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Case Report

Pseudocavitation sign at chest CT scan due to COVID-19 pneumonia: A report of 5 cases and literature review $^{a, \star \pm}$

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ABSTRACT

Coronavirus disease 2019 (COVID-19) pneumonia computed tomography imaging features have been described in detail in many studies. The pseudocavitation sign has not been described in the previous COVID-19 studies. We present chest computed tomography scans of 5 reverse transcriptase-polymerase chain reaction positive patients with COVID-19 pneumonia who has bare areas among pulmonary infiltrates. All 5 also had previous scans with similarly sized low attenuated areas in the same location prior to the addition of pulmonary infiltrates. The pre-existing cystic changes had become remarkable due to the contrast around them after the pulmonary infiltrates added. Therefore, they should be termed as "pseodocavity" according to Fleischner Society glossary. Small air-containing spaces between pulmonary infiltrates have been termed in previous COVID-19 studies as a new sign called "round cystic changes/air bubble sign/vacuolar sign." We would like to draw attention that the vacuolar sign and the synonyms may be the pseudocavity sign that is due to pre-existing changes rather than a new defined sign.

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Introduction

An outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection occurred in China. In February 2020,

World Health Organization (WHO) officially named the novel coronavirus disease as coronavirus disease 2019 (COVID-19) [1]. WHO on March 11, 2020 has declared the COVID-19 outbreak a global pandemic [2]. Chest computed tomography (CT) had an important role in describing and differentiating

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Abbreviations: COVID-19, novel coronavirus disease 2019; GGO, ground-glass opacification; RT-PCR, reverse transcriptase-polymerase chain reaction; ICU, intensive care unit; CT, computed tomography; WHO, World Health Organization; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ER, emergency room.

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inding of COVID-19 pheumonia.					
Publication data (chronologically)	Methodology	Author [Ref. No.]	Total number of CT scans	Manifestation	Term
Feb 2020	Case series	Kong et al. [9]	3	1 (33.3%)	Cavity
Feb 2020	Original research	Shi et al. [7]	81	8 (10%)	Round cystic changes
Feb 2020	Original research	Yang et al. [13]	149	12 (8%)	Cystic change
Feb 2020	Original research	Cheng et al. [14]	11	1 (9.1%)	Cystic change
April 2020	Original research	Wang et al. [15]	93	7 (7.5%)	Cavity sign
June 2020	Original research	Zhou et al. [11]	62	34 (45.2%)	Vacuolar sign
April 2020	Original research	Lomoro et al. [16]	42	None (0%)	Vacuolar sign
July 2020	Original research	Zhu et al. [17]	72	36 (50%)	Vacuolar sign
July 2020	Original research	Cinkooglu et al. [18]	147	15 (10.2%)	Air bubble sign
Dec 2020	Original research	Zhang et al. [12]	34	6 (17.65%)	Intralesional vacuole sign
Oct 2020	Original research	Tekcan Sanli et al. [19]	102	2 (2%)	Vacuolar sign (air bubble sign)
Oct 2020	Original research	Zhou et al. [20]	100	149 (54.8%)	Vacuolar sign
Oct 2020	Research letter	Rodrigues et al. [21]	43	13 (30.2%)	Cystic airspace

Table 1 – Summary table of studies evaluating small bare areas among pulmonary infiltrates observed as a chest imaging finding of COVID-19 pneumonia.

COVID-19 pneumonia and appears to be a sensitive imaging modality. The findings in the scans were similar to the other viral pneumonias [3,4]. Chest CT findings of COVID-19 pneumonia were reported as ground-glass opacification (GGO), mixed GGO with interlobular septation, consolidation or linear densities, reverse halo sign, bronchial wall thickening, arcade-like pattern, bronchiectasis, and CT halo sign [5-8]. The vacuolar sign and the synonyms (cavity, cystic changes, and air bubble sign) were reported as COVID-19 pneumonia CT scan feature of unknown pathophysiology (Table 1) [9-22]. We present 5 cases of reverse transcriptase-polymerase chain reaction positive patients with COVID-19 pneumonia who had bare areas (pseudocavities) among pulmonary infiltrates in their CT scans. They had previous scans with emphysematous/cystic changes or low attenuated areas in the same location.

All scans were performed in a single center on 2 CT devices in a single center. ([Aquilion Lightning, Canon Medical Systems, 16-row 32 slice helical CT; 5 mm slice thickness, 120 kVp, 100 mAs, noncontrast CT] and [GE Optima CT660, 128-slice CT scanner;1.3 mm slice thickness, 120 kVp, 100 mAs, noncontrast CT]).

