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Postmortem CT lung findings in decedents with Covid-19: A review of 14 decedents and potential triage implications

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ABSTRACT

Objective: Computed tomography has significant utility as a diagnostic tool for coronavirus disease 2019 (COVID-19) in the clinical setting. COVID-19 deaths are sometimes examined by forensic pathologists, often in the setting of an unknown diagnosis. We assessed the utility of postmortem computed tomography (PMCT) for use as a triage tool for these autopsy examinations.
Materials and methods: We reviewed PMCT findings in 14 and histopathology in 11 decedents who were positive for COVID-19.
Results: The predominant imaging findings were bilateral mixed densities, in either a diffuse or peripheral distribution, with traction bronchiectasis, and/or crazy paving. In particular, traction bronchiectasis, ill-defined rounded consolidations, and reverse halo sign are useful when distinguishing from other postmortem changes.
Conclusion: We conclude that triage with a PMCT may aid the forensic pathologist in diagnosing possible COVID-19 infection prior to autopsy examination.

Introduction

The coronavirus disease 2019 (COVID-19) is a newly described acute respiratory syndrome with clinical manifestations ranging from asymptomatic infection, to mild upper-respiratory symptoms, to fatal pneumonia [1,2]. This ongoing outbreak has had major global implications with 737,417 deaths and over 20 million cases worldwide, as of August 12, 2020 [3]. Containment and control of this pandemic relies heavily on detecting infection in affected individuals, allowing for contact tracing with isolation of contacts to decrease transmission of the virus.

Chest computed tomography (CT) was initially thought to be an important tool in the diagnosis of COVID-19 infected patients as it is easy to perform, provides rapid data, and is relatively sensitive for diagnosis. In fact, early studies of CT imaging in these patients have shown a higher sensitivity for the diagnosis of COVID-19 than real time polymerase chain reaction (RT-PCR) testing [4-6]. However, as with any diagnostic tool, there is the potential for false negative detection. Early reports of CT findings in COVID-19 patients suggested that nearly all positive patients (regardless of symptom severity) had positive CT lung findings [7-10]. Yet later reports revealed that negative findings are possible, particularly in early infection and in asymptomatic cases [11-12]. With these limitations in mind, chest CT imaging is still an efficient and sensitive diagnostic tool for symptomatic or severe cases of COVID-19, at least in the clinical setting.

Postmortem CT (PMCT) imaging is used by some forensic pathologists as an effective, non-invasive way to screen for natural disease, trauma, and infectious diseases prior to autopsy [13]. Its potential utility as a triage tool for the evaluation of COVID-19 infection in certain decedents is therefore reasonable to consider. This is particularly true in

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situations where adequate history is not available to the pathologist, or when the preceding symptoms or circumstances may not be typical or directly lead to suspicion of COVID-19 infection. While standard clinical symptoms such as fever, cough and dyspnea are commonly described, a myriad of atypical presentations have been reported to include diarrhea, nausea, and headache. [14-16]. This suggests that triaging cases for potential COVID-19 infection on investigative and clinical data alone (when available) may not be sufficient.

Another confounding issue is that, when compared to other types of pneumonia, COVID-19 seems to cause milder symptoms which are paired with more severe pulmonary findings on CT; so while an individual may by asymptomatic or have only mild symptoms, that does not reliably correlate to COVID-19 negativity [7]. Triage with PMCT and detection of COVID-19 lung pathology can raise suspicion enough to obtain the appropriate samples for testing. This may prevent cases with atypical presentations from going undetected and can allow for additional precautions and appropriate personal protective equipment for autopsy personnel prior to autopsy.

