



# Non-COVID-19 Viral Respiratory Tract Infection as Causes of Death amid the Pandemic: a Report of Two Autopsy Cases and Tips for Safe Practice

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## Abstract

Autopsy practice is one of the most well-defined procedures in medicine, with strict safety instructions in place to protect medical personnel from infectious agents. However, for various reasons, these precautionary measures are often overlooked. Herein we report two autopsy cases of patients who died during the COVID-19 pandemic and the national state of emergency declared in Bulgaria. One patient was a 77-year-old female who had a medical history of a viral respiratory tract infection in February 2020 but had not undergone any test. She had multiple comorbidities including hypertension, cerebral and cardiovascular disease, and type 2 diabetes. The other patient was a 53-year-old female with morbid obesity with previous medical history of malignancy, hypertension, and type 2 diabetes. Both patients were tested for COVID-19 during the autopsy. Gross and histological findings in both patients showed respiratory tract viral infection with severe complications, incompatible with life. The first patient had serous desquamative tracheitis, hemorrhagic pneumonia, pericarditis, meningitis, and acute necrotizing encephalitis. The second patient had serous tracheitis, interstitial pneumonia, and diffuse alveolar damage and pneumocyte cytopathic effect, the alveolar septi had undergone a fibrotic change, with serous meningitis and non-necrotizing encephalitis also noted histologically. Autopsy-wise, it is always important, against the backdrop of an epidemic, to use full precautionary measures and exclude epidemic strands in cases where gross findings are suggestive of a viral infection.

## Keywords

autopsy, COVID-19, histopathology, viral infections

## INTRODUCTION

Autopsy practice is one of the most well-defined procedures in medicine, with strict safety instructions in place to protect the medical personnel from infectious agents.<sup>1,2</sup> However, due to different reasons, often these precautionary measures are overlooked.<sup>1,2</sup> This posed great difficulty

in the novel coronavirus 2019 (COVID-19) pandemic, as most autopsy theatres were ill-equipped to perform autopsies of patients with respiratory viral infections.<sup>3,4</sup> Herein we report two autopsy cases of patients who died during the COVID-19 pandemic and the national state of emergency declared in Bulgaria.

## CASE REPORT

Both patients were female, the one was 77 years old, and the other was 53 years old.

The first patient had a medical history of a viral respiratory tract infection in February 2020, but had not undergone any test. She had multiple comorbidities including hypertension, cerebral and cardiovascular disease, and type 2 diabetes. At admission to hospital, she presented with progressive neurological deficits and acute renal failure.

The second patient was morbidly obese and had a history of previous malignancy, hypertension, and type 2 diabetes. Current symptoms induced exacerbation of chronic respiratory failure; however, the patient died in the emergency department before proper investigations could be conducted.

Both autopsies were video documented in full.

Due to the epidemiological data and the short hospital stay of both patients, a full infectious disease autopsy protocol was used. Both the pathologist and hall attendant were equipped with an N-95 respirator mask, respiratory helmet, and infectious disease suit with full-body protection. The autopsy theatre was well aerated with maximum air exchange being provided.

