
Forensic Autopsy-Confirmed COVID-19-Induced Out-of-Hospital Cardiac Arrest: Case Report

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Received: April 20, 2021; **Accepted:** April 28, 2021; **Published:** May 15, 2021

Abstract

Background: In the setting of severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) infection, data from autopsy in subjects who died at home during lockdown are scarce. We here report a forensic autopsy series of coronavirus disease 2019 (COVID-19)-related out-of-hospital cardiac arrest (OHCA).

Methods and Results: Between March and April 2020, four COVID-19-related OHCA were autopsied at the Institute of Legal Medicine of the metropolitan area of Lyon (France). Autopsies of 3 individuals reported natural death by acute respiratory failure implicating SARS-CoV-2 with typical COVID-19 pulmonary aspect of gross findings and pulmonary microscopy findings, i.e. diffusely congestive edematous lungs with peripheral thrombi and diffuse alveolar damage (DAD) at different stages of inflammatory reaction. For one individual, autopsy concluded of violent death due to suicidal acute alcohol intoxication in a patient that could no longer endure COVID-19 lockdown. No significant lesions were found in the heart.

Conclusions: We report here OHCAs of non-cardiac cause directly implicating COVID-19 at various stages of SARS-CoV-2-related DAD. This, autopsy remain of interest during this epidemic, both legally and medically to better understand the pathogenic processes of this infectious disease.

Keywords: Autopsy; COVID-19; SARS-CoV-2 infection; Cardiac arrest

Abbreviations

BMI: Body mass index; COVID-19: Coronavirus disease 2019; DAD: Diffuse alveolar damage; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; OHCA: Out-of-hospital cardiac arrest

Introduction

On January 25, 2020, Europe was hit by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic which broke out on December 31, 2019 in Wuhan (Hubei, China) [1]. On April 20, 2021, the World Health Organization coronavirus disease 2019 (COVID-19) situation report counted 3,021,397 deaths, including 1,042,683 in Europe and 101,209 in France [2]. A strong association between cumulative incidence of COVID-19 and of out-of-hospital cardiac arrest (OHCA) was previously reported in the Lombardy region of Italy [3]. Some autopsy data on deaths within the health system clarified the pathophysiology of this emerging infection [4,5]. However, there is little information regarding cause of death in subjects who died at home in a context of suspected COVID-19 during lockdown [6]. We hear a forensic autopsy series of COVID-19-related OHCA. Between March 19, 2020 and April 21, 2020, COVID-19-related OHCA were autopsied at the Institute of Legal Medicine of the metropolitan area (1.5 million inhabitants) of Lyon (France). Autopsies adhered to Council of Europe Circular N°1159 and safe operating procedures [7]. RT-PCR assay for SARS-CoV-2 was conducted on endotracheal swabs and pulmonary samples. Standard histology staining (hematoxylin-eosin) was performed on all organs. General unknown drug screening was carried out using gas chromatography/mass spectrometry and liquid chromatography/diode array detector/mass spectrometry. Concentrations of detected molecules were measured by specific chromatographic techniques. Blood ethanol concentration was measured by gas chromatography/flame ionization detector. This study was approved by our local institutional review board (Comité d’Ethique du CHU de Lyon).

Case Presentation

Four Caucasian individuals presenting virosis and laboratory-confirmed COVID-19 were autopsied. Individual #1 was a 59-year-old obese woman (body mass index (BMI): 40 kg/m²) with mental deficiency, who suffered OHCA in presence of her brother (also mentally deficient). Individual #2 was a 57-year-old man (BMI: 29 kg/m²) with myeloma, who suffered OHCA in presence of his wife 5 days after a chemotherapy course. Individual #3 was a 57-year-old man (BMI: 22.7 kg/m²) with manic-depressive psychosis treated by valproic acid, found dead at home; a farewell letter said he could no longer endure COVID-19 lockdown. Individual #4 was a 54-year-old man (BMI: 26.3 kg/m²) with untreated Crohn’s disease, found dead in bed by his wife.