The typical pulmonary changes of COVID-19 pneumonia on CT evaluation have been well documented in the clinical settings. They consist of bilateral, multifocal ground glass opacities (GGOs) and/or consolidations, distributed mostly within the lower lobes, and with peripheral/subpleural predilection. "Crazy paving" pattern (reticular interlobular septa thickening within ground glass opacities), septal thickenings, and traction bronchiectasis are common findings [4,7,9, 11-12,17]. In addition, an evolution of these pulmonary findings is described as the disease progresses, with pure GGOs seen in the early/less severe phase of the pneumonia, and diffuse GGOs with progression to crazy paving pattern and consolidation in the later/more severe phases [17]. The degree of symptoms also seems to play a role, with asymptomatic patients demonstrating a GGO predominance, and symptomatic cases showing a consolidation predominance [11]. Pleural effusion, lung cavitation, lymphadenopathy and calcifications are rarely present [12].

It is important to note that usual postmortem changes have characteristic PMCT imaging findings as well. These include bilateral GGOs evolving to consolidations, localized in the dependent (typically posterior) areas of the lungs. Crazy pavings and septal thickenings may or may not be present [18]. Therefore, it is important to differentiate these similar, non-pathological postmortem findings from those that are characteristic of COVID-19.

Recently published reports have described the autopsy findings of COVID-19 decedents, some of which describe PMCT findings, although this has been limited [19-20]. We aim to expand upon the previously described PMCT findings, compare these with the clinical imaging findings described above, and distinguish these findings from normal postmortem changes.

Materials and methods

Decedents

This review consists of fourteen COVID-19 positive decedents from March-May of 2020. All deaths fell under the jurisdiction of the New Mexico Office of the Medical Examiner. This is a statewide system that investigates any death occurring in the State of New Mexico that is sudden, violent, untimely, unexpected, or where a person is found dead and the cause of death is unknown. Therefore, all the decedents in this series had symptoms suspicious for COVID-19, PMCT findings suspicious for pneumonia, or were known to be COVID-19 positive and were not being treated by a physician at the time of their death.

All of the decedents were screened at the time of examination by nasopharyngeal and/or lung swab with RT-PCR testing. All decedents received a full body PMCT prior to examination. Cases were excluded if significant decomposition was present. A full autopsy (internal and external examination with histology) was performed on eleven of the decedents (79%). These cases utilized Biosafety Level 3 (BSL-3) level precautions, to include high-efficiency particulate air (HEPA) filtration, downdraft table ventilation, and personal protective equipment consisting of powered air-purifying respirators (PAPRs). The remaining three decedents (21%) had a limited "external examination only" performed without histology, since they had a history of significant natural disease or evidence of natural disease on PMCT to potentially explain their deaths. These three decedents underwent COVID-19 RT-PCR testing at external examination due to reported histories of COVID-19 symptoms and/or recent positive COVID-19 testing prior to their deaths.

PMCT and analysis

Whole body post-mortem CT was performed in the morning, prior to autopsy, on the same day the case was scheduled for autopsy. Decedents were imaged using a Philips Brilliance Big Bore 16 Slice CT scanner with an 85 cm bore and a flat bariatric table, with Big Bore version 4.2 software. The standard adult, non-decomposed scanning protocol was used and was performed over two volumes: 1) vertex of cranium to just below the upper extremities (with arms crossed over the chest/abdomen) and 2) sternal notch to just below the toes (with arms raised over the head). The total time required to scan one decedent (including transport time) averaged 16 minutes. Axial slices were reconstructed from both volumes with a 3 mm slice thickness (3 mm spacing) and a 1 mm slice thickness (0.5 mm spacing), using both a soft tissue algorithm and a bone algorithm. Other reconstructions include sagittal and coronal reformats (bone and soft tissue), axial brain, dental, coronal and axial lung views.

Images were reviewed by a board-certified forensic radiologist with postmortem imaging experience of eleven years. The presence or absence of the following lung findings were reviewed for each case: GGOs, consolidations (including ill-defined rounded consolidation), crazy paving pattern, interseptal thickenings, reverse halo, honey combing, tree-in-bud appearance, cavitation, emphysema, pneumothorax, pleural effusion, and lymphadenopathy. The presence or absence of posterior-dominant GGOs, which are frequently seen in PMCT as a postmortem changes, was also reviewed (designated "postmortem lung changes").

