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Atypical Chest Computed Tomography Finding of Predominant Interstitial Thickening in a Patient with Coronavirus Disease 2019 (COVID-19) Pneumonia

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 77-year-old
Final Diagnosis: COVID-19 pneumonia
Symptoms: Cough • shortness of breath
Medication: —
Clinical Procedure: —
Specialty: Radiology

Objective: Challenging differential diagnosis

Background: Coronavirus disease 2019 (COVID-19) is caused by a novel coronavirus, SARS-CoV-2, and is associated with severe respiratory disease. There are extensive publications on the chest computed tomography (CT) findings of COVID-19 pneumonia, with ground-glass opacities (GGO) and mixed GGO and consolidation being the most common findings. Those with interstitial thickening manifesting as reticular opacities typically show superimposed ground-glass opacities, giving a crazy-paving pattern.

Case Report: We report the case of a 77-year-old man with a background of asthma-chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS) who presented with progressive cough and shortness of breath for 2 days. He was in close contact with a confirmed COVID-19 case. Reverse-transcription polymerase chain reaction analysis of a nasopharyngeal swab was positive for SARS-CoV-2. The initial chest radiograph was negative for lung consolidation and ground-glass opacities. During admission, he had worsening shortness of breath with desaturation, prompting a chest CT examination, which was performed on day 14 of illness. The chest CT revealed an atypical finding of predominant focal subpleural interstitial thickening in the right lower lobe. He was provided supportive treatment along with steroid and antibiotics. He recovered well and subsequently tested negative for 2 consecutive swabs. He was discharged after 34 days.

Conclusions: Interstitial thickening or reticular pattern on CT has been described in COVID-19 pneumonia, but largely in association with ground-glass opacity or consolidation. This case demonstrates an atypical predominance of interstitial thickening on chest CT in COVID-19 pneumonia on day 14 of illness, which is the expected time of greatest severity of the disease.

MeSH Keywords: Coronavirus • COVID-19 • Multidetector Computed Tomography

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/926781

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Background

Coronavirus disease 2019 (COVID-19) is caused by a novel coronavirus and is associated with severe respiratory disease and significant morbidity and mortality. The first cluster of reported cases originated from Wuhan, in Hubei province of China, with the causative virus subsequently named SARS-CoV-2 [1,2]. Currently, it is a global pandemic with over 17.6 million confirmed cases and more than 680 000 deaths as of August 2, 2020 [3].

Since the outbreak of COVID-19, there have been many publications discussing the different radiologic manifestations of COVID-19, with a focus on chest CT due to its high sensitivity in depicting subtle changes, especially ground-glass opacities (GGO), in COVID-19 pneumonia. While widely used in the clinical setting for diagnosis and management of COVID-19, chest radiograph and chest CT studies are not currently recommended as first-line investigations for diagnosis of this disease over virology testing, due to non-specificity and overlap of imaging findings with infections and inflammatory lung conditions [4,5]. A confirmatory test using reverse-transcription polymerase chain reaction (RT-PCR) analysis of respiratory samples is still essential for a diagnosis.

The most typical CT imaging features of COVID-19 pneumonia are GGO and mixed GGO and consolidation, with preference for peripheral distribution and bilateral lung involvement [6–10]. Other findings, such as reverse halo sign, crazy-paving pattern, subpleural bands, and airway abnormalities like bronchial wall thickening and bronchiectasis, have been described [6–10]. Crazy-paving pattern, which refers to ground-glass opacities with thickened interlobular septa and intralobular lines, is a less common finding in COVID-19, reportedly seen in 5-36% of cases [11]. Interstitial thickening manifesting as a reticular pattern has been described in COVID-19 pneumonia and is typically superimposed on GGO or consolidation [12–14]. We report a case of COVID-19 pneumonia with an atypical predominant finding of subpleural interstitial thickening on chest CT during the peak disease severity.

