Inside the lungs of COVID-19 disease

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Case Report

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Abstract

In the setting of COVID-19 pandemic, only few data regarding lung pathology induced by SARS-CoV-2 is available, especially without medical intervention interacting with the natural evolution of the disease. We present here the first case of forensic autopsy of a COVID-19 fatality occurring in confinement and in a young female. Diagnosis was made at necropsy and lung histology revealed diffuse alveolar damage, edema and interstitial pneumonia with a geographically heterogeneous pattern, affecting mostly central part of the lungs. This death related to COVID-19 pathology highlights the heterogeneity and severity of central lung lesions when the disease naturally evolves.

Introduction

In 2019 a novel human coronavirus, later named SARS-CoV-2, was discovered in Wuhan (China) [1]. Coronaviruses are known to induce a wide range of pathology ranging from common cold to severe acute respiratory syndrome. Most of the viruses present in the family of *Coronaviridae* are known to induce primarily self-limited upper respiratory diseases with the exceptions of two Betacoronaviruses, namely SARS-CoV and MERS-CoV. The former was responsible for a pandemic of viral pneumonia which began in the Guangdong province (China) in late 2002 and peaked globally in the early 2003. The latter was discovered in 2012 and was responsible for cases of fatal viral pneumonia mainly located in the Arabic peninsula, especially in Saudi Arabia. In late December 2019 SARS-CoV-2 was related to cases of fatal viral pneumonia. Since then thousands of cases have been confirmed in the population worldwide becoming a new pandemic. To this date, only limited data exists regarding the lung pathology induced by SARS-CoV-2. Forensic investigations continue to be necessary during COVID-19 pandemic when death is violent or undetermined in nature. In mid-march 2020 our services were confronted for the first time to a potentially infected young woman who collapsed at home during confinement. No specific diagnosis was performed antemortem according to local recommendations at the time. We present here the results of an exceptional case of forensic autopsy, showing extremely severe lung lesions of a COVID-19 disease diagnosed on postmortem samples. This is to our knowledge, the first forensic autopsy performed on a young women who died in confinement and was later known to have COVID-19 disease.

Case Presentation

A 31 years old woman was found unconscious at her apartment, during the outbreak of the coronavirus disease (COVID-19) pandemic. Antitussive opioid sirup and ibuprofen were found at the death scene. Paramedics were send to the residence and after thirty minutes of unsuccessful resuscitation maneuvers, the patient was pronounced dead at the scene and the police was called because of her young age. After preliminary police investigation, the diseased manifested herself for the last time alive approximatively two and a half hours before having been found unconscious. Her medical history was only relevant for a morbid obesity. Seven days prior to her death she has started presenting cough. She attended medical attention two times in the previous days and was confined at home since then.

Death scene investigation by the forensic pathologist revealed in particular a body rectal temperature of 41,4°C two hours after death was established. A medico-legal autopsy was ordered by the authorities and performed the next day at the University Center of Legal Medicine in Geneva, Switzerland.

Gross autopsy findings were a morbid obesity (body mass index of 61,2 kg/m^2), overweighed lungs grossly firm and rubbery (1220 g right; 1000 g left) with hemorrhagic edema bilaterally, tracheobronchial and pleural effusion and acute signs compatible with shock (petechiae of the skin, petechial hemorrhages of the visceral and parietal serosa of the abdomen, variegated “nutmeg” liver appearance, cortical pallor with medullary congestion of the kidneys). Cut sections of the lungs revealed heterogeneous areas of whitish consolidation without any purulent discharge.

Histological analysis of the lungs revealed alveolar damage with a geographically heterogeneous pattern, central part of the lungs being mostly affected (figure 1a). Alveolar compartment showed mainly edema, diffuse alveolar damage (DAD) in his exudative phase with the presence of hyaline membranes in some alveoli (figure 1c), deposit of fibrin as cotton wools within the alveoli (figure 1b) and moderate type II pneumocytes hyperplasia which were mainly desquamated (figure 2a). In the alveolar exudate, there were also moderate amount of intra-alveolar macrophages (figure 2b) and only scant polymorphonuclear neutrophils (PMN) and lymphocytes. Focal areas of intraalveaolar hemorrhage and bacterial proliferation were also present. No viral inclusions nor giant multinucleated cells were noted. Interstitial compartment showed edema, vascular stasis, lympho-monocytic infiltrates (majority of T lymphocytes (CD3+, figure 2d) over monocytes and exempt of B lymphocytes (CD20+)) and abundant megakaryocytes. Within the alveolar septa and mainly into the capillaries, abundant PMN were also seen, indicating margination and diapedesis process. No signs of increase collagen deposition within the alveoli nor the intersitium was noticed (Masson trichrome stain). Bronchi and bronchioles showed only minimal lymphocytic infiltrates within their walls and did not displayed any signs of mucosal necrosis. Histological analysis of other organs showed mild chronic tracheitis and microabscess in the liver parenchyma.