Results

Demographics

Our decedents ranged in age from 29 to 82 years and consisted of eleven men and three women. Most suffered from one or more comorbidities, the most common being atherosclerotic and/or hypertensive heart disease (nine decedents, 64%). Other common comorbidities included chronic ethanol abuse (five decedents, 36%) and lung disease of any type (three decedents, 21%). Obesity, diabetes mellitus type 2, and homelessness were also observed in a minority of the cases.

Four decedents (29%) had atypical presenting symptoms by our available investigative data; this included nausea, vomiting, abdominal pain, and fatigue/weakness without cough, shortness of breath or fever. One decedent was reportedly asymptomatic. The remaining decedents exhibited typical symptoms such as fever, dyspnea, and cough. Four decedents (29%) had tested positive for COVID-19 prior to their death.

Gross and histopathologic findings

Gross findings of the lungs in the eleven decedents who underwent full autopsy universally included parenchymal congestion and edema. Frothy fluid in the airways, arterial microthrombi, consolidation and airway mucus were variably present in 20% of the cases.

Histologic examination of the decedents receiving full autopsy universally exhibited varying amounts of interstitial inflammation (acute and/or chronic). Intra-alveolar edema and hyaline membrane formation

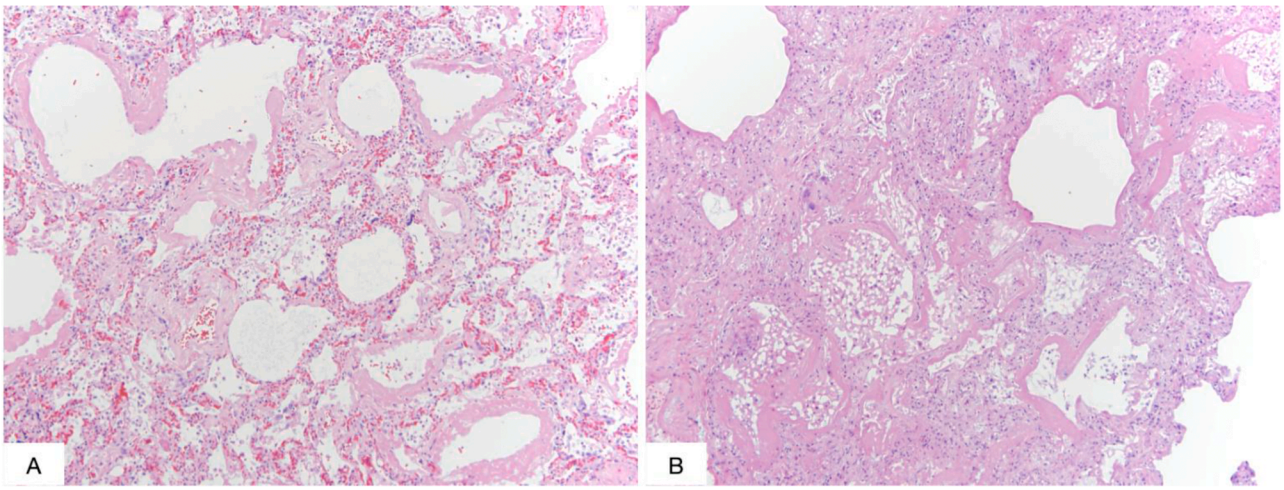

Image 1. A and B: Sections of lungs from two separate decedents show lymphocytic interstitial inflammation, atypical pneumocytes within and along the alveolar spaces, and hyaline membrane formation. B: Diffuse alveolar damage with exuberant hyaline membrane formation, obliterating alveolar spaces.