Case report

A 77-year-old Chinese man presented to our Emergency Department with progressive cough and shortness of breath on exertion for 2 days. He was epidemiologically linked to a confirmed COVID-19 case at another hospital and was considered to be at risk for COVID-19. RT-PCR of a nasopharyngeal swab (GenXpert system) was performed and showed a

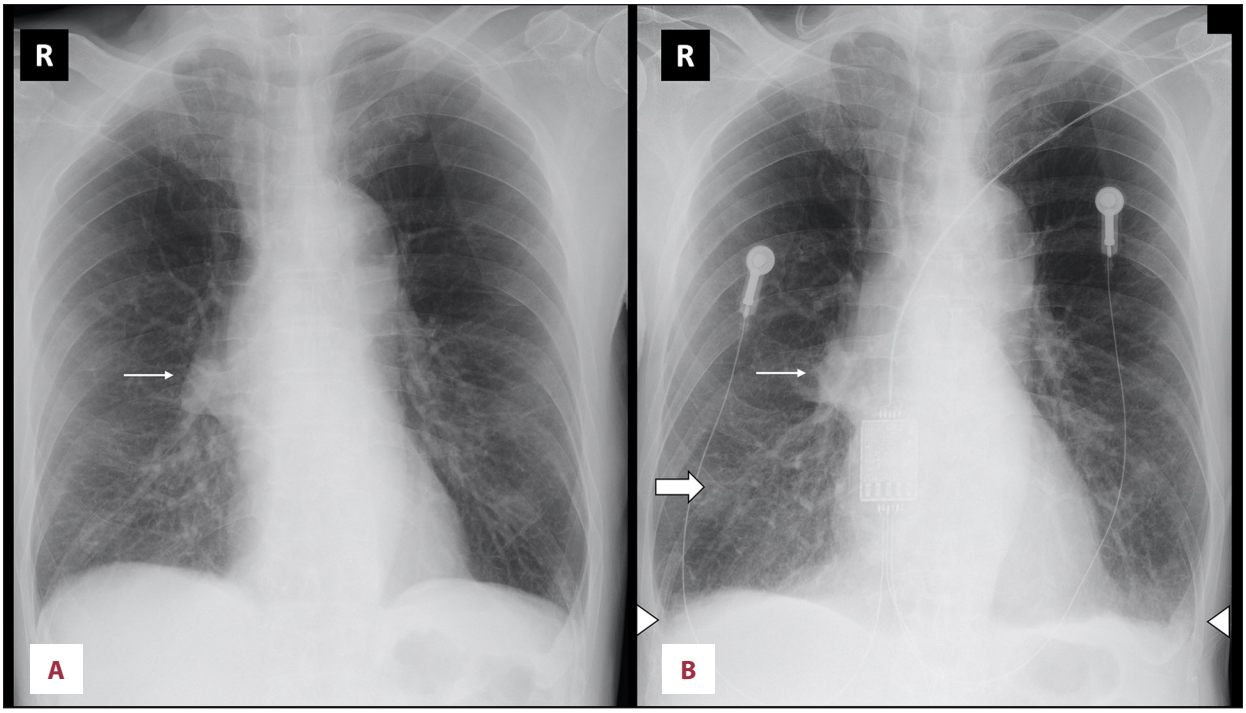

Figure 1. Serial chest radiographs of a 77-year-old man who presented with progressive cough and shortness of breath for 2 days. (**A**) Initial chest radiograph performed on admission showed a right perihilar opacity (thin arrow), in keeping with known chronic middle-lobe collapse of uncertain etiology. There was no ground-glass opacity, consolidation, or pleural effusion. (**B**) A follow-up radiograph performed 10 days later showed interval development of subtle increased reticular opacities in the right lower zone (broad arrow). There were bilateral small pleural effusions (arrowheads).

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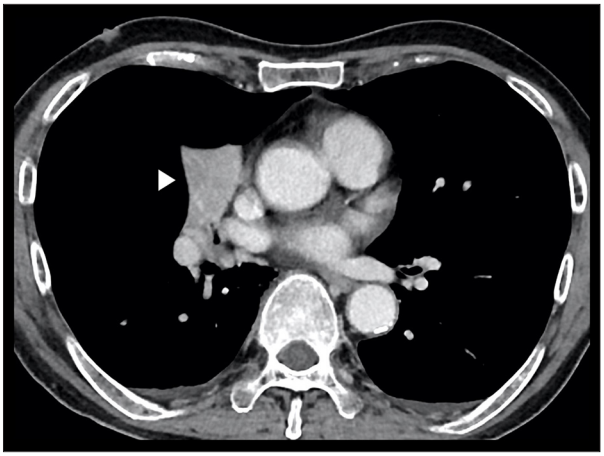

Figure 2. An axial contrast-enhanced CT image of a 77-year-old man who presented with progressive cough and shortness of breath for 2 days. A chronic middle-lobe collapse (arrowhead) is noted, which is probably a long-standing sequelae of prior infection. No associated mass, foreign body, or lymphadenopathy were detected.

