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Nidhi Rai
Consultant Pathologist,
Raipur, Chhattisgarh, India

Utsav Raj
Senior Resident, Department
of Community and Family
Medicine, All India Institute of
Medical Sciences, Raipur,
Chhattisgarh, India

Corresponding Author:
Nidhi Rai
Consultant Pathologist,
Raipur, Chhattisgarh, India

Pathological findings of COVID 19: All we know till now

Nidhi Rai and Utsav Raj

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Abstract

The emergence of severe acute respiratory virus (SARS-CoV) that year stimulated major research into these viruses. Corona viruses usually cause respiratory symptoms, but occasionally enteric, hepatic, and neurological symptoms can also be seen. Pulmonary involvement is the most common manifestation of all three of these viruses, which may manifest as acute respiratory distress syndrome and mortality. Lung involvement is responsible for high viral transmission. Lack of autopsies and biopsies include the suddenness of the outbreak, the vast patient volume in hospitals, shortage of healthcare personnel, and the high rate of transmission, which makes invasive diagnostic procedures less of a clinical priority so trying to summarize all we know about pathological findings of COVID 19 patients. Histopathological findings included heterogeneous acute alveolar damage (DAD), predominantly lymphocytic interstitial inflammation and the identification of reactive pneumocytes and multinucleated syncytial cells. The differential diagnoses of COVID-19 pneumonia might include but are not limited to acute or chronic pneumonia resulting from other infections

Keywords: Respiratory, Acute alveolar damage (DAD), predominantly lymphocytic, interstitial inflammation

Introduction

Corona viruses belong to the family Coronaviridae, are enveloped viruses with a single-stranded, positive-sense RNA genome approximately 26–32 kilo base in size, which is the largest known genome for an RNA virus^[1]. The term 'corona virus' refers to the appearance of CoV virions when observed under electron microscopy, in which spike projections from the virus membrane gives the appearance of a crown or *corona* in Latin^[2, 3]. The family *Coronaviridae* encompasses a broad spectrum of animal and human viruses, all characterized by a distinctive morphology. Prior to 2003 members of this family were believed to cause only mild respiratory illness in humans, other corona viruses then are known to be large of importance only to the livestock industry. But the emergence of severe acute respiratory virus (SARS-CoV) that year stimulated major research into these viruses, to the effect that many new coronaviruses have since been discovered, some with a zoonotic potential of causing serious outbreaks of disease in humans. The more recent emergence of MERS-CoV is exemplary. Most corona viruses first replicate in epithelial cells of the respiratory or enteric tracts. Because corona viruses are enveloped, virions are less stable in the environment and in clinical specimens compared to most non-enveloped viruses.

Corona viruses usually cause respiratory symptoms, but occasionally enteric, hepatic, and neurological symptoms can also be seen. Six corona virus species are identified which are known to cause human diseases. Four of the already known corona virus species 229E, OC43, NL63, and HKU1, are commonly circulating viruses in the human population and cause mild common cold-like symptoms^[4]. Two of the already known strains of corona virus are zoonotic in origin and cause serious illnesses which can be fatal, these are severe acute respiratory syndrome corona virus (SARS CoV) and Middle East respiratory syndrome CoV (MERS-CoV) and now the recently pandemic causing SARS CoV2^[5]. SARS CoV caused the SARS outbreak in China (2002 and 2003)^[5] and MERS-CoV caused the severe respiratory disease outbreak in the Middle East (in 2012)^[6]. At the end of 2019, a novel corona virus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China. It rapidly spread, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries throughout the world.

In February 2020, the World Health Organization designated the disease COVID-19, which stands for corona virus disease 2019 [7]. The virus that causes COVID-19 is designated severe acute respiratory syndrome corona virus 2 (SARS-CoV-2); previously, it was referred to as 2019 nCoV. Corona viruses such as SARSCoV2, MERS CoV, and SARS-CoV can cause significant morbidity and mortality in infected persons. Pulmonary involvement is the most common manifestation of all three of these viruses, which may manifest as acute respiratory distress syndrome and mortality. Lung involvement is responsible for high viral transmission. Patients initially present with fever with or without respiratory symptoms, but all patients later develop various degrees of pulmonary abnormalities on chest CT imaging [8, 9]. Although the vast majority of patients only have a common, mild form of illness, about 15-20% of the patients fall into the severe group, meaning they require assisted oxygenation as part of treatment [9]. The severe group has a high mortality rate and is associated with older age, underlying diseases such as diabetes, and medical procedures. Although there have been several studies describing clinical features and characteristic radiographic findings (mainly chest CT scans) [8, 9], less pathologic studies have been conducted based on autopsies or biopsies. Some of the reasons for the lack of autopsies and biopsies include the suddenness of the outbreak, the vast patient volume in hospitals, shortage of healthcare personnel, and the high rate of transmission, which makes invasive diagnostic procedures less of a clinical priority so trying to summarize all we know about pathological findings of COVID 19 patients.

