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Case Report

COVID-19 in an HIV-infected patient. Lessons learned from an autopsy case

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\section*{ABSTRACT}

Despite measures put in place to curb the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) across South Africa, there has been a rapid spread which caused extensive morbidity and mortality. Whilst there is currently increased COVID-19 associated death, autopsies on COVID positive individuals are not routinely performed. An autopsy was performed on a 19 years old African patient who was recently diagnosed with human immunodeficiency virus (HIV). He presented with clinical features suggestive of SARS-CoV-2, which he subsequently tested positive for. Important histopathological findings included diffuse alveolar damage and fibrin thrombi. No superimposed infections were noted. The cause of death was attributed to COVID-19. We report the first autopsy case of an HIV-infected individual with COVID-19 as the cause of death.

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\section*{Introduction}

The first confirmed case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was reported in China in December 2019. This viral infection has since spread across the globe with the first case reported in South Africa on March 20, 2020.

Coronaviruses are enveloped, non-segmented, positive-sense single-stranded RNA viruses. The other two that are known to cause human diseases are beta coronaviruses—severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) (Carsana et al., 2020; Barton et al., 2020).

The clinical features range from asymptomatic to mild symptoms such as cough, fever, dyspnea and severe disease which leads to acute respiratory distress syndrome and death (Carsana et al., 2020; Shalev et al., 2020). Older patients and individuals with hypertension, diabetes and cancer are at increased risk of infection (Shalev et al., 2020). There is little knowledge on HIV/AIDS and its impact on the clinical outcomes in patients with COVID-19\textsuperscript{(3)}. To the best of our knowledge, this manuscript represents the first published report of an autopsy performed on an HIV infected patient with cause of death attributed to COVID-19.

\section*{Autopsy case report}

\subsection*{Clinical features}

The patient was a 19 years old African male who was referred from a local clinic with one-week history of generalised weakness, fatigue, cough and shortness of breath. He was recently diagnosed with human immunodeficiency virus (HIV) with CD4 T lymphocytes of 17 cell/\textmu L and viral load of 1,487,946 copies/mL. He was not yet on anti-retroviral therapy (ART). He had no other co-morbidities. On examination, his blood pressure was 95/33 mmHg, heart rate of 103 beats/minute, fever of 38.7°C and saturation of 95% on 40% oxygen. He was confused, pale and hypovolemic with generalised lymphadenopathy. He had bilateral crackles on chest examination. Abdominal examination revealed massive splenomegaly and hepatomegaly. He was given an intravenous stat dose of ceftriaxone and acetaminophen, and admitted to a patient under investigation (PUI) ward for COVID-19 suspects. The chest x-ray showed extensive bilateral infiltrates (Figure 1a). The full blood count showed bicytopaenia with low haemoglobin and platelets of $100 \times 10^{9}$/$L$, and 3 units of red blood cells were transfused.
The liver function tests were mildly deranged. C-reactive protein, ferritin and procalcitonin were raised. The renal function tests revealed pre-renal acute kidney injury most likely secondary to the hypovolaemia (see Table 1 for investigations). Despite SARS-CoV-2 infection, in view of the retroviral disease, pneumocystis pneumonia, bacterial pneumonia and tuberculosis could not be excluded. He was started on trimethoprim-sulfamethoxazole 1920 mg 6-hly, hydrocortisone 200 mg 8-hly, azithromycin 500 mg daily and enoxaparin 60 mg daily. Polymerase chain reaction of the nasopharyngeal swab detected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Three days post admission, his confusion worsened; he developed cardiorespiratory failure and died.

**Autopsy findings**

A complete autopsy was performed in a negative pressure autopsy room with personal protective equipment (PPE), including N95 masks, eye protection, gloves and gowns.

**Gross features**

The patient’s body mass index was 18.1 kg/m². He was emaciated, hypovolaemic and pale with generalized lymphadopathy. He had serosanguineous bilateral pleural effusion and ascites. The right and left lungs weighed 884 g and 772 g (n = 360–570 g and 325–480 g) respectively. They were oedematous, firm with alternating pale and red areas (Fig. 2b). The spleen weighed 1310 g (n = 156) with haemorrhagic cut surface. The liver weighed 2400 g (n = 1500–1800) with pale, greasy and yellowish cut surface. The kidneys had smooth surface with good corticomedullary differentiation on cut section. The brain and heart were unremarkable. The bone marrow was pale and soft.

**Microscopic features**

Sections of the lungs showed extensive oedema with bilateral diffuse alveolar damage (DAD) evidenced by hyaline membrane formation (Figure 1c-e). Adjacent small calibre blood vessels with fibrin thrombi were noted (Figure 1f). Granulomatous inflammation or infectious pathogens were not seen. The spleen was poorly

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**Figure 1.** a, chest x-ray shows extensive bilateral infiltrates with left pleural effusion; b, firm lung with alternating red and pale areas, and oedema. No visible thrombus; c–e, diffuse alveolar damage with hyaline membrane formation ( ); f, Small vessels with fibrin thrombi ( ).
preserved; however, infectious pathogens or neoplastic infiltrate were not seen. Sections of the liver showed microvesicular steatosis and lobular inflammation. The heart, brain and bone marrow were unremarkable. The kidney, lymph nodes and pancreas were poorly preserved. The well preserved glomeruli did not show features of hypertension, diabetes mellitus or HIV associated nephropathy. Furthermore, fibrin thrombi were not seen within the glomerular capillaries.