Post-mortem microbiological (bacterial and virological) analysis were performed. A lower respiratory tract (tracheobronchial) swab was performed for sanitary purposes and tested positive for SARS-CoV-2 (ARN, PCR, E-gene), with a C_t (threshold cycle) value of 21,4 (Qia QS5). Bacterial analysis performed on blood, lungs, liver, spleen and cerebrospinal fluid revealed mixed flora. Post-mortem biochemistry was indicative of an inflammatory process with elevated c-reactive protein of 48 mg/l (norm ≤10 mg/l), but showed no signs of systemic bacterial infection according to a normal value of procalcitonin (0,06 µg/l). Dextromethorphan was found in blood screening.

Discussion

SARS-CoV-2 virus is clinically known to generate acute respiratory distress syndrome. To this date, only few data regarding lung pathology are available [2-4]. So far, those findings were performed on surgical material [4], post-mortem biopsies [3], or minimal invasive autopsy [2]. To our knowledge, we report here the first case of forensic autopsy of a young COVID-19 fatality diagnosed at necropsy without any

medical intervention interacting with the evolution of the disease. Lung pathology revealed DAD and interstitial pneumonia. The pattern of injury was geographically heterogeneous affecting primarily central parts of the lungs and preserving peripheral parts. Early phase of secondary bacterial infection was noticed within the alveoli and with margination of PMN. Abundant megakaryocytes can also be explained by an early stage of infection, reflecting release of hemopoietic cells by the bone marrow. However, according to the post-mortem biochemistry, death was related to pulmonary changes related to SARS-CoV-2 and high fever without implication of a secondary bacterial infection (normal procalcitonin).

Our findings are in agreement with those found in literature [3]. Some features were different, such as the absence of multinucleated syncytial cells [2-4], fibroblastic plugs [4], or hyaline thrombi in microvessels [2]. Overall the induced lesions of SARS-CoV-2 were similar with the patterns of other members of the *Coronaviridae* family infection, especially the Betacoronaviruses SARS-CoV [5,6], and MERS-CoV [7].

This community setting death of a young woman related to COVID-19 pathology highlights the heterogeneity and severity of central lung lesions after natural evolution of the disease in confinement.

Declarations

Compliance with Ethical Standards

Funding: None.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Zhu N, Zhang D, Wang W et al. (2020) A novel coronavirus from patients with pneumonia in China. N Engl J Med 382(8): 727–33.
2. Yao XH, Li TY, HE ZC et al. (2020) [A pathological report of three COVID-19 cases by minimally invasive autopsies]. Zhonghua Bing Li Xue Za Zhi 49(0): E009. https://doi.org/10.3760/cma.j.cn112151-20200312-00193.
3. Xu Z, Shi L, Wang Y et al. (2020) Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med S2213-2600(20): 30076–X. https://doi.org/10.1016/S2213-2600(20)30076-X.
4. Tian S, Hu W, Niu L, Liu H, Xu H, Xiao S-J. (2020) Pulmonary pathology of early-phase 2019 novel coronavirus (COVID-19) pneumonia in two patients with lung cancer. J Thorac Oncol S1556-0864(20): 30132–5. https://doi.org/ 10.1016/j.jtho.2020.02.010.
5. Hwang DM, Chamberlain DW, Poutanen SM, Low DE, Asa SL, Butany J. (2005) Pulmonary pathology of severe acute respiratory syndrome in Toronto. Mod Pathol 18(1): 1– https://doi.org/10.1038/modpathol.3800247.