Autopsies of individuals #1, #2 and #4 revealed diffusely purplish-red, firm, heavy, congestive edematous lungs (Figure 1A) with parenchymal congestion, and, for individual #4, an inferior cerebellar hemorrhagic lesion (Figure 1C). Cross-section of the fixed lung showed a typical COVID-19 aspect (Figure 1B). The heart was free of significant lesions and the pulmonary arteries were free of thrombi at the hilum in the 3 individuals. Autopsy of individual #3 showed vomiting, alcoholic body-odor, and airway aspiration.

Histology confirmed diffuse alveolar damage (DAD) with typical alveoli lined with hyaline membranes at different stages of inflammatory reaction: vasculo-exudative phase (individual #1, Figure 1D), early cellular phase (individual #2, Figure 1E) and resorptive/organizing phase (individual #4, Figure 1F). Interestingly, foci of atypical pneumocytes showing characteristic viral cytopathogenic effect were disseminated across the DAD lesions.

No inflammatory lesions of vessels or endothelial cell alteration were found. Lung tissue from individuals #1 and #4 (Figure 1G) showed multiple non-organized thrombi. The cerebellar lesion in individual #4 was small hemorrhagic infarct, a few days old, with a venous thrombus walled with endothelial cells. Histology of lung tissue from individual #3 confirmed the diagnosis of airway aspiration. For all individuals, no significant lesions were found in the other organs, including the heart. No evidence of toxic involvement was found for individuals #1, #2 or #4. For individual #3, blood-alcohol was 5.04 g/L, and valproic acid blood concentration 27 µg/mL (therapeutic range: 40-100 µg/mL). In all, autopsy reported natural death by acute respiratory failure implicating SARS-CoV-2 for individuals #1, #2 and #4, and violent death due to suicidal acute alcohol intoxication for individual #3.

