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ORIGINAL RESEARCH

Pathology of Major Organs in Autopsy Specimens of Covid Positive Patients

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Abstract
Background: Pathological Autopsy has been the mainstay of understanding the concepts of diseases. Histopathological changes due to Covid 19 infection in various organs are not well documented, especially in the heart.
Objective: Describe the histomorphology in major organs - heart, lung and brain in autopsy specimens of COVID positive patients. Determination of a possible pathophysiological outcome as cause of death.
Materials and methods: Descriptive Cross-sectional Autopsy Study conducted in the Departments of Pathology and Forensic Medicine, Government Medical College, Manjeri over a one-year period. All RTPCR proven COVID positive deaths, irrespective of any other known / medicolegal cause of death were included in the study.
Results: Eleven autopsy cases were studied in the 1-year period. Diffuse alveolar damage of Lung was observed in 2 of the eleven patients. 4 of the eleven patients had histologic findings consistent with Ischemic Heart Disease. The rest of the patients (5 in number) were 50 years and below and had no evidence of coronary artery disease. These cases had Myocarditis with myofiber loss in random sections. The youngest case in this series was 16 years of age.
Conclusions: Cardiovascular disease appeared to be the major finding related to death in majority of COVID patients; this included Myocardial infarction as well as Myocarditis. COVID induced inflammatory changes in the heart appear to play a major role in its pathogenesis.
Keywords: Diffuse alveolar damage Lung, Ischemic heart disease, Myocarditis, SARS-CoV-2.

Introduction

The Corona virus pandemic has left thousands of people dead all over the world. The cause of death stated most of the times is severe viral pneumonia with massive immune response. COVID 19 infection in humans is also known to affect the heart, kidneys, intestine and brain. It is indicated that the virus travels to the various organs from the respiratory tract via the blood stream.[1] Histopathological changes in these various organs are also not well

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documented, especially in the heart. MRI scan and Troponin levels at the time of infection indicate a possible Myocarditis occurring in COVID patients alongside respiratory distress.
Pathological Autopsy has always been the mainstay of understanding the concepts of diseases which have ravaged mankind since ages. Pathological Autopsy in cases of death related to a new infectious agent like SARS-CoV- 2 can make better understanding of the physiology of changes that occur in major organs leading to death.

Aims & objectives

1. Describe the histomorphological changes in major organs- Heart, Lung and Brain in autopsy specimens of COVID positive patients
2. Estimation of a possible pathophysiological outcome as cause of death in these patients

Materials and methods

It was a Descriptive Cross-sectional Study done in the Departments of Pathology and Forensic Medicine, Government Medical College, Manjeri during one year from April 2020 to March 2021. Autopsy specimens of all RTPCR proven COVID positive deaths, irrespective of any other known / medicolegal cause of death were included in the study. Autolyzed specimens were excluded from the study.
Autopsy was performed on cadavers kept in the mortuary cooler at 4 degree centigrade and post mortem examination was done after 72 to 96 hour after death abiding to Covid protocol. Institutional and Ethical clearance were obtained for performing the study. Gross examination was done in detail by the Forensic surgeon, relevant tissue pieces were then sent to the department of Pathology.
Autopsy specimens received in the department of Pathology were fixed in Formalin for a period of not less than 48 hours to avoid possible infectivity from virus. The specimens included would be tissue from Heart, Lung and Brain.
Tissue bits were subjected to processing in an Automated tissue processor and stained with Haematoxylin and Eosin. Detailed histopathological examination was done and concurrence of findings obtained between a minimum of 3 expert pathologists.

Results

In our hospital-based study on autopsies done on eleven COVID positive patients, respiratory failure secondary to Diffuse Alveolar Damage (DAD) as a cause of death was plausible in only two out of 11 patients. In all other patients inflammation in the lung was interstitial, in the form of diffuse loose collections of lymphocytes or in follicular aggregates.
Lungs in the two patients who had ARDS were histologically remarkable in that they were characterized by epithelial denudation, widespread hyaline membrane formation, foci of intra alveolar haemorrhage and intra alveolar fibrinous material. The lungs appeared to have been washed over by a cytokine storm (Fig 1). Thrombi were not noted in small arterioles or in any major pulmonary vessel.
In the rest nine of 11 patients, respiratory disease could not account for the sudden onset in breathing difficulty and uneasiness leading to death. Lung in all these patients showed oedema (interstitial or alveolar) in addition to interstitial inflammation. The pulmonary oedema in these cases appeared to be secondary to Cardiovascular disease. Cardiovascular disease in these cases took on a constellation of findings. Four of these nine patients had evidence of chronic heart disease in the form of ventricular muscle hypertrophy and fibrosis. The fibrous tissue in the hearts of these patients were collagenized scars of previous myocardial infarction. Evidence of fresh infarcts in the form of areas of myocardial interstitial oedema / wavy hypereosinophilic fibres / RBC extravasation indicating infarcts> 12 hours old were seen on additional tissue sections. Coronaries in these cases showed

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luminal obstruction by atheromatous plaques with ***secondary events***. Secondary events in these cases were plaque rupture, haemorrhage or superimposed thrombus. Plaques of coronaries showed significant number of lymphocytes and plasma cells; these were also seen within the wall layers. Luminal obstruction was > 70% in all these cases (Fig 2,3&4).