6. Lang Z-W, Zhang L-J, Zhang S-J et al. (2003) A clinicopathological study of three cases of severe acute respiratory syndrome (SARS). Pathology 35(6): 526–
7. Ng DL, Hosani FA, Keating MK et al. (2016) Clinicopathologic, immunohistochemical, and ultrastructural findings of a fatal case of Middle East respiratory syndrome coronavirus infection in the United Arab Emirates, April 2014. Am J Pathol 186(3): 652–

Figures

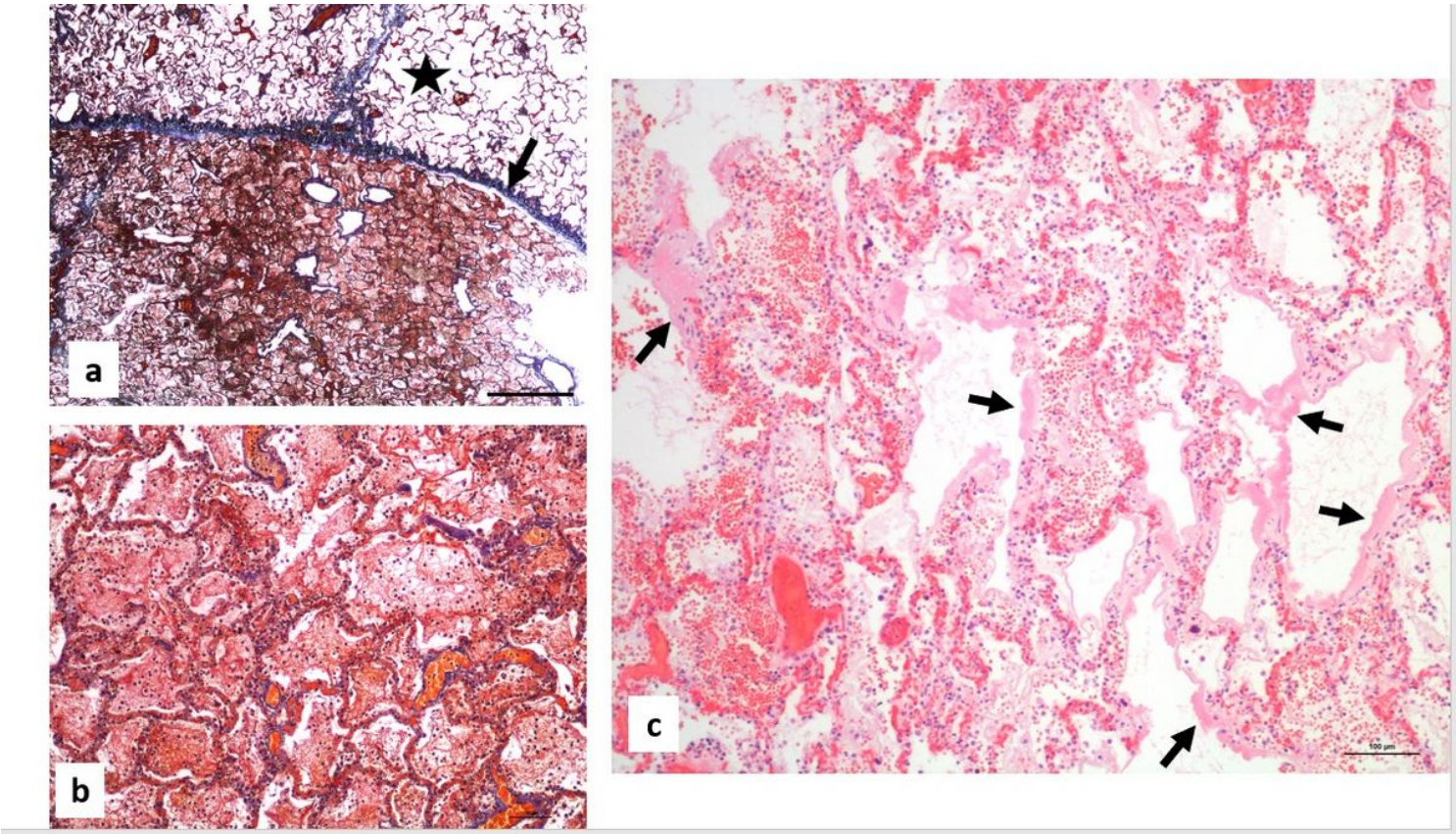

Figure 1

(a) Geographical heterogeneity of pulmonary lesions, with two samples of lung parenchyma in contact. The central sample is at the bottom presenting diffuse filling of the alveolar space with fibrin and the peripheral sample is at the top (black star) with clear open alveolar space. Arrow indicate visceral pleura (Acid fuchsin – Orange G stain (SFOG), 20x). (b) Magnification of diffuse filling of the alveolar space with fibrin (Acid fuchsin – Orange G stain (SFOG), 100x). (c) Hyaline membranes (black arrows) indicating diffuse alveolar damage (hematoxylin and eosin, 100x).