Case descriptions

Case 1

The first patient was a 72-year-old male with a history of recent travel to Spain 10 days ago in March 2020. He had been complaining of fever and cough for a week. In the initial CT scan, there were peripherally distributed insignificant GGOs in the lower lobes. There were also peripherally distributed thin-walled cystic changes that are not related with the pneumonia in the upper lobes (Figs. 1a and c). The follow-up scan on the 17th day of the onset of the illness showed involvement of all 5 lobes with consolidation in the upper lobes. The pre-existing cystic changes had become remarkable due to the contrast around them. The pseudocavities were seen as small cystic lakes among the areas of consol-

idation (Figs. 1b and d). He was discharged after a 17-day hospitalization.

Case 2

The second patient was a 65-year-old male complaining of fever for a day. He had the initial CT scan on the first day of the disease and the follow-up scans on the fourth and ninth days. The initial scan showed a few insignificant GGOs in the right lower lobe (Figs. 2a and d). On the first followup scan multifocal GGOs located peripherally were noted. On the second follow-up scan on the ninth day, GGOs were enlarged and merged forming diffuse GGOs located peripherally. Among the GGOs small low-attenuated areas (pseudocavity) were recorded (Figs. 2b and e). When the initial scan was reevaluated, it was noted that there were already small thinwalled low-attenuated insignificant areas in the same location (Figs. 2a and d). He was discharged after an 11-day hospitalization.

A third CT scan was performed when the patient was admitted to the hospital again due to cough 5 months after discharge. In the scan, GGOs were observed to have almost completely regressed and pseudocavitation areas were seen as barely distinguishable air spaces, similar to imaging before COVID involvement (Figs. 2c and f).

Case 3

The third patient was a 72-year-old male who visited the emergency room (ER) complaining of fever and coughing in April 2020. He had gastric cancer and had undergone gastric surgery 15 days ago. The thoracoabdominal CT scan before the surgery showed emphysematous changes in lung parenchyma, especially located peripherally, in the subpleural areas without the features of pulmonary infiltrates (Fig. 3a). The chest scan on the day of admission had pneumonia manifestations. There was bilateral lung involvement including marked cystic areas (pseudocavitations) among the consolidation (Fig. 3b). Bilateral pleural effusion was also recorded. He required admission to intensive care unit (ICU) on the fourth

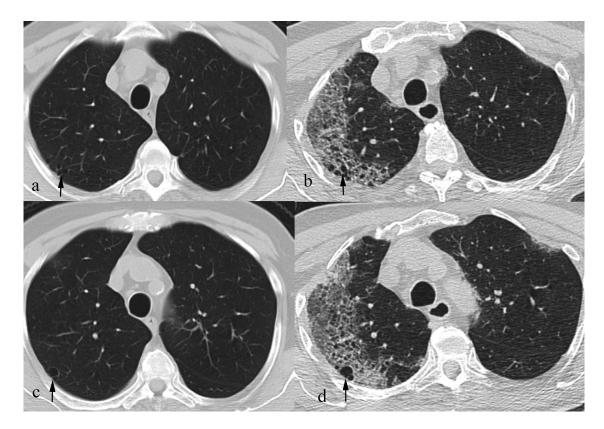


Fig. 1 – 72-year-old male patient with COVID-19 pneumonia. Findings: (a, c) Initial scans showing thin walled-cystic changes (arrow) on the right lung without signs of pneumonia on the 7th day of the onset of the illness. (b, d) Follow-up scan 17 days later showed added pneumonia features bilaterally with pseudocavities (arrow) as low-attenuated cystic areas among consolidation.

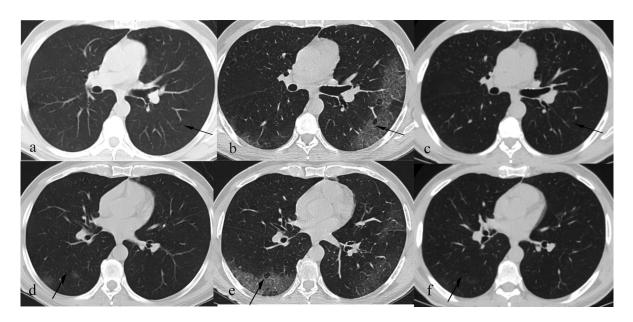


Fig. 2 – 65-year-old male patient with COVID-19 pneumonia. Findings: (a, d) Initial scan without pneumonia features showing insignificant low-attenuated areas (arrow) in right lower lobe. (b, e) Follow-up scan on the ninth day of the illness pointing the pseudocavities (arrow) among the diffuse peripherally located GGO on the right and left lower lobes. (c, f) The third CT scan 5 months after discharge of the patient showing regressed GGOs and barely distinguishable air spaces (arrow), similar to imaging before COVID involvement.