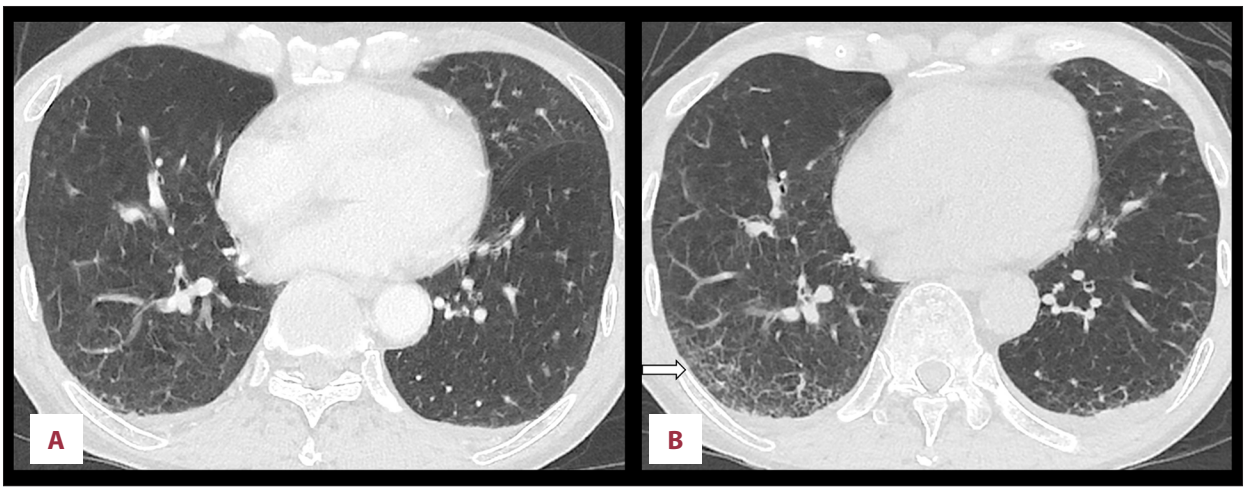

Figure 3. An axial chest CT images of a 77-year-old man who presented with progressive cough and shortness of breath for 2 days, placed side-by-side for comparison. The initial contrast-enhanced CT study (**A**) performed on day 6 of illness onset showed no evidence of ground-glass opacity or consolidation. A repeat plain CT study (**B**) obtained on day 14 of illness onset in view of worsening shortness of breath demonstrated new subpleural interstitial thickening at the posterior aspect of the right lower lobe (arrow). There were also small bilateral pleural effusions.

Figure 4. An axial plain CT image of a 77-year-old man who presented with progressive cough and shortness of breath for 2 days. This was performed on day 14 of illness onset. Subpleural smooth reticular opacities at the posterior aspect of the right lower lobe representing interstitial thickening were demonstrated. There were subtle adjacent ground-glass changes, which may be attributed to atelectasis or inflammation. No lung consolidation was detected, and no bronchiolectasis or peribronchial thickening was seen.

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positive result for SARS-CoV-2. The patient was admitted on the same day. He was isolated and managed in an airborne infection isolation room (AIIR).

The patient was an ex-smoker of 60 pack-years, with a significant background medical history of hypertension, hyperlipidemia, minor coronary artery disease, and asthma-COPD overlap syndrome (ACOS). His vital signs and physical examination were unremarkable. Laboratory results revealed a mild increase in C-reactive protein of 7.0 mg/L; (0.0–5.0 mg/L), eosinophilia of 0.84×10^9/L (0.00–0.60×10^9/L), and mild lymphopenia of 1.00×10^9/L (1.10–3.10×10^9/L). The total white blood cell count was within the normal range.