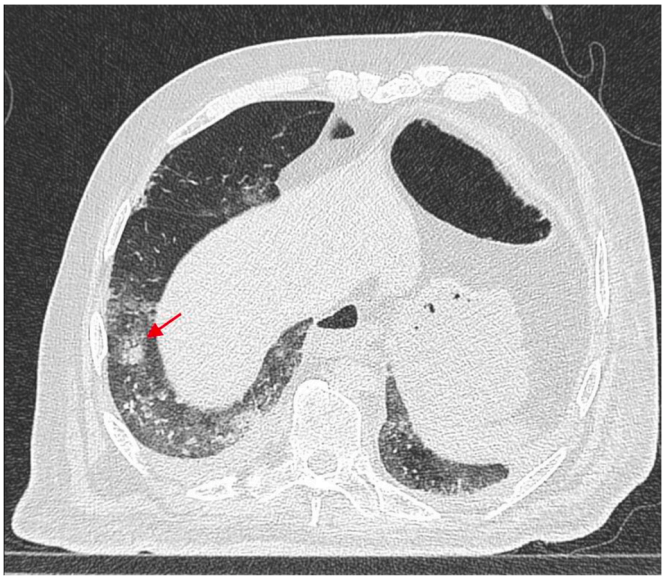

Image 2. Axial PMCT image of the lungs shows ill-defined rounded consolidation (arrow) in the right lung. Also note the right-sided pleural effusion.

were present in seven decedents (64%), consistent with diffuse alveolar damage. Two decedents (18%) demonstrated arterial microthrombi. Additional pathologies included type II pneumocyte hyperplasia and fibroblastic activity, likely demonstrating a more organizing phase of the disease process (Image 1).

Imaging

Eleven decedents (79%) demonstrated mixed densities (near-equal amounts of both GGOs and consolidations). Two decedents (14%) had GGOs without consolidations (or with a small amount of consolidations). Seven decedents (50%) had ill-defined rounded consolidations (Image 2).

One decedent (7%) had consolidations without GGOs. In all decedents, these findings were present bilaterally and in either a diffuse or peripheral distribution. Traction bronchiectasis (eleven decedents, 79%), interseptal thickenings (ten decedents, 71%) and crazy paving pattern (nine decedents, 64%) were the most commonly observed features, with pleural effusion (five decedents, 36%), lymphadenopathy

Table 1
PMCT features of COVID-19 decedents.

PMCT Features	Decedents (n=14)
Densities	
Mixed densities	11
Ill-defined rounded consolidations	7
GGOs without consolidations (or with a small amount of consolidations)	2
Consolidations without GGOs	1
Other Findings	
Traction bronchiectasis	11
Interseptal thickenings	10
Crazy paving pattern	9
Pleural effusion	5
Mild lymphadenopathy	4
Reverse halo sign	2
Honey combing	1
Tree-in-bud opacities	0
Cavitation	0
Emphysema	0
Pneumothorax	1
Postmortem lung changes	4
Distribution	
Bilateral	14
Diffuse	8
Peripheral	4
Centrilobular	2

(four decedents, 29%), and reverse halo sign (two decedents, 14%) present in a subset of cases (Table 1, Images 3 and 4).

The remaining three cases (21%) demonstrated atypical findings: one decedent had diffusely distributed consolidations, which obscured other findings and made interpretation difficult. The second decedent demonstrated centrilobular GGOs without septal thickenings and sparing of the subpleural area; findings that are not typically reported for COVID-19 (Image 5).

Of note, this decedent was atypical in many ways, with presenting symptoms of only nausea/vomiting and abdominal pain, and with nonspecific histology (intra-alveolar macrophages, bacterial colonies and mild chronic interstitial inflammation without features of diffuse alveolar damage). The third atypical decedent again demonstrated centrilobular GGOs without septal thickenings, which is inconsistent with COVID-19 pneumonia. However, this decedent did have ill-defined, rounded consolidations, which is suggestive of COVID-19.