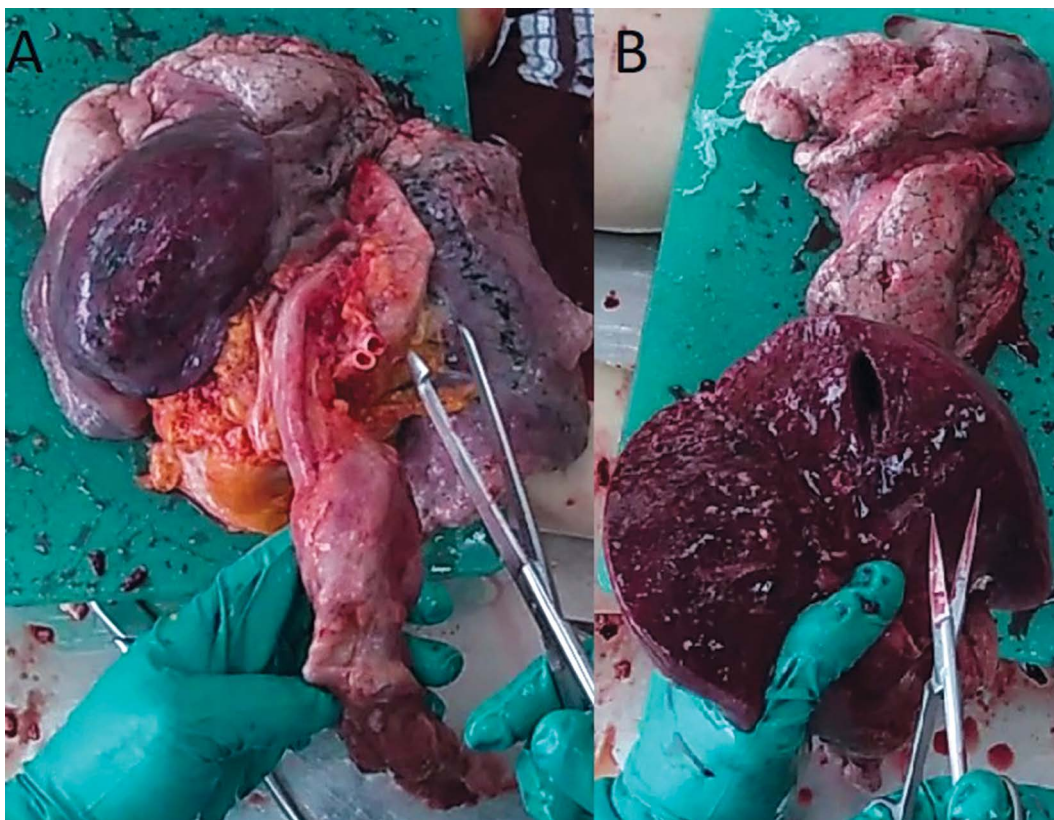
The thoracic section of the first patient revealed sero-desquamative tracheitis and hemorrhagic pneumonia located in the upper lobe of the right lung (Fig. 1). Based on the medi-

cal history, gross characteristics of the respiratory system, and epidemiological data, a tracheal swab and blood sample were acquired for a quantitative real-time polymerase chain reaction (qRT-PCR) during the autopsy to test for COVID-19. The rest of the autopsy was uneventful apart from hypertension and atherosclerosis complications. A few hours after the autopsy the qRT-PCR results for COVID-19 came back negative.

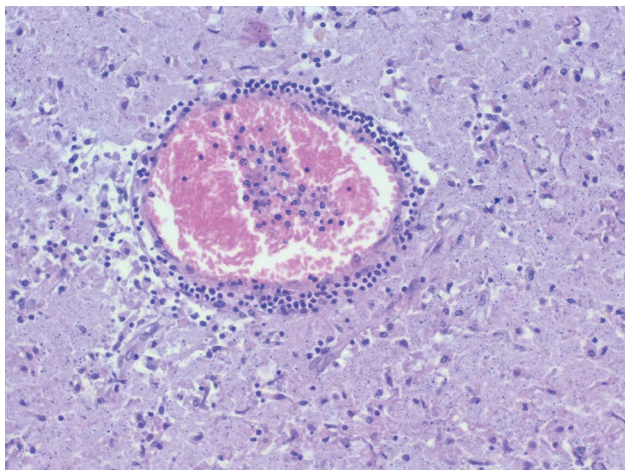
Histopathology from the collected specimens revealed serous desquamative tracheitis, hemorrhagic pneumonia, pericarditis, meningitis, and acute necrotizing encephalitis (Fig. 2).

Thoracic section of the second patient revealed sero-desquamative tracheitis and a diffuse acute respiratory distress syndrome (ARDS) changes in both lungs (Fig. 3), with grossly detectable thromboembolism. A fast immunoglobulin (Ig) test was used during the autopsy, with both IgM and IgG being negative.