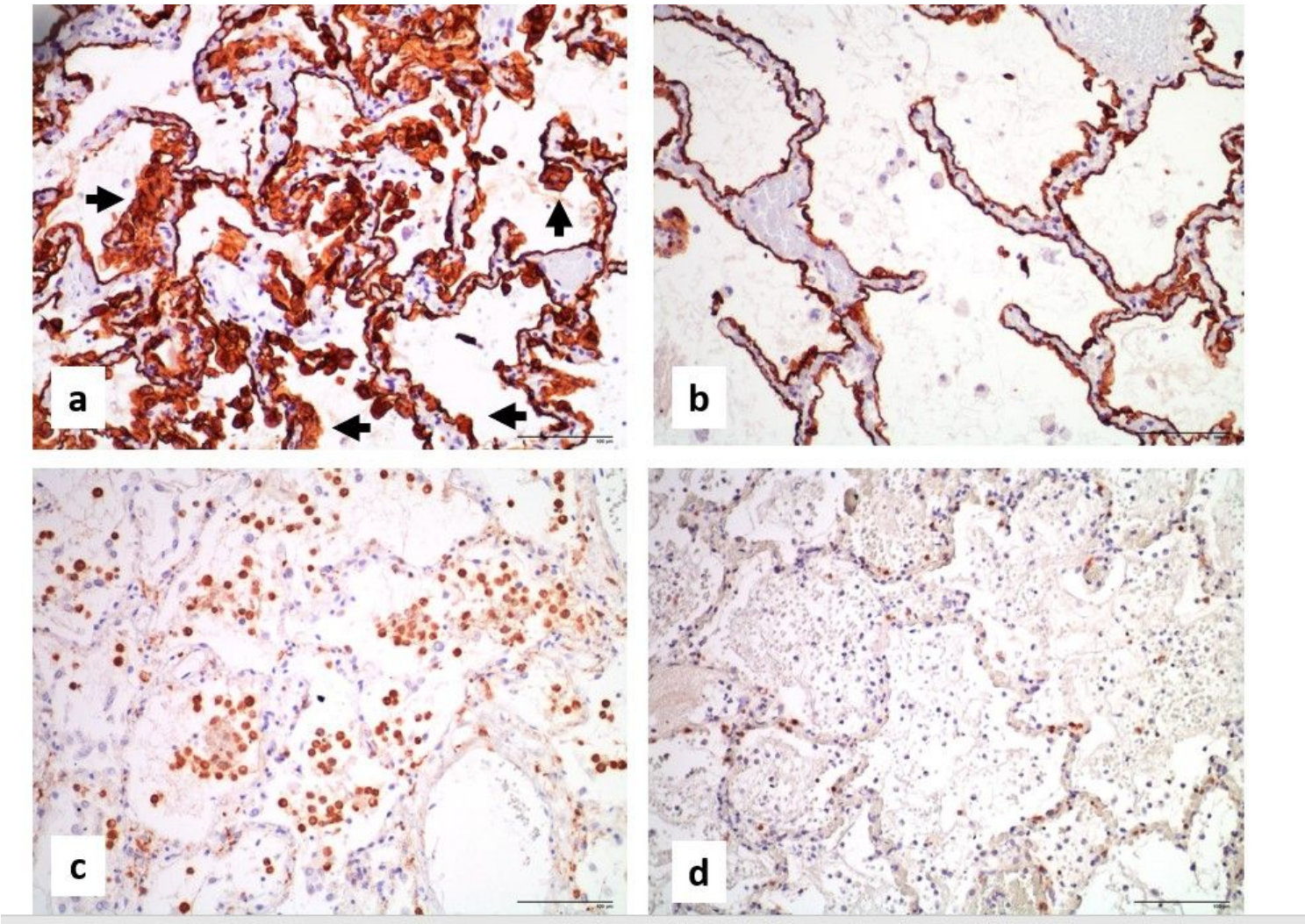

Figure 2

(a) Moderate type II pneumocytes hyperplasia (black arrows) with some desquamation (pankeratin, 200x). (b) Unaffected area of lung parenchyma with normal pneumocytes I and II morphology (pankeratin, 200x).(c) Moderate intraalveolar macrophages (CD68, 200x). (d) Moderate amount of lymphocytes infiltration in the interstitium (CD3, 100x).

Supplementary Files

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