Findings such as tree-in-bud opacities, cavitation, and emphysema were not observed in these decedents. Peripheral honeycombing was

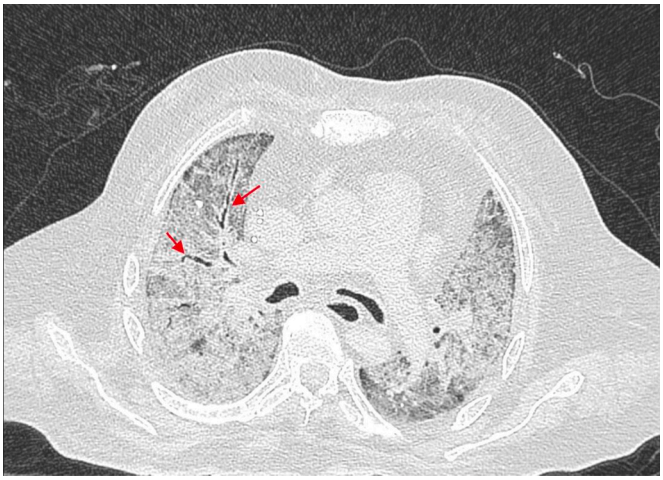

Image 3. Axial PMCT image of the lungs shows diffuse ill-defined mixed densities with traction bronchiectasis in the right lung (arrows). Crazy pavings and interseptal thickenings are also present.

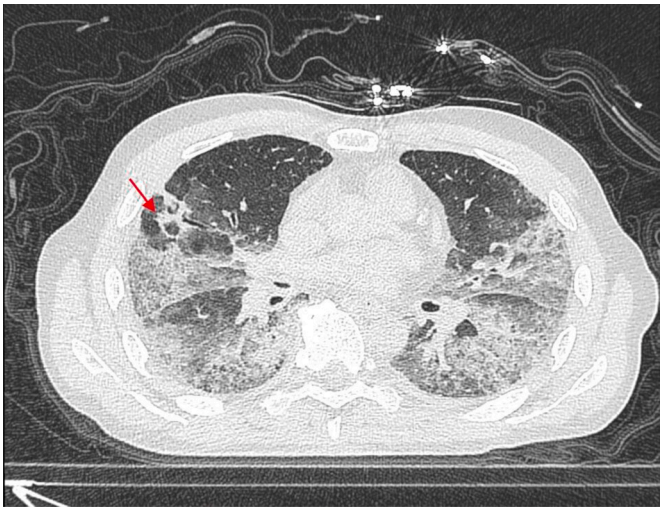

Image 4. Axial PMCT image of the lungs shows mixed densities in posterior-dominant areas, which is compatible with typical postmortem lung changes. Reverse halo sign is seen (arrow) in the right lung.

present in one decedent (7%) who had a history of oxygen dependency with unknown clinical history. Postmortem lung changes were present in four (29%) decedents (Image 6).

Discussion

Our review of 14 COVID-19 positive decedents demonstrates similar gross and histologic findings when compared with the previously reported (yet limited) literature [19-22]. The observed gross findings are nonspecific (congestion of the parenchyma with occasional findings of consolidation, frothy airway fluid or microthrombi). These findings are unlikely to be useful as a triage tool at autopsy, especially in the absence of consolidation. The histologic findings point to a viral interstitial pneumonia characterized by diffuse alveolar damage with hyaline membranes and interstitial inflammation. Arterial microthrombi and proliferation of fibroblasts and type II pneumocytes were present in a subset cases.

Our observed CT findings are comparable to those reported in the clinical setting. Recently published, limited reports that include PMCT findings in COVID-19 decedents are also compatible with our findings

Image 5. Axial PMCT image of the lungs shows centrilobular pure GGOs without crazy pavings or traction bronchiectasis, rather than the diffuse or peripheral-dominant mixed-density pattern that is typical for the COVID-19 cohort.

[19-23]. Mainly, we observed bilateral, mixed pattern of GGOs and consolidations, in either a diffuse or a peripheral distribution. Traction bronchiectasis, crazy paving pattern and septal thickenings were commonly present. Prior reports have suggested that pleural effusion and lymphadenopathy are not typically seen with COVID-19 infection. Our findings indicate that these findings were present in a subset of cases. Five of these decedents (36%) demonstrated mild pleural effusions, while four (29%) had mild lymphadenopathy.

