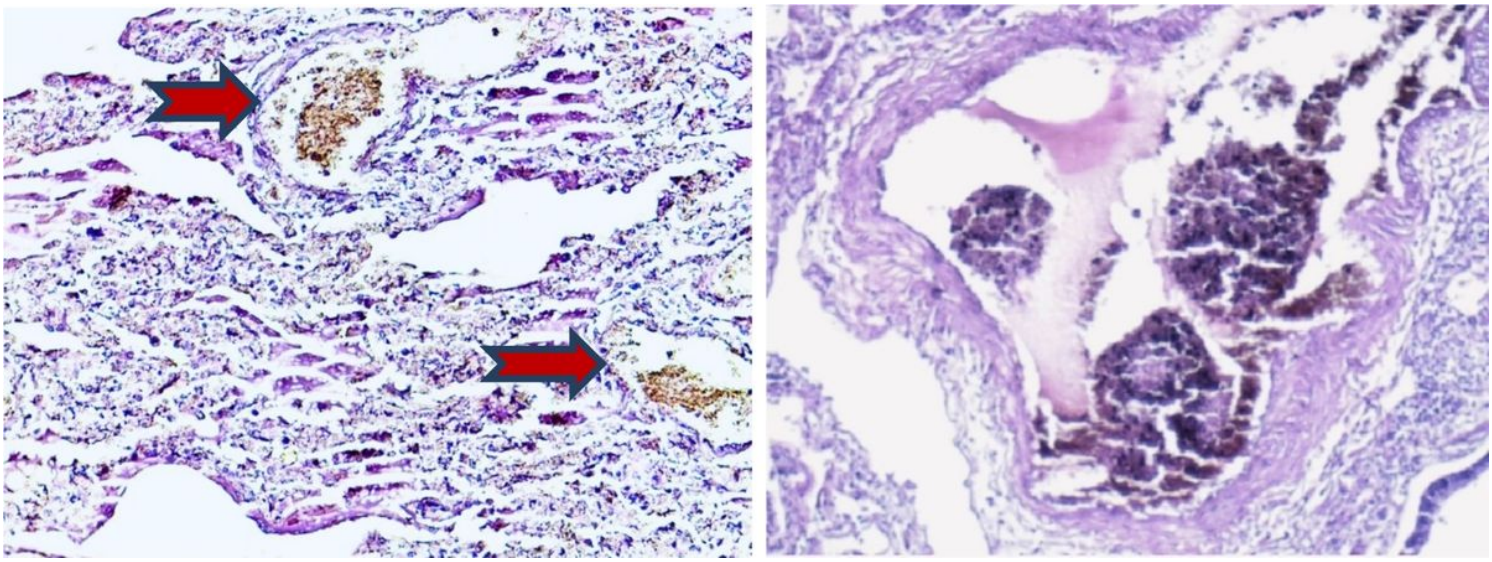

Figure 2

diffuse alveolar damage with capillary congestion .