Rest of the five patients had flabby hearts as recorded by the forensic expert performing the autopsy. These hearts on microscopic examination of random tissue bits revealed foci of interstitial oedema and lymphocytic infiltration of myocardial tissue consistent with Myocarditis. Myofiber loss was patchy and not seen in all five cases. Myocarditis was accompanied by pericarditis in one case. It is to be noted that some of the myocardial tissue bits only showed mild inflammation in contrast to other tissue bits with more significant inflammation substantiating the fact that histological findings of Myocarditis are not uniform throughout the heart (Fig 5). Myocarditis alone as a cause of death was possible only in two of these five patients; one patient had DAD Lung and the other two patients had medico legal causes of death respectively. Brain in all these patients only showed congestion.

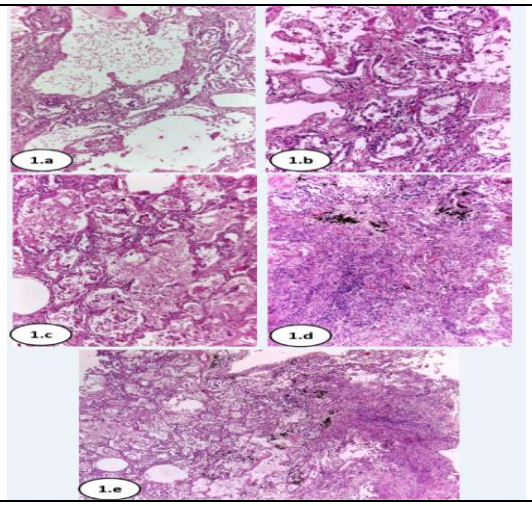

Figure 1: Lung pathology in COVID: a) Alveolar rupture b) Epithelial denudation c) Fibrinous material in alveolar lumen d) Interstitial inflammation lung e) Hyaline membrane and lung collapse

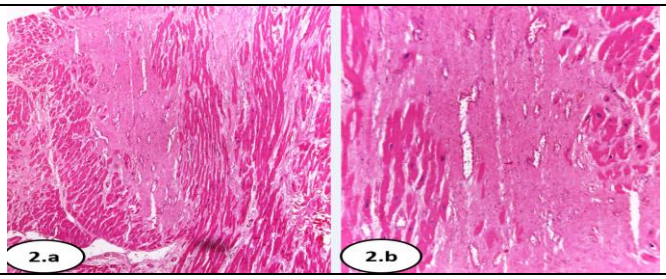

Figure 2: Old infarct in COVID patient: a) 100X b) 200X

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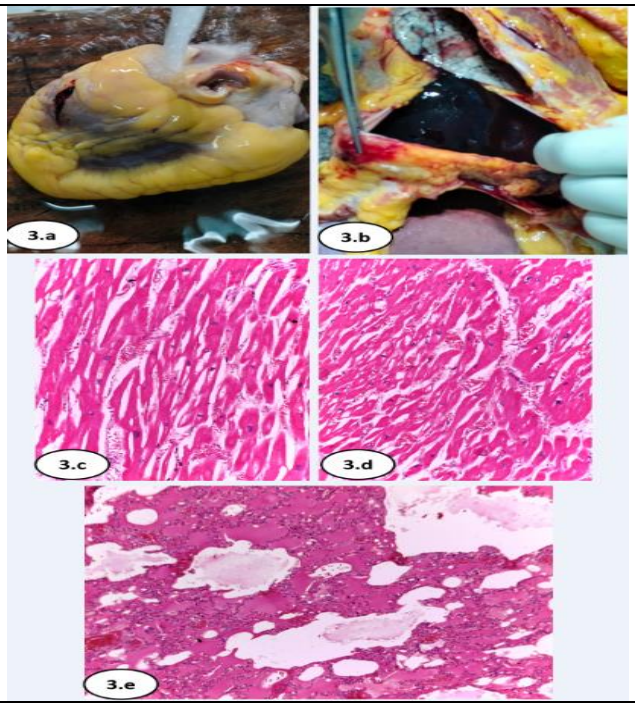

Figure 3: Fresh infarct findings in COVID patients: a) Site of ventricular wall rupture b) Hemopericardium c & d) Histopathologic findings in fresh infarct e) Pulmonary edema