The initial chest radiography performed on admission was negative for lung consolidation or GGO (Figure 1). There was a right perihilar opacity on radiography (Figure 1) related to a chronic middle-lobe collapse of uncertain etiology (Figure 2). On day 6 of onset of illness, a contrast-enhanced CT thorax was performed to investigate clinical desaturation despite a negative chest radiograph, but the CT scan was negative for lung consolidation and ground-glass opacity (Figure 3). There were also no stigmata of chronic lung disease such as honeycombing (fibrosis) or bronchiectasis. The pulmonary arteries were opacified, with no findings to suggest pulmonary embolism. There was no endobronchial mass causing middle-lobe collapse.

The patient was admitted to the Intensive Care Unit 8 days later, having developed type 1 respiratory failure secondary to COVID-19 pneumonia and presumed exacerbation of ACOS. Worsening shortness of breath associated with a further episode of desaturation warranted a repeat CT thorax on day 14 of illness onset. A plain CT thorax showed a new finding of subpleural interstitial thickening along the posterior aspect of the right lower lobe (Figures 3, 4), and there were subtle adjacent ground-glass changes, possibly due to inflammation or atelectasis. There was no evidence of peribronchial thickening associated with ACOS, nor was there evidence of fluid overload or cardiac failure.

On the same day, the patient was started on off-label anti-retroviral drugs (Lopinavir and Ritonavir) for a period of 4 days, but this was subsequently stopped as he no longer desired to be treated. Supportive treatment along with steroids and antibiotics were the mainstay of treatment during hospitalization. He showed interval improvement in clinical symptoms and tested negative for 2 consecutive swabs before being discharged well after 34 days.

Discussion

Interstitial thickening manifesting as a reticular pattern has been described in COVID-19 pneumonia and is typically superimposed, with GGO or consolidation as the predominant findings [12–14]. Carotti et al. described the presence of GGO and thickened interstitial structures in COVID-19 patients during the intermediate and remission stages of the illness [15]. In the present case, the atypical CT findings of predominant interstitial thickening with subtle ground-glass changes occurred on day 14 after onset of symptoms, just after the expected time of greatest severity of CT change at around 9-13 days, as reported in prior studies [12,16]. The presence of interstitial thickening on CT is related to interstitial infiltrates of lymphocytes, predominantly mononuclear cells [16]. In addition, the CT finding of bilateral pleural effusions is a relatively uncommon imaging feature, typically reported in severe or fatal cases [7].

The imaging findings of subtle interstitial thickening and small bilateral pleural effusions in this patient are discordant with his clinical severity, which required monitoring in the Intensive Care Unit for low oxygen saturation. We believe that his desaturation was partly due to acute exacerbation of asthma-COPD overlap syndrome, but this was not manifested on CT. In ACOS, patients develop emphysematous changes, but to a lesser degree compared to patients with COPD alone [17]. The emphysematous changes in our patient were predominantly in the upper lobes. ACOS patients have been reported to show greater airway thickness and higher pulmonary microvascular density on CT compared to those with COPD alone [18]. Interstitial thickening is not a diagnostic feature in ACOS.

Interstitial lung thickening may be related to a broad list of differential diagnoses. Viral pneumonias can present with interstitial thickening, giving a reticular appearance, as in herpes simplex virus (HSV), cytomegalovirus (CMV), Epstein-Barr virus (EBV) pneumonias, and severe acute respiratory syndrome (SARS) [19,20]. However, it is a rare finding and is also frequently accompanied with airspace disease. CMV and EBV belong to the same Herpesviridae family as HSV, and SARS-CoV and SARS-CoV-2 of COVID-19 also belong to the same Coronaviridae family. Although not seen in all cases, it is interesting to note that there can be imaging pattern similarities on the basis of viridae [19].

Pulmonary edema can manifest with features of pulmonary interstitial edema, like smooth septal thickening, which are often seen with a gravitational or perihilar distribution, but is commonly associated with airspace opacities and pleural effusion [21]. Reticular interstitial thickening can be due to lymphangitic spread of cancer (i.e., lymphangitic carcinomatosis). These, however, often appear more nodular and irregular and less frequently appear as subtle smooth thickening [22,23]. The documented onset of these findings in a short interim of 8 days and the absence of underlying malignancy rule out lymphangitis carcinomatosis. Interstitial thickening can also be

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observed in idiopathic pulmonary fibrosis, non-specific interstitial pneumonia, sarcoidosis [24–26], and rare cases of pulmonary amyloidosis, which otherwise typically present with diffuse reticulonodular thickening [27].