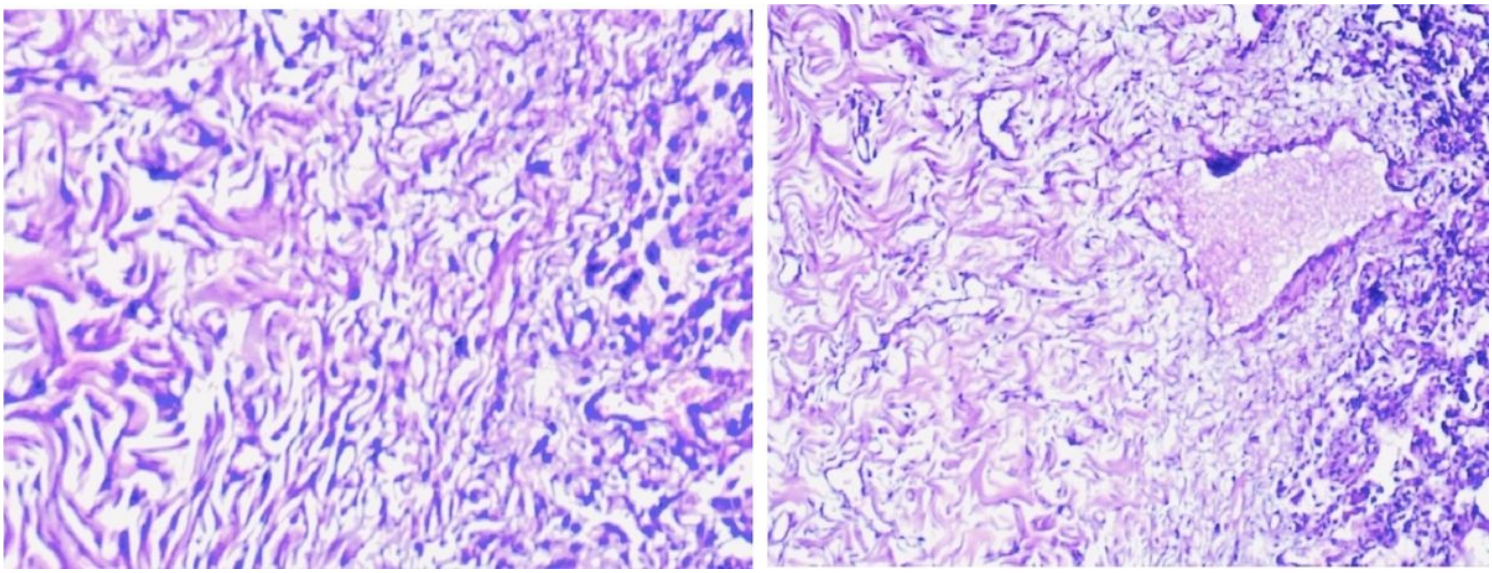

Figure 3

diffuse alveolar fibrosis

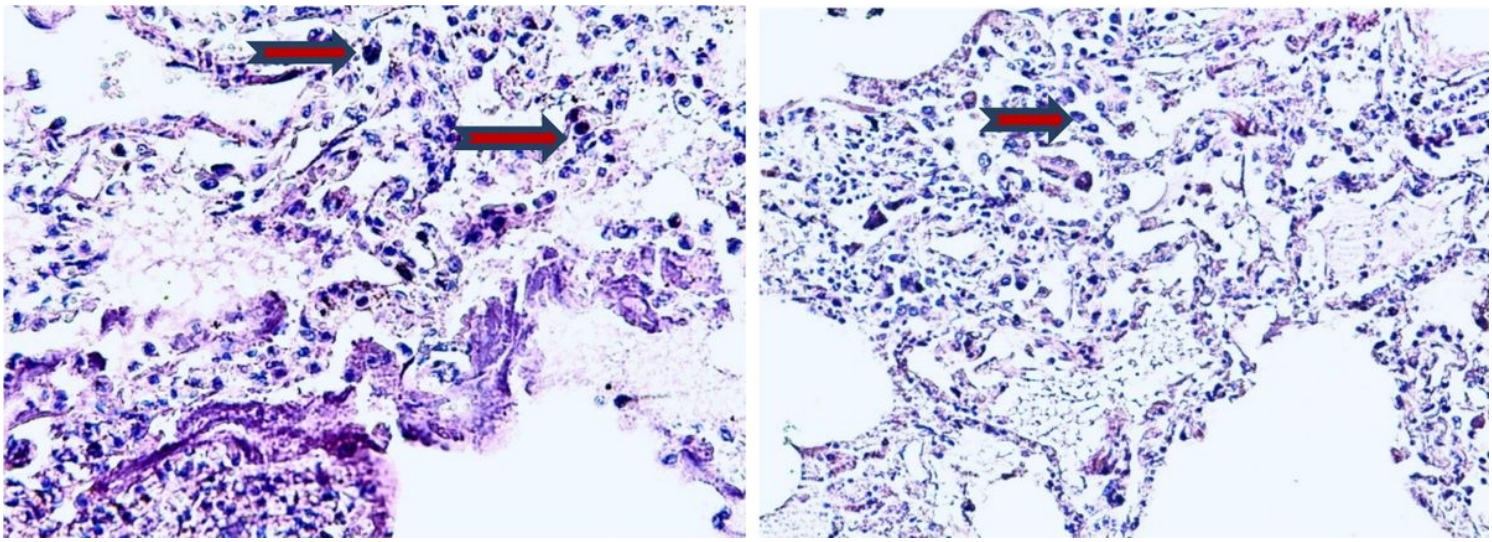

Figure 4

intra-alveolar atypical large cells (reactive).

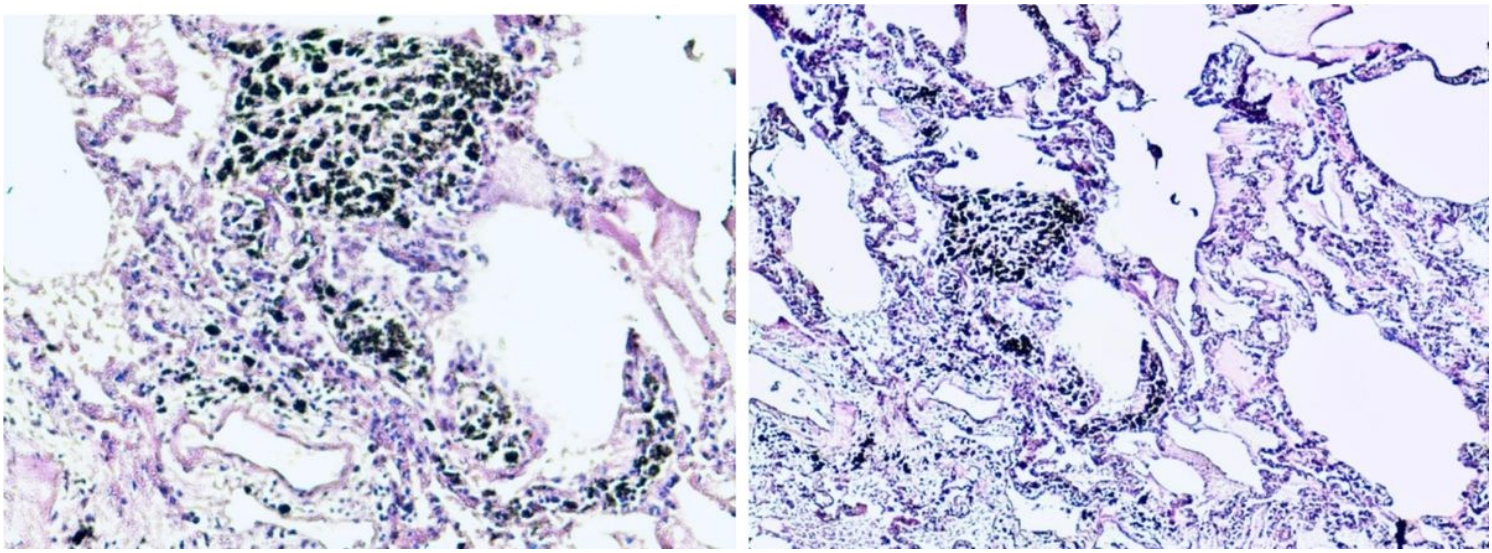

Figure 5

carbon particle deposition

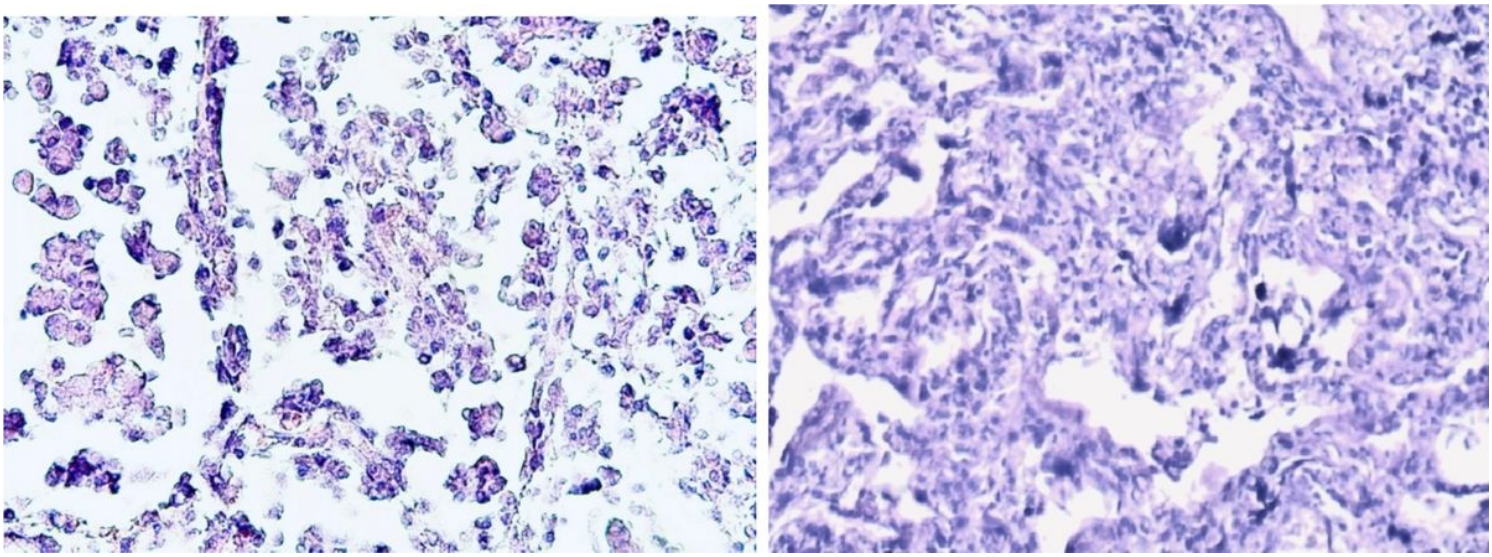

Figure 6