The final cause of death was SARS-CoV-2 (COVID-19) infection in an HIV infected patient.

### Discussion

Much as performing autopsies on COVID-19 positive individuals is still not routinely performed due to safety reasons, there has been a recent increase in COVID-19 autopsy. The spectrum of pathological findings has emerged from this.

The most consistently described autopsy findings are diffuse alveolar damage with associated desquamation of pneumocytes, oedema and capillary congestion (Carsana et al., 2020). Increased intra-alveolar macrophage and enlarged, atypical pneumocytes have also been seen in advanced disease (Fox et al., 2020).

ALP values were elevated in most cases and are suggestive of hepatic injury. The vasculature was not affected in any case.

Vascular microthrombi were seen in areas of diffuse alveolar damage with diffuse endothelial damage. Whilst this feature is not pathognomonic for COVID-19, it has been postulated to be specific to COVID-19 as this is not a normal finding in DAD (Fox et al., 2020; Bradley et al., 2020).

Luca Carsana et al. found that fibrin thrombi of small vessels were observed in 87% of lung cases and high levels of D-dimers in the blood (Carsana et al., 2020).

Elevated D-dimers are associated with increased thrombin generation in COVID-19 (Fan, 2020). The existence of fibrin thrombi and high serum levels of D-dimers may explain the severe hypoxaemia that indicates acute respiratory distress syndrome in these patients (Carsana et al., 2020). D-dimer levels of >1 μg/mL are associated with increased mortality in COVID-19 patients (Fan, 2020).

In accord with what is already published, the lung findings on the index patient showed an early phase of diffuse alveolar damage with associated microthrombi that is seen in COVID-19. The lung findings on this patient were not different from the ones reported on non-HIV infected patients.

Little is known of the interaction between HIV infection and SARS-CoV-2 pathogenesis. Furthermore, there is little knowledge on the impact of HIV infection on the clinical outcomes of patients infected with SARS-CoV-2.

Whilst HIV infected people on treatment with normal CD4 count and low viral load may not be at a high risk of serious illness, the presence of other chronic conditions may increase their overall risk (Gervasoni et al., 2020).

The fact that SARS-CoV-2 can cause transient immune deficiency denotes that HIV and COVID-19 interaction may have adverse immunological and clinical outcomes. Therefore, defective cellular immunity in HIV infected patients may be paradoxically protective for severe cytokine dysregulation in patients with COVID-19 (Härter et al., 2020). The index patient's clinical emaciation suggests that the low CD4 count was pre—COVID-19.

Shalev et al. hypothesized that the absence of T-cell activation alleviates the severe immunopathological phenomena seen in COVID-19. While his study had its limitations, he further suggested that SARS-CoV-2 does not act as an opportunistic pathogen in patients with uncontrolled HIV or AIDS (Shalev et al., 2020).

Tuohy et al. suggested that HIV status did not significantly impact clinical outcomes in patients with SARS-CoV-2 infection, albeit he detected trends suggestive of worse course outcome in HIV-positive patients (Karmen-Tuohy et al., 2020).

Although the index patient was HIV infected, he was young without co-morbidities. He had lymphopenia and was not yet on antiretroviral therapy. This is contrary to the few published cases which show that high mortality rate of COVID-19 in HIV infected patients is usually associated with older patients (>50 years) with diabetes, hypertension, etc.

Furthermore, in view of the index patient’s low CD4 count, secondary or opportunistic infection such as tuberculosis, pneumocystis pneumonia or cryptococcal infection would be expected. However, there was no superimposed infection identified on lung sections examined. This further favoured COVID-19 as the sole cause of death in this patient.

### Conclusion

With its own limitations, this autopsy has not shown any distinct pathological findings specific to HIV infection in contrast to what is already described in non-HIV infected patients. In lieu of this, more studies regarding HIV and COVID-19 association are warranted as typical clinicopathological findings may likely have important treatment implications for these patients.

### Limitation

The autopsy was done seven days after he died, awaiting written informed consent from the family. Hence some of the organs were autolysed.
Author contributions

MCK, TCN and NM conceptualised the report and wrote the manuscript. All authors have read and approved the submitted version of this manuscript.

Availability of data and materials

All materials and data described in this manuscript are available upon reasonable request to the corresponding author, and if complying with patients’ privacy.

Consent for publication

Written informed consent was obtained from the patients’ parents for scientific publication of this case report.

Ethical approval and consent to participate

Sefako Makgatho Health Sciences University Research Ethics Committee (SMUREC) approved the publication of these case series.

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Conflicts of interest

The authors declare that they have no conflicts of interest

Declaration of Competing Interest

The authors report no declarations of interest.

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