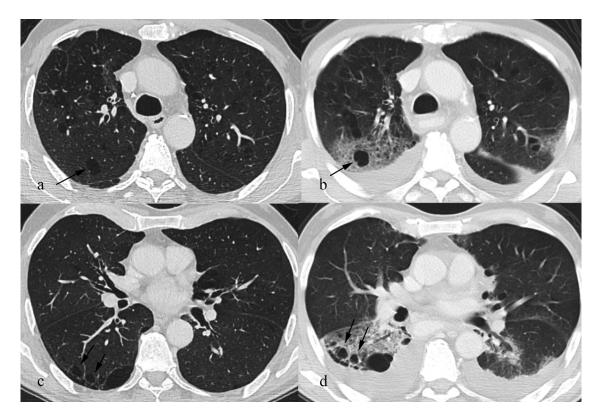


Fig. 3 – 72-year-old male patient with COVID-19 pneumonia. Findings: (a, c) CT scan showing emphysematous and cystic pulmonary changes before the pneumonia features added. (b, d) Second chest scan taken 15 days later showing bilateral lung involvement with marked pseudocavities (arrow) among the consolidation.

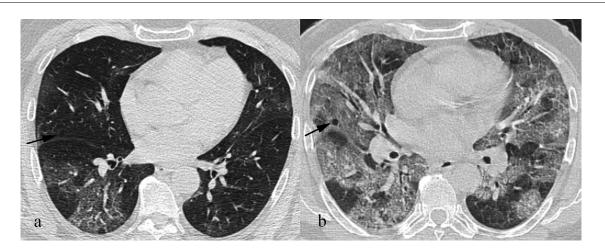


Fig. 4 – 63-year-old male patient with COVID-19 pneumonia. Findings: (a) CT scan showing lucent area among normal lung parenchyma. (b) Second chest scan taken 8 days later showing a spare area (arrow) among the GGO.

day of hospitalization. He had also accompanying gastrointestinal problems (abscess) and died after an 8-day hospitalization in the ICU.

Case 4

The fourth patient was a 63-year-old male who visited the ER complaining of coughing for 14 days in March 2020. There were patchy GGOs on all 5 lobes in the initial CT scan (Fig. 4a). He

had the second chest scan 8 days later when he complained of shortness of breath. The follow-up scan showed consolidation within enlarged and merged GGOs. On the right middle lobe, there was a spare area (pseudocavitation) within the GGOs (Fig. 4b). When the initial scan was re-examined, it was noted that there was already a small area more lucent than peripheric lung tissue (Fig. 4a). He was transferred to another hospital's ICU after 10-day hospitalization and died 13 days later in the ICU.

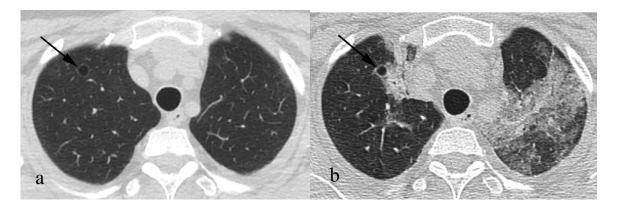


Fig. 5 – 43-year-old female patient with COVID-19 pneumonia. Findings: (a) CT scan showing thin walled cyst among normal lung parenchyma. (b) Second chest scan taken 20 days later showing a pseudocyst (arrow) among the consolidation.

Case 5

A 43-year-old female patient with a history of asthma and rheumatoid arthritis visited ER complaining of a cough. The initial CT scan showing thin-walled cyst within normal lung parenchyma on the right upper lobe, which did not have the pulmonary infiltrates (Fig. 5a), and she was not hospitalized. She applied to the ER again with the complaint of a cough that would not go away, but had gotten worse. A follow-up chest scan (Fig. 5b) taken 20 days later showed consolidation within GGOs in all lobes. The cyst in the initial scan on the right upper lobe was seen as a pseudocyst among the consolidation in the control scan. She was transferred to another hospital's ICU after 7-day hospitalization. She died on the 13th day of hospitalization in ICU.

Discussion

The CT findings of COVID-19 pneumonia were reported in detail in the previous studies [5,6,8]. CT manifestations of COVID-19 resemble those seen in viral pneumonias [3,4]. In previous studies, the low attenuated spaces among consolidated areas were reported in different names as cavity [9], round cystic change [7], air bubble sign [10], or vacuolar/intralesional vacuole sign [11,12] in COVID-19 pneumonia (Table 1) [7,9,11-21]. The pathophysiology of these cystic changes in areas of infiltrates remains unclear. Shi et al. [7] described round cystic changes in 10% of patients and suggested that they might be associated with the process of resorption of consolidation which might be explained by the infection causing damage to the alveolar walls and leading to pneumatoceles. Ye et al. [10] referred these small air containing spaces as air bubble sign and suggest that they might be the pathological dilation of a physiological space or a cross section of the bronchiolectasis, or associated with the process of consolidation resorption. Zhou et al. [11] was the first authors referring to as the vacuolar sign. They described as a vacuole-like transparent shadow of <5 mm in length observed in the lesion. They reported 45.2% of the patients' scans show vacuole sign, and observed vacuolar sign often in the advanced phase of COVID-19