While the COVID-19 imaging findings in the clinical setting are more often reported as peripheral/subpleural in distribution with lower lung predilection, our cohort demonstrated a much more diffuse pattern. This distribution is consistent with more severe infection, which would be the most likely to cause death and explain why this pattern is predominant in our postmortem population.

A potential confounding issue is postmortem changes, which may consist of posterior/dependent GGOs, consolidations, crazy paving pattern and interseptal thickenings. These findings can also be seen in COVID-19 patients and are therefore nonspecific. However ill-defined rounded opacities, traction bronchiectasis and reverse halo sign are *not* reported as typical postmortem changes; their presence can be key findings when differentiating COVID-19 from normal postmortem changes. Traction bronchiectasis is particularly useful and was present in 79% of our COVID-19 decedents. Ill-defined rounded consolidations are also considered useful in 50% of our cohort. While reverse halo sign was only present in 2 cases (14%), both cases had concurrent postmortem change. Therefore we believe the presence of reverse halo inside or near postmortem changes can be suggestive of COVID-19.

Understanding the characteristic imaging features of COVID-19 is also useful for differentiating from other types of community-acquired and atypical pneumonias. The presence of multiple lesions involving multiple segments and lobes of both lungs is typically not seen in bacterial pneumonias [7]. Similarly, viral pneumonia is more likely to have central involvement, lymphadenopathy and pleural effusions when compared to the peripheral distribution, GGOs, and crazy paving pattern of COVID-19 pneumonia [24]. Further investigation is underway to determine if specific PMCT findings can reliably distinguish COVID-19 from other pneumonias in the postmortem setting.

PMCT is not without limitations. Although PMCT is becoming more common in death investigation settings world-wide, in some regions,

Image 6. Axial PMCT image of the lungs shows typical postmortem lung changes, which include posterior-dominant GGOs.

including the U.S., it is not yet widely available. Additionally, previous underlying lung pathology, other comorbidities, and decomposition can obscure or alter the classic COVID-19 features. While negative CT imaging has been reported clinically in COVID-19 patients, this is typically in asymptomatic or mild infections [11-12]. This limitation is probably somewhat less significant in the postmortem setting, as COVID-19 is not likely to cause or significantly contribute to death in early infections without severe lung manifestations. Our case review supports this presumption, as every decedent demonstrated worsening symptoms over a period of days prior to their death.

Interestingly we report one case of fatal COVID-19 infection with a lack of any reported symptoms. Fortunately, this decedent was tested prior to death, and positivity was known prior to autopsy. The PMCT findings were characteristic of COVID-19 infection, supporting prior observations that asymptomatic individuals can have COVID-19 lung pathology [12]. We believe this case highlights the broad presentation and the lack of reliability of clinical and investigative data for triage purposes and confirms that decedents with no reported symptoms can still have distinctive lung pathology on imaging.

Overall, we believe that PMCT is a rapid and effective way to screen decedents for COVID-19 infection prior to autopsy, particularly in situations where the preceding symptoms or circumstances may not be typical or highly suspicious of infection. Bilateral, mixed densities in either a diffuse or peripheral distribution with traction bronchiectasis and/or crazy paving are the constellation of imaging findings most frequently seen. In particular, traction bronchiectasis, ill-defined rounded consolidations and reverse halo sign are useful when distinguishing from other postmortem changes. The additional benefits of efficiency and the lack of dependency on investigative/clinical data and nonspecific gross findings are extremely beneficial when determining if RT-PCR testing is needed. Therefore the characteristic CT findings, if present at triage, can guide the pathologist to test decedents who may not have had severe or typical COVID-19 symptoms, increasing the overall detection of the disease.

Declaration of Competing Interest

None declared.

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