At present, the American College of Radiology, Fleischner Society, and British Society of Thoracic Imaging do not recommend the use of chest radiographs and CT imaging as first-line diagnosis for COVID-19 [4,5,28]. Patients with COVID-19 infection, particularly asymptomatic patients, may have no or few abnormalities on CT; therefore, in these cases, the diagnosis of COVID-19 might be missed without nucleic acid or serologic tests [29,30]. This further emphasizes that CT should not be utilized as a first-line screening tool for detection of COVID-19. There have been documented cases of COVID-19 patients primarily presenting with gastrointestinal symptoms (e.g., diarrhea and abdominal pain) and only mild respiratory symptoms, and this makes early diagnosis of COVID-19 even more challenging for clinicians, especially in patients with unknown epidemiological history and atypical symptoms [31].

CT is, however, indicated for patients who show signs and symptoms of worsening respiratory disease, as it better delineates the extent of the disease and aids prognostication. CT is more sensitive for detection of early parenchymal disease, disease progression, and complications, and provides additional information on conditions such as acute heart failure and pulmonary embolism [32]. However, factors such as limited availability, high costs, exposure to radiation, risk of transmission to uninfected healthcare workers and other patients, and consumption of personal protective equipment (PPE) should also be taken into consideration. It can be argued that for asymptomatic COVID-19 patients, steps such as isolation and recommended antiviral treatment can be implemented without the economic and physical burden on the patient arising from performing a CT scan [30].

In our patient, CT was warranted due to the discordance between CXR with minimal findings and dyspnea requiring supplemental oxygen. Unfortunately, we were not able to obtain histological and microbiological correlation for the chest CT findings via lung biopsy, which might have been able to provide additional information about whether they were due to diffuse alveolar damage, organizing pneumonia, fibrosis, or granulomatous disease. However, this was not clinically indicated, as the patient's condition improved and no further investigation was required. Pleural fluid drainage and culture were not performed as it was attributed to COVID-19 pneumonia and the effusions were small.

Conclusions

This case highlights the atypical predominant CT finding of subpleural interstitial thickening at the expected peak severity of imaging findings of COVID-19. It is significant in that the subtle pulmonary abnormalities on imaging were matched by a disproportionately high degree of respiratory distress. Greater understanding of the pathophysiologic mechanisms in COVID-19 pneumonia may shed light on the unusual imaging manifestation reported in the present case.

Acknowledgement

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Conflicts of interest

None.

References:

1. Zhu N, Zhang D, Wang W et al: A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med, 2020; 328: 727–33
2. Guarner J. Three emerging coronaviruses in two decades. Am J Clin Pathol, 2020; 153: 420–21
3. World Health Organization: Coronavirus disease 2019 (COVID-19) situation report – 195. 2020 Available from: *https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200802-covid-19-sitrep-195.pdf?sfvrsn=5e5da0c5_2*
4. Americal College of Radiology: ACR recommendations for the use of chest radiography and computed tomography (CT) for suspected COVID-19 infection. 2020 Available from: *https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for-Suspected-COVID19-Infection*
5. British Societ of Thoracic Imaging: COVID-19 BSTI statement and guidance. 2020 Available from: *https//www.bsti.org.uk/standards-clinical-guidelines/clinical-guidelines/covid-19-bsti-statement-and-guidance/*
6. Bernheim A, Mei X, Huang M et al: Chest CT findings in coronavirus disease-19 (COVID-19): Relationship to duration of infection. Radiology. 2020: 295: 200463
7. Zhao W, Zhong Z, Xie X et al: Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: A multicenter study. Am J Roentgenol, 2020; 214: 1072–77
8. Zhou S, Wang Y, Zhu T, Xia L: CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. Am J Roentgenol. 2020; 214: 1287–94
9. Zu ZY, Jiang MD, Xu PP et al: Coronavirus disease 2019 (COVID-19): A perspective from China. Radiology, 2020; 296: E15–25
10. Chung M, Bernheim A, Mei X et al: CT Imaging features of 2019 novel coronavirus (2019-nCoV). Radiology, 2020: 295: 202–7
11. Ye Z, Zhang Y, Wang Y et al: Chest CT manifestations of new coronavirus disease 2019 (COVID-19): A pictorial review. Eur Radiol, 2020; 30: 4381–89
12. Shi H, Han X, Jiang N et al: Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: A descriptive study. Lancet Infect Dis, 2020; 20: 425–34
13. Wu J, Wu X, Zeng W et al: Chest CT findings in patients with coronavirus disease 2019 and its relationship with clinical features. Invest Radiol, 2020; 55(5): 257–61