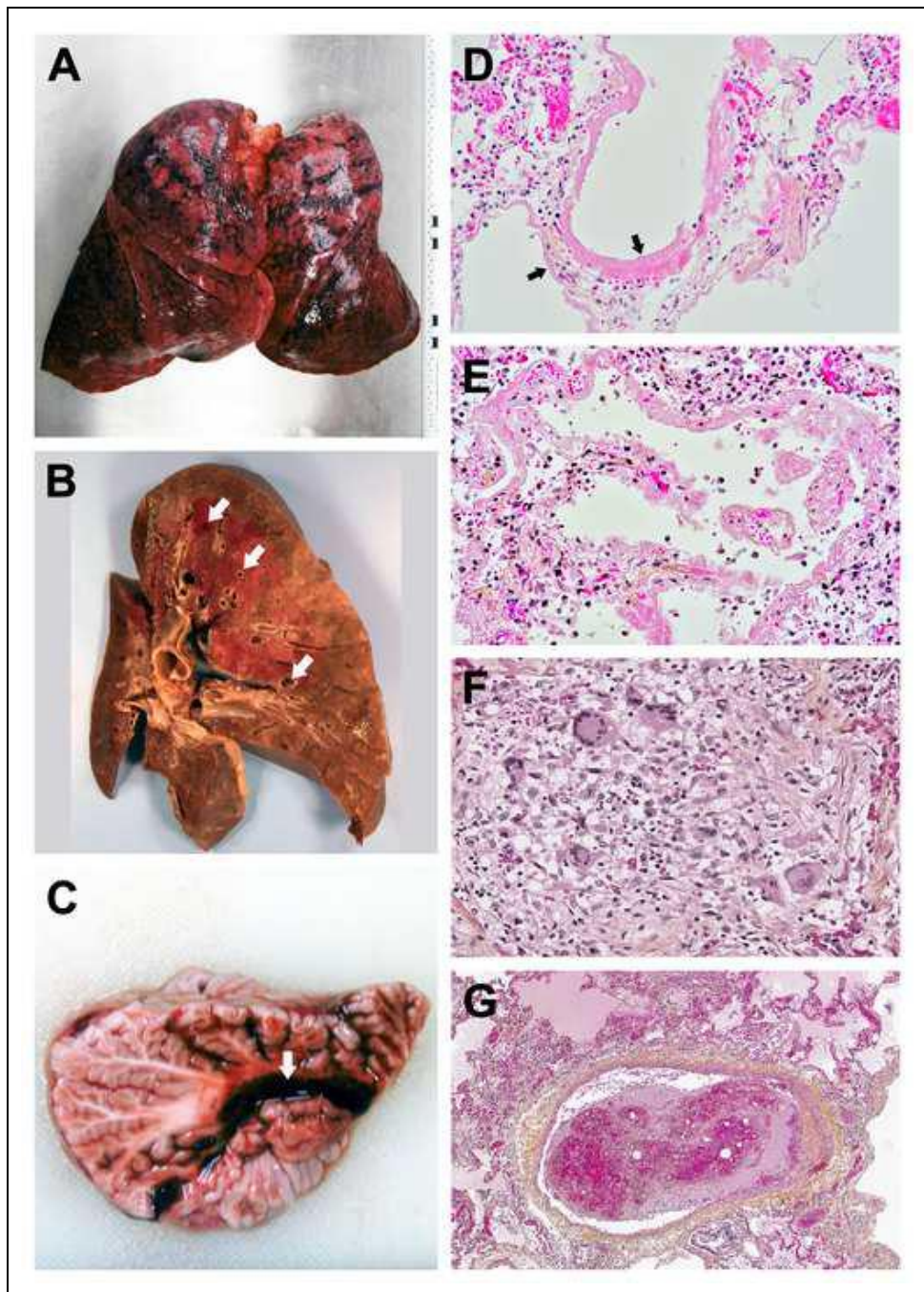


Figure 1: Gross findings and pulmonary microscopy findings in COVID-19-related out-of-hospital cardiac arrest; **(A):** Diffusely purplish-red, firm, heavy lungs from individual #4. Right lung: 1,110 g (normal: 651 ± 241 g); left lung: 740 g (normal: 579 ± 201 g); **(B):** Cross-section of fixed right lung from individual #1 showing light brown areas, (consolidation), dark brown areas (congestion), and small peripheral thrombi (arrows); **(C):** Right cerebellar small (0.8 x 2 cm) inferior infarct (arrow) without tonsillar involvement in individual #4; **(D):** Vasculo-exudative phase of diffuse alveolar damage (DAD) with alveoli lined hyaline membranes (arrows), interstitial edema, congestion and rare lymphomonocytic infiltrate (hematoxylin and eosin stain, X 200) from individual #1; **(E):** Early cellular phase of DAD with macrophage, lymphocytic and neutrophilic infiltrates (hematoxylin and eosin stain, X 200) from individual #2; **(F):** Resorptive/organizing phase of DAD with light alveolar walls thickening, giant multinucleated cells infiltrate in lumen and bronchiolar metaplasia of alveoli (hematoxylin and eosin stain, X 200) from individual #4; **(G):** Non-organized thrombi in lung tissue (hematoxylin and eosin stain, X 100) from individual #4.

Discussion

Only forensic autopsy determines both cause and circumstances of death. We report here 3 OHCAs of non-cardiac cause directly implicating COVID-19 and 1 suicide related to the lockdown. Interestingly, sudden death can occur at various stages of SARS-CoV-2-related DAD. Unlike what was reported in a series of hospital autopsies [4], the cause of death appears mainly due to lung damage without any major additional mechanism, in particular cardiovascular (e.g., pulmonary embolism).

Conclusion

In agreement with a previous commentary, this report emphasizes that autopsy, with appropriate indications and technical and safety protocols [7], is of obvious interest during this pandemic, both legally and medically. Finally, it seems important to consider that autopsy can dramatically help in the understanding of the pathogenic processes of this emerging infectious disease.

Contributors

Pr. Fanton and Pr. Argaud had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Fanton, Argaud.

Acquisition, analysis, or interpretation of data: Fanton, Nahmani, Epain, Meyronet, Argaud.

Drafting of the manuscript: Fanton, Argaud.

Critical revision of the manuscript for important intellectual content: Nahmani, Epain, Meyronet.

Supervision: Fanton, Argaud.

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