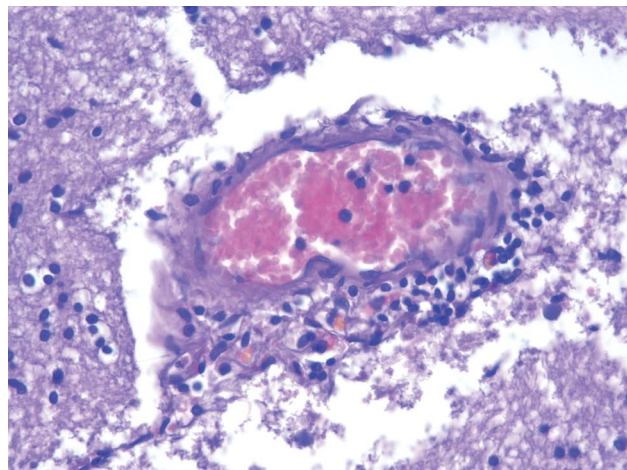
Histopathology from the collected specimens revealed serous tracheitis, interstitial pneumonia with hyaline membranes, multiple megakaryocytes and desquamation of the alveolar epithelium with cytopathic effect - some of the cells were enlarged with ground-glass opacity cytoplasm and an enlarged eccentric nucleus, whilst others were multinucleated, parts of the alveolar septi had undergone a fibrotic change (Fig. 4). Serous meningitis and non-necrotizing encephalitis were also noted histologically (Fig. 5).



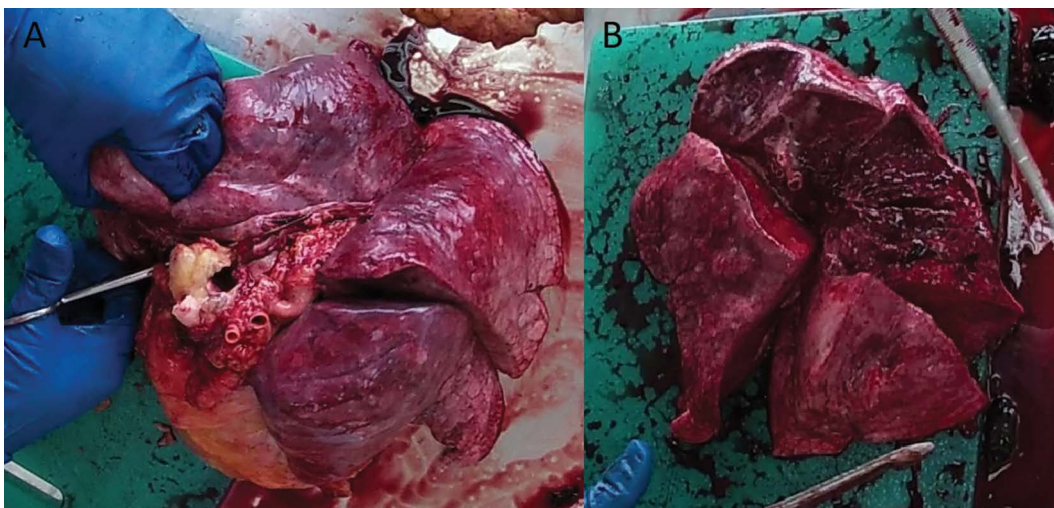
**Figure 1.** Cervicothoracic complex: (A) posterior view, upper right lobe is hemorrhagic in appearance and firm; (B) section of the upper right lobe reveals hepatization, left lung without changes visible on the backdrop. Note: images are snapshots from the video recording of the autopsy.



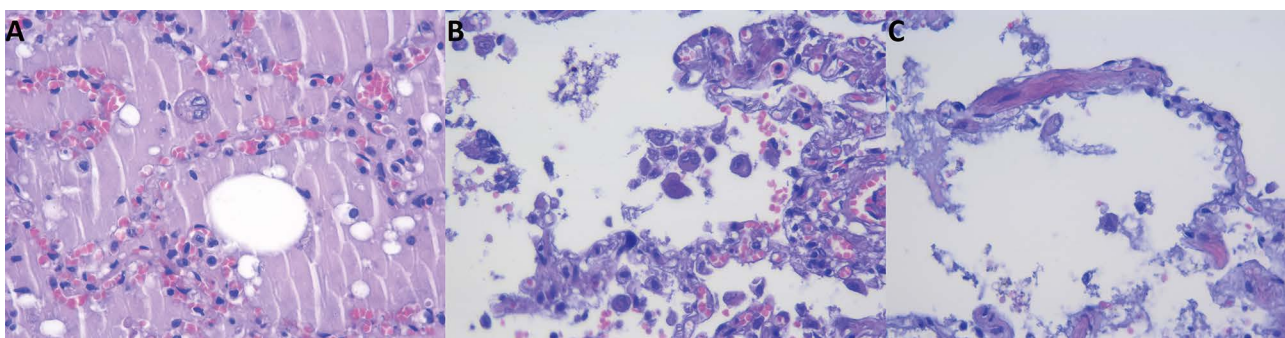
**Figure 2.** Acute necrotizing viral encephalitis (encephalopathy)-lymphocytic vascular cuffs and neuronal necrosis with granulation tissue in the periphery. Hematoxylin and Eosin, original magnification  $\times 200$ .