Common pathological findings in COVID-19 as reported in various studies are as follows [9-13].

- Diffuse alveolar damage with cellular fibromyxoid exudates.
- Interstitial mononuclear inflammatory infiltrates dominated by lymphocytes.
- Multinucleated syncytial cells with atypical enlarged pneumocytes characterized by large nuclei, amphophilic granular cytoplasm, and prominent nucleoli in the interalveolar spaces, showing viral cytopathic-like changes.
- Serous exudation and fibrin exudation, edematous, and widened alveolar septa. Dilated blood vessels and monocytic and lymphocytic infiltrates.
- Formation of the hyaline membrane with pulmonary edema suggestive of early phase ARDS.
- Proliferation of type2 alveolar epithelia and focal desquamation of alveolar epithelia.
- Presence of Coronavirus particles in bronchial mucosal epithelia and Type II alveolar epithelia under an electron microscope
- SARSCoV2 antigen: Presence on the alveolar epithelium and Macrophages (immunohistochemistry positive)
- Real-time polymerase chain reaction positive for 2019CoV nucleic acid.
- In addition, the liver biopsy specimens of the patient with COVID-19 showed moderate microvesicular steatosis and mild lobular and portal activity, indicating the injury could have been caused by either SARS-CoV-2 infection or drug-induced liver injury. There

were a few interstitial mononuclear inflammatory infiltrates, but no other substantial damage in the heart tissue.

Studies also found out that common laboratory findings among hospitalized patients with COVID-19 were lymphopenia, elevated aminotransaminase levels, elevated lactate dehydrogenase levels, and elevated inflammatory markers (eg, ferritin, C-reactive protein, and erythrocyte sedimentation rate). It was found that lymphopenia is especially common, while the total white blood cell count is variable. In a study conducted in New York City with 393 adult patients hospitalized with COVID-19, 90 percent had a lymphocyte count <1500/microL; leukocytosis (>10,000/microL) and leukopenia (<4000/microL) were each reported in approximately 15 percent. Serum procalcitonin levels are more likely to be elevated in patients requiring ICU care. Several laboratory features, including high D-dimer levels and more severe lymphopenia, have been associated with mortality [9-13]. Xu *et al.* [14] presented the first description of the postmortem histopathological findings of a severe acute respiratory syndrome corona virus 2 (SARS CoV2) infection in a 50 years old male. Although the pathological the analysis was limited to tissue from the lung, heart, and liver and utilized only light microscopic examination. These data suggest similarities in the pathogenesis and the mechanisms of tissue damage and inflammatory response to coronaviruses infections. Histopathological findings included heterogeneous acute alveolar damage (DAD), predominantly lymphocytic interstitial inflammation and the identification of reactive pneumocytes and multinucleated syncytial cells. The right lung showed evidently desquamation of pneumocytes and hyaline membrane formation, indicating acute respiratory distress syndrome. The left lung tissue displayed pulmonary edema with hyaline membrane formation, suggestive of early-phase ARDS. Interstitial mononuclear inflammatory infiltrates, dominated by lymphocytes, was seen in both lungs. These histopathological findings were similar to those described in SARSCoV [15, 16] and Middle East respiratory syndrome coronavirus (MERS-CoV) [17].

Imaging findings

Chest radiographs may be normal in early or mild disease. In a retrospective study of 64 patients in Hong Kong with documented COVID-19, 20 percent did not have any abnormalities on chest radiograph at any point during the illness [18]. Common abnormal radiograph findings were consolidation and ground-glass opacities, with bilateral, peripheral, and lower lung zone distributions; lung involvement increased over the course of illness, with a peak in severity at 10 to 12 days after symptom onset. Chest CT in patients with COVID-19 most commonly demonstrates ground-glass opacification with or without consolidative abnormalities, consistent with viral pneumonia [19, 20].

Discussion

The main pathologic findings from the lungs of fatal cases of COVID-19 pneumonia include diffuse alveolar damage and acute fibrinous and organizing pneumonia patterns of acute lung injury, hyaline membrane formation, fibrin exudates, epithelial damage, and diffuse-type II pneumocyte

hyperplasia, which are all features of DAD. Mild thickening of alveolar walls is also evident in some cases, suggesting a more advanced stage. However, mature fibrosis is not seen. The differential diagnoses of COVID-19 pneumonia might include but are not limited to acute or chronic pneumonia resulting from other infections. Comprehensive clinical analysis of the epidemiological status, CT scan, and nucleic acid test can easily exclude such possibilities. Changes in the liver and heart are limited or related to the underlying diseases. To further understand the pathogenesis of COVID-19, studies including more patients with different ages and physiological backgrounds are needed

Conclusion

Our clinical and pathological findings in these severe cases of COVID-19 can not only help to identify a cause of death, but also provide new insights into the pathogenesis of SARS-CoV-2-related pneumonia, this might help physicians to formulate a timely therapeutic strategy for similar severe patients and reduce mortality.

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