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

14. Song F, Shi N, Shan F et al: Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology, 2020; 295(1): 210–17
15. Carotti M, Salaffi F, Sarzi-Puttini P et al: Chest CT features of coronavirus disease 2019 (COVID-19) pneumonia: Key points for radiologists. Radiol Med, 2020; 125(7): 636–46
16. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology, 2020; 295: 715–21
17. Cosentino J, Zhao H, Hardin M et al: Analysis of asthma-chronic obstructive pulmonary disease overlap syndrome defined on the basis of bronchodilator response and degree of emphysema. Ann Am Thorac Soc, 2016; 13(9): 1483–89
18. Suzuki T, Tada Y, Kawata N et al: Clinical, physiological, and radiological features of asthma-chronic obstructive pulmonary disease overlap syndrome. Int J Chron Obstruct Pulmon Dis, 2015; 10: 947–54
19. Koo HJ, Lim S, Choe J et al: Radiographic and CT features of viral pneumonia. Radiographics, 2018; 38(3): 719–39
20. Franquet T: Imaging of pulmonary viral pneumonia. Radiology, 2011; 260(1): 18–39
21. Storto ML, Kee ST, Golden JA, Webb WR: Hydrostatic pulmonary edema: High-resolution CT findings. Am J Roentgenol, 1995; 165(4): 817–20
22. Ikezoe J, Godwin JD, Hunt KJ, Marglin SI: Pulmonary lymphangitic carcinomatosis: Chronicity of radiographic findings in long-term survivors. Am J Roentgenol, 1995; 165(1): 49–52
23. Johkoh T, Ikezoe J, Tomiyama N et al: CT findings in lymphangitic carcinomatosis of the lung: Correlation with histologic findings and pulmonary function tests. Am J Roentgenol, 1992; 158(6): 1217–22
24. Sverzellati N, Lynch DA, Hansell DM et al: American Thoracic Society-European Respiratory Society Classification of the idiopathic interstitial pneumonias: Advances in knowledge since 2002. Radiographics, 2015; 35(7): 1849–71
25. Grosse C, Grosse A: CT findings in diseases associated with pulmonary hypertension: A current review. Radiographics, 2010; 30(7): 1753–77
26. Cozzi D, Bargagli E, Calabrò AG et al: Atypical HRCT manifestations of pulmonary sarcoidosis. Radiol Med, 2018; 123(3): 174–84
27. Czeyda-Pommersheim F, Hwang M, Chen SS et al: Amyloidosis: Modern cross-sectional imaging. Radiographics, 2015; 35(5): 1381–92
28. Rubin GD, Ryerson CJ, Haramati LB et al: The role of chest imaging in patient management during the COVID-19 pandemic: A multinational consensus statement from the Fleischner Society. Radiology, 2020; 158: 106–16
29. Xu C, Xu Q, Du C et al: Radiological follow-up of twelve COVID-19 patients with initially normal chest CT. Quant Imaging Med Surg, 2020; 10(5): 1153–57
30. Zeng Y, Fu J, Yu X et al: Should computed tomography (CT) be used as a screening or follow-up tool for asymptomatic patients with SARS-CoV-2 infection? Quant Imaging Med Surg, 2020; 10(5): 1150–52
31. Tang L, Cheng X, Tian C et al: Computed tomography (CT) intestinal alterations of Coronavirus Disease 2019 (COVID-19) from the imaging perspective: A case description. Quant Imaging Med Surg, 2020; 10(5): 1145–49
32. Driggin E, Madhavan MV, Bikdeli B et al: Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. J Am Coll Cardiol, 2020; 75: 2352–71

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