**Figure 5.** Non-necrotizing viral encephalitis - lymphoplasmacytic vascular cuffs and a few siderophages. Hematoxylin and Eosin, original magnification  $\times 400$ .



**Figure 3.** Cervicothoracic complex: (A) posterior view, both lungs are enlarged livid and firm with minimal aerated parenchyma remaining in the periphery; (B) section of the left lung reveals hepatization. Note: images are snapshots from the video recording of the autopsy.



**Figure 4.** Pulmonary histopathology from the second case: (A) edema and desquamated enlarged binucleated pneumocyte; (B) desquamated enlarged and a few multinucleated pneumocytes with lymphoplasmacytic infiltration in the alveolar interstitium; (C) alveolar septa fibrosis. Hematoxylin and eosin stain, original magnifications  $\times 200$ .

## DISCUSSION

Epidemiological data is always important when performing an autopsy, especially in cases where patients have had a very brief hospital stay, before death, or in cases where a viral disease was suggested but no test was performed.<sup>2,5</sup> In such cases, extreme precautions should be taken with the goal of both protecting the medical and non-medical hospital personnel and to properly identify any infectious agent to allow for more epidemiological data to be gathered.<sup>5</sup>

It is also important to note that even despite the epidemiological data, non-prevalent viral agents can also be the cause of death, as in our two cases, where influenza viruses were considered to be the most probable cause for the diffuse changes.<sup>5,6</sup>

Also worth noting is that the second case had pulmonary histology very close to some of the changes depicted in COVID-19 autopsies; however, even with the low-specificity of the rapid antibody test, without serology or qRT-PCR, the viral causative agent cannot be defined.<sup>3,7,8</sup>

## CONCLUSION

Viral respiratory tract infections are amongst the leading causes of epidemic outbreaks. From an autopsy perspective, it is important, against the backdrop of an epidemic, to always use full precautionary measures and exclude

epidemic strands, using serology tests or qRT-PCR, in cases where gross findings are suggestive of a viral infection.

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# Вирусная инфекция дыхательных путей, не связанная с COVID-19, как причина смерти в условиях пандемии: отчёт о двух случаях вскрытия трупа и советы по безопасной практике

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## Резюме

Вскрытие – одна из наиболее чётко определённых процедур в медицине со строгими инструкциями по безопасности для защиты медицинского персонала от инфекционных агентов. Однако по разным причинам эти меры предосторожности часто игнорируются. Здесь мы сообщаем о двух вскрытиях пациентов, умерших во время пандемии COVID-19 и чрезвычайного положения, объявленного в Болгарии. Одна пациентка была 77-летней женщиной, у которой с февраля 2020 года в анамнезе была вирусная инфекция дыхательных путей, но она не была обследована. У неё было несколько сопутствующих заболеваний, таких как гипертония, церебральные и сердечно-сосудистые заболевания и диабет 2 типа. Другой пациенткой была 53-летняя женщина с патологическим ожирением, в анамнезе которой были злокачественные новообразования, гипертония и диабет 2 типа. Оба пациента прошли обследование на COVID-19 при вскрытии. Общие и патологические данные у обоих пациентов показали вирусную инфекцию дыхательных путей с тяжёлыми осложнениями, несовместимыми с жизнью. У первого пациента был тяжёлый дескваматозный трахеит, геморрагическая пневмония, перикардит, менингит и острый некротический энцефалит. У второго пациента был тяжёлый трахеит, интерстициальная пневмония и диффузное альвеолярное поражение, пневмоциты с вирусным цитопатическим действием, альвеолярные перегородки претерпели фиброзные изменения с серозным менингитом и некротическим энцефалитом, что также установлено гистологически. При вскрытии всегда важно соблюдать меры предосторожности, особенно на фоне эпидемии, и исключать признаки эпидемии в тех случаях, когда основные результаты указывают на вирусную инфекцию.

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## Ключевые слова

вскрытие, COVID-19, гистопатология, вирусные инфекции

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