pneumonia (8-14 days after symptom onset), associated with interstitial involvement and accompanied by repair changes. In their later study, the same group suggested that the vacuolar sign might be due to the inhomogeneous involvement and incomplete filling of alveoli and it was characteristic especially during the advanced stage [20]. Zhang et al. [12] reported the intralesional vacuole sign in 17.65% of the patients in their study and mentioned that it might be the dilation of alveolar ducts and alveolar sac, indicating the alveolar destruction and onset of fibrosis and also argued that it could be a feature of the progressive stage. Zhu et al. [17] mentioned that young group showed the vacuolar sign 21%, while elderly group had 15%. Cinkooglu et al. suggested that air bubbles could not be seen easily on the source images, and that might be the reason for the relatively low rate [18]. Rodrigues et al. [21] mentioned that 30.2% patients presented cystic changes; 11.6% patients had cystic airspaces only in the subpleural region and along the peribronchovascular interstitium; and 18.6% had cystic airspaces admixed with areas of opacity in the lung parenchyma. There was a difference in the frequency of these changes among studies (Table 1) [7,9,11-21].

Cavities are described as the gas-filled spaces or lowattenuation areas within consolidations that appear as a solution of the drainage of a necrotic part of the lesion [23]. During the course of the disease, cavitation can develop in viral pneumonias [24]. But the small bare areas among pulmonary infiltrates in the presented case series were already in the area before consolidation or GGO occurred.

According to Fleischner Society, pseudocavity is a term used to describe small lakes or vacuoles among masses or consolidation areas. Pseudocavity represents spared parenchyma, normal or ectatic bronchi, or focal emphysema rather than cavitation. It was described in patients with some malign disease as well as some benign conditions as infectious pneumonia [12]. The case series we presented had emphysematous or cystic changes in the initial scans. Although these cystic areas remained the same in size and shape, they became more prominent due to the contrast in the surrounding consolidated areas after pulmonary infiltration was added.

Pseudocavity was described in other viral pneumonias as influenza A (H5N1) [3,4,24]. The initial imaging findings

of COVID-19 pneumonia are not organism specific and can overlap with H1N1 influenza, cytomegalovirus pneumonia, and other atypical pneumonias [8]. Studies have shown that the advanced phase signs in scans were also similar to the other pneumonias [6,25]. Therefore, we suggest that COVID-19 pneumonia is not expected to be organized differently from all known pneumonias.

In the previous studies similar cystic changes seen among consolidations were discussed to be a result of resorption of consolidation or alveolar destruction as a feature of the progressive stage. Our data indicate that it is not possible to decide on the pathogenesis of such changes observed in pneumonia, without the knowledge of pre-existing pathological changes in the lungs.

Conclusion

The purpose of presenting and terming these changes is to draw attention since the so-called vacuolar sign and the synonyms described in COVID-19, may be due to preexisting emphysematous changes/focal areas of air trapping due to chronic small airway disease, rather than due to a postulated theory of resolution of opacities/focal sparing/due to bronchiolar destruction.

Notation of prior abstract/presentation

Poster Presentation: 41th Turkish Radiology Congress, October 24–November 1, 2020, Antalya/Turkey.

Patient consent

This study was approved by the Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (Approval Number: HNEAH-KAEK 2020/99). All patients were diagnosed and treated in Haydarpasa Numune Training and Research Hospital.

Availability of supporting data

All data available upon request.

Human and animal rights

This study was approved by the Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (Approval Number: HNEAH-KAEK 2020/99) and the Republic of Turkey Ministry of Health, COVID-19 Scientific Research Committee.

Authors' contributions

E. Gurdal Kosem conceived of the presented idea and wrote the manuscript. R. Balik followed-up the patients and arranged their treatment in the clinic. E. Gurdal Kosem collected the scans and commented on them. Both authors give final approval of the version to be submitted and any revised version.

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REFERENCES

- WHO. Novel coronavirus—China. 2020. Available at: http://www.who.int/csr/don/ 12-january-2020-novel-coronavirus-china/en/ (Accessed January 19, 2020)
- [2] Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed 2020;91(1):157–60 PMID: 32191675; PMCID: PMC7569573. doi:10.23750/abm.v91i1.9397.
- [3] Koo HJ, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral pneumonia. Radiