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Original Research Article

Postmortem Lung Biopsy in a Sample of COVID-19 Patients in Iraq

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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 higher mortality. An autopsy can reveal the pathogenesis and determine the cause of death. ***Objectives:*** To understand the pathophysiological changes in lung tissue in COVID-19-affected individuals. ***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 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 because of COVID-19. Their slides and paraffin-embedded blocks of lung biopsies, as well as their reports, were collected and sent to two pathologists for further evaluation of COVID-19-related changes in the lungs. ***Results:*** Only two of the six 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. In another case, there were atypical large cells, ischemic necrosis, and severe inflammation with macrophages and pneumocyte hyperplasia inside the alveoli. ***Conclusion:*** the thromboembolic events suggest a role for COVID-19-induced coagulopathy. Molecular mechanisms and clinical features of COVID -19 should be studied. Atypical alterations need to be investigated to confirm their relation to COVID-19 infection.

Keywords: Postmortem Pathological Findings, Clinical pathology, COVID-2019, Autopsy, SARS-Cov-2, Diffuse alveolar damage.

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: asymptomatic, mild upper respiratory tract infection (URTI), anosmia and/or ageusia as the only symptoms, and 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 higher mortality [3, 4]. An

autopsy can reveal the pathogenesis and determine the cause of death. To our knowledge, there is limited data on the 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.

MATERIALS & METHODS

In this study, we collected postmortem lung biopsy slides of six deceased adults who tested positive for SARS- CoV-2 by reverse transcriptase polymerase chain reaction (PCR) and subsequently passed away in the Imamein Kadhimein Medical City in Baghdad between July and September 2020 because of COVID-19. Their slides and paraffin- embedded blocks regarding lung biopsies were obtained and reviewed by two pathologists for further assessment of lung changes caused by COVID-19. The Medico-legal directorate in Baghdad provided the slides, blocks, and their earlier postmortem histopathology report.

Ibn Sina University of Medical and Pharmaceutical Sciences/Research Ethics Committee reviewed and ethically approved this study.

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

RESULTS

Clinical Findings

Table 1: Clinical data of the six patients

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	DM + HT	-	-
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

This study 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).

Histology

The histopathological findings included the following: two of the six patients confirmed features of diffuse alveolar damage with alveolar hyaline layer and pulmonary artery fibrin thrombi, small vessel congestion, and pulmonary infarction (Fig. *1* & 2).

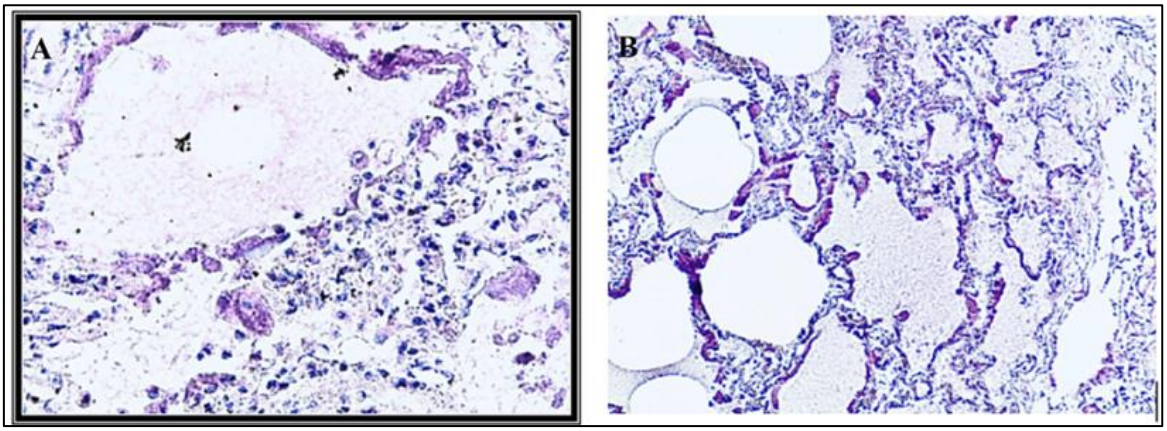

Figure 1: Intra-alveolar hyaline with inflammatory cells infiltration (mainly lymphocytes and plasma cells), X40

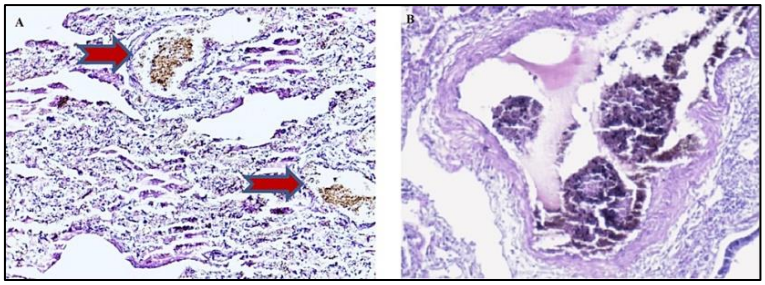

Figure 2: Diffuse alveolar damage with capillary congestion

Two patients demonstrated diffuse alveolar fibrosis (organizing pneumonia), severe inflammation, and foci of squamous metaplasia, in addition to the deposition of carbon particles (fig. *3*, *4* & 5).

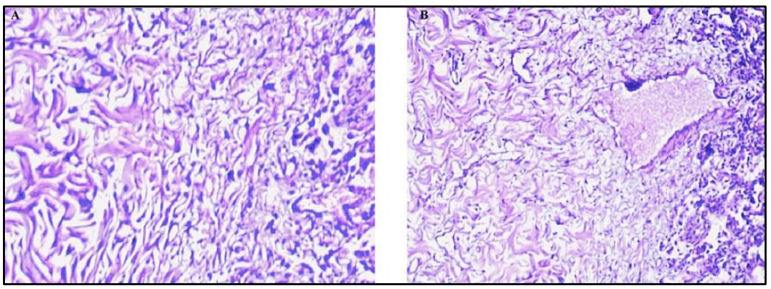

Figure 3: Diffuse alveolar fibrosis

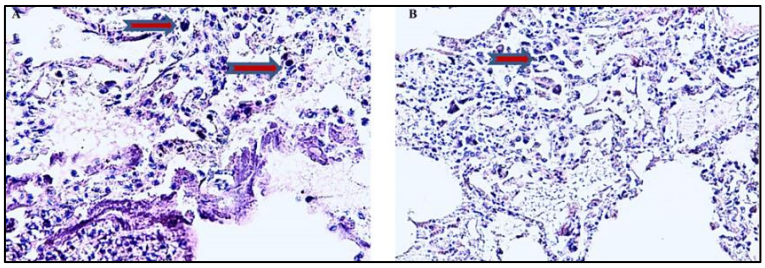

Figure 4: Intra-alveolar atypical large cells (reactive)

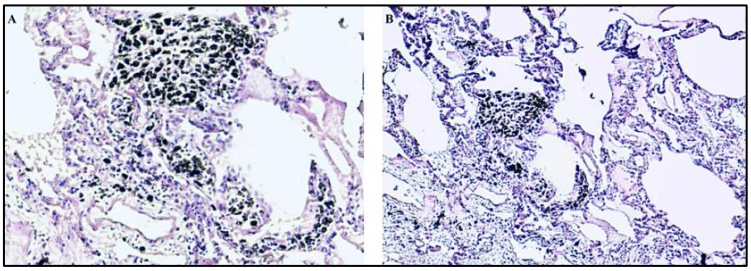

Figure 5: Carbon particle deposition

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).

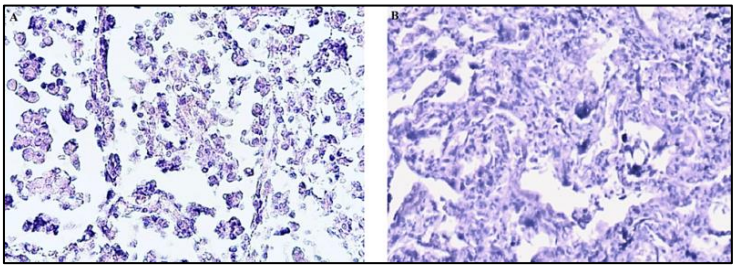

Figure 6: Intra-alveolar macrophages with severe pneumonia.

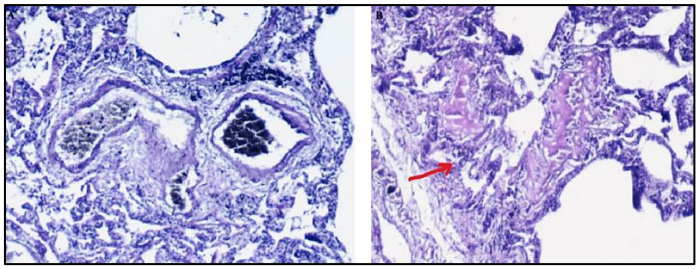

Figure 7: Fibrin clot and pneumocytes hyperplasia.

No microbial or fungoid organisms were cultured in any of our samples. Table *2* summaries the histopathological finding.

Table 2: The histopathological findings

Patient	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 deposition
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 pulmonary histopathological outcome in six patients with COVID-19 from the autopsy of the lung. 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 the deposition of carbon particles, intra-alveolar atypical large cells, ischemic necrosis with intra-alveolar macrophages, and pneumocyte hyperplasia. 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 who died because of 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 Carsana *et al.*, study [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 the habit of the patient "smoking," and this may play a role in the 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 linked to more thrombotic events and may be the reason why patients with circulatory risk and signs of myocardial damage die more often. Both Llitjos *et al.,* and Connors and Levy demonstrate similar findings [7, 8]

Pulmonary infarction has also been described by other studies in SARS_CoV during the pandemic [3], and even in SARS 2005 [9].

In our study, four cases revealed bronchopneumonia. This also was found in Edler *et al.*, and Konopka *et al.,* studies [10, 11].

In one case, atypical enlarged pneumocytes with pleomorphic enlarged nuclei, amphiphilic granulated cytoplasm, and conspicuous nucleoli with viral-related cytopathic changes in the intra-alveolar areas were found. These changes may be a reaction to a severe inflammatory process or may have been there before the COVID-19 infection. This goes with what Tian *et al.*, found [12].

CONCLUSIONS

The thromboembolic events seen in this sample suggest an important role for COVID-19-induced coagulopathy in the course of the disease. It is important to consider the full clinical picture when studying COVID-19 and to dig deeper into the underlying molecular pathways. There has to be further research on atypical changes to determine if they are caused by COVID-19 or not.

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