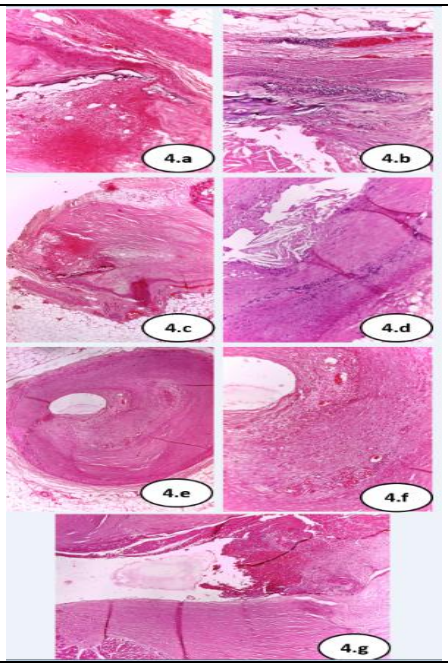

Figure: 4 Secondary changes in atheromatous plaque: a) Aortic plaque with haemorrhage b) Aortic Plaque with inflammation c) Coronary plaque with haemorrhage d) Coronary plaque with inflammation e) Thrombus on coronary plaque 100X f) Thrombus on coronary plaque 200X g) Thrombus attached to myocardial wall

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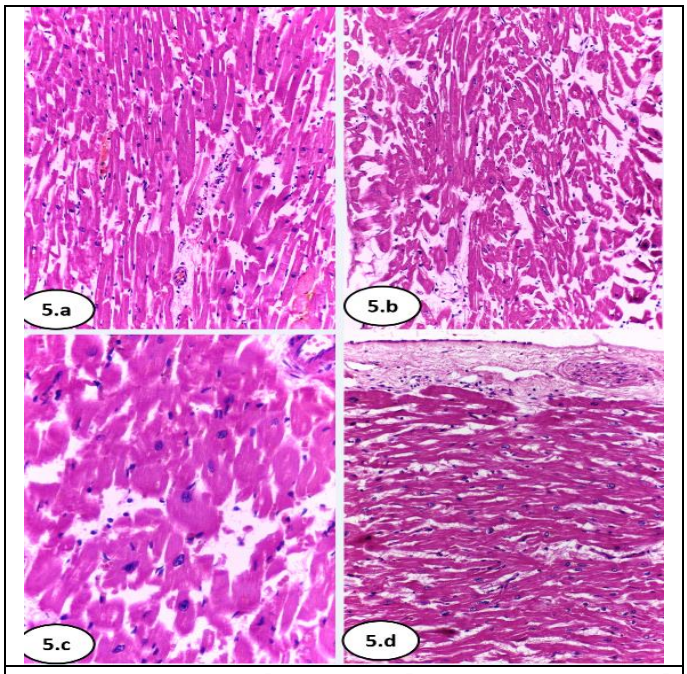

Figure 5: Myocarditis: a & b) 200X c) 400X d) Pericarditis accompanying Myocarditis

Discussion

Studies indicate that the SARS -CoV- 2 virus infects host target cells through the ACE 2 receptor.[2] ACE 2 receptor is primarily stated to be on pneumocytes and endothelial cells.[3] In patients who develop severe disease, aberrant immune response has been noted.[4]

Pneumocyte injury leading to epithelial cell necrosis, entry of neutrophils into alveolar lumen and cytokine release with formation of hyaline membrane and thus respiratory distress syndrome is now a fairly well recognized cause of death in COVID 19 patients based on autopsy study details revealed over the past one year since onset of the pandemic as well as the clinical scenario of patients in the ICUs world over.[5-8]

The acute coronary syndrome in 4 of the patients with ischemic heart disease were evidently due to ***acute plaque change***. Atherosclerosis is stated to be an inflammatory disease elicited by cholesterol accumulation in the artery.[9] Inflammatory cells and pathways contribute to the initiation, progression and complications of atherosclerotic lesions.[10]Binding of the Corona virus to the endothelial cells through the ACE receptor likely results in endothelial dysfunction. Ackermann and colleagues [11] report an increased number of ACE receptors on endothelial cells and alteration in endothelial function subsequent to viral infection. Endothelial dysfunction leads to augmented expression of adhesion molecules that promote sticking of WBCs to the surface. The plaques in these 4 patients showed significant infiltration by inflammatory cells which could very well be due to chemotactic factors released by the virus. Release of pro inflammatory cytokines and pro thrombotic mediators by these inflammatory cells could trigger abrupt changes in plaque configuration with superimposed thrombosis / haemorrhage. It is now recognized that plaques that are responsible for myocardial infarction and other acute coronary syndromes are often asymptomatic before undergoing a sudden typically unpredictable change.[12] One of the patients in this context even had cardiac rupture with hemopericardium.