intra-alveolar macrophages with severe pneumonia

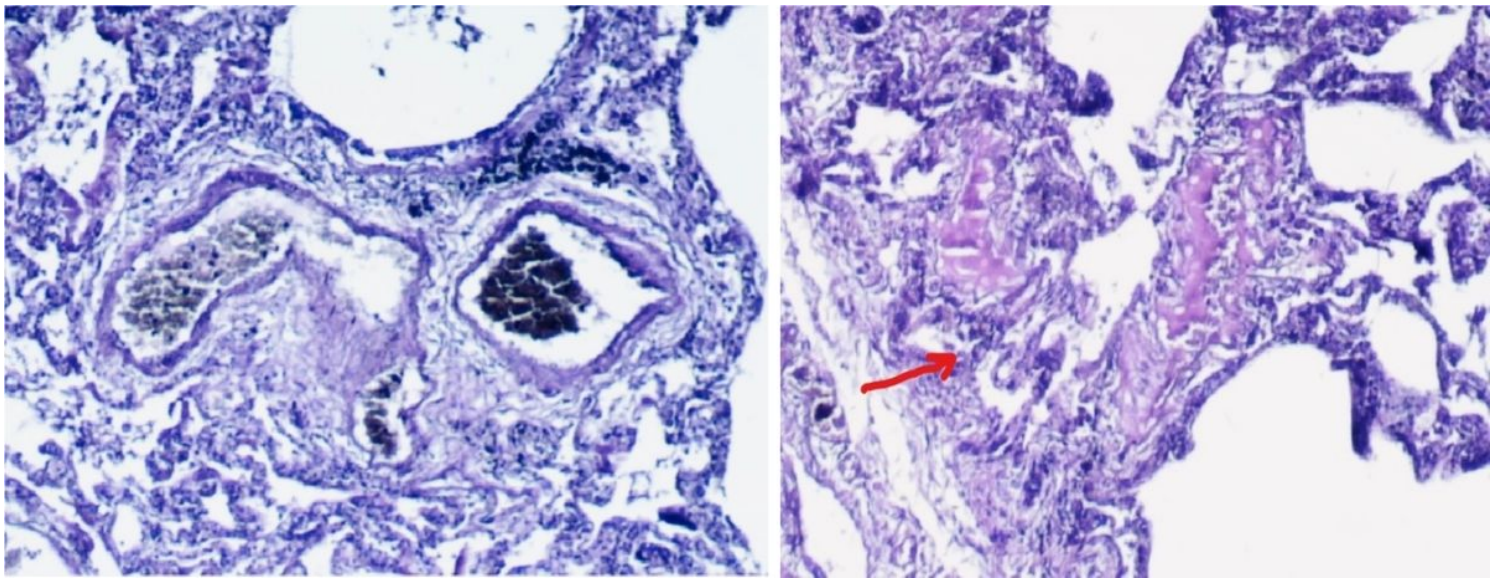

Figure 7

fibrin clot and pnemocytes hyperplasia