Causes of Myocarditis have always traditionally been attributed to viral infections such as Coxsackie, ECHO, Influenza, HIV and so on. The SARS- CoV-2 virus can easily be implicated as a causative agent in Myocarditis. Myocarditis in viral infections occur as a

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result of direct cytopathic effect by the offending agent or damage secondary to an associated immune response with cytokine release.[13] Given the fact that ARDS with associated complications have been recorded in most studies related to COVID infections -; it is likely the myocarditis is immunologically induced and related to cytokine release. Myocarditis is very often patchy and focal; this being supported by the fact that random multiple biopsies of the heart in all five cases showed varying degrees of inflammation. Another point of note is that the ages of these five patients were 50 years and less and they seemed to have no significant coronary disease – a point of caution for those in the younger age group. The youngest in this group was 16 years old.

Thromboembolic phenomena in major organs affected by COVID as recorded in several autopsy studies [6,7,14] were not observed in our study. The brain in all eleven patients did not show features of meningoencephalitis indicating that the virus did not have the property of neurotropism.

Summary

Autopsy was done on SARS-CoV-2 cases based on a positive RTPCR on nasopharyngeal swab. Autopsy cases were 11 in number in the study period from April 2020 to April 2021. Majority of the patients were male except two. Diffuse alveolar damage was observed in two of the eleven patients. Four of the eleven patients had histologic findings consistent with ischemic heart disease. Evidence of fresh myocardial infarction was obtained in these patients; the cause of this could be attributed to Acute Plaque Change in the atherosclerotic plaques. The acute plaque change was possibly induced by an increase in inflammatory cell infiltration in the plaque brought about by an aberrant immune response. The rest of the patients (five in number) were 50 years and below and had no evidence of coronary artery disease. These cases had Myocarditis with myofiber loss in random sections. The youngest case in this series was 16 years of age.

Conclusion

Cardiovascular disease appeared to be the major finding related to death in majority of Covid patients; this included Myocardial infarction as well as Myocarditis. The cause of myocardial infarction in those patients could be attributed to Acute Plaque Change in the atherosclerotic plaques which was possibly induced by an increase in inflammatory cell infiltration in the plaque brought about by an aberrant immune response. Myocarditis was more prevalent in a younger age group.

Acknowledgement

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References

1. Zhang Y, Geng X, Tan Y, et al. New understanding of the damage of SARS-CoV-2 infection outside the respiratory system. Biomed Pharmacother. 2020 Jul;127:110195.
2. Cevik M, Kuppalli K, Kindrachuk J, Peiris M. Virology, transmission, and pathogenesis of SARS-CoV-2. BMJ. 2020 Oct 23
3. Cevik M, BamfordCGG, Ho A. COVID-19 pandemic-a focused review for clinicians. ClinMicrobiol Infect. 2020 Jul;26(7):842-847
4. Blanco-Melo D, Nilsson-Payant BE, Liu WC, et al. Imbalanced Host Response to SARS-CoV-2 Drives Development of COVID-19. Cell. 2020 May 28;181(5):1036-1045
5. Sekhawat V, Green A, Mahadeva U. COVID-19 autopsies: conclusions from international studies. DiagnHistopathol (Oxf). 2021 Mar;27(3):103-107

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 02, 2023

6. Carsana L, Sonzogni A, Nasr A, et al. Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study. Lancet Infect Dis. 2020 Oct;20(10):1135-1140
7. Elsoukkary SS, Mostyka M, Dillard A, et al. Autopsy Findings in 32 Patients with COVID-19: A Single Institution Experience. Pathobiology. 2021;88(1):56-68
8. Falasca L, Nardacci R, Colombo D, et al. Postmortem Findings in Italian Patients With COVID-19: A Descriptive Full Autopsy Study of Cases With and Without Comorbidities. J Infect Dis. 2020 Nov 9;222(11):1807-1815
9. Hansson GK. Inflammation and Atherosclerosis: The End of a Controversy. Circulation. 2017 Nov 14;136(20):1875-1877
10. Libby P, Theroux P. Pathophysiology of coronary artery disease. Circulation. 2005 Jun 28;111(25):3481-8
11. Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. N Engl J Med. 2020 Jul 9;383(2):120-128
12. Mitchell RN, Connolly AJ. The Heart. In: Kumar V, Abbas AK, Aster JC, editors. Robbins &Cotran Pathologic Basis Of Disease. 10th ed. Philadelphia: Elsevier; 2021. p. 527-582
13. Kang M, An J. Viral Myocarditis. 2020 Aug 11. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan
14. Remmelink M, De Mendonça R, D'Haene N, et al. Unspecific post-mortem findings despite multiorgan viral spread in COVID-19 patients. Crit Care. 2020 Aug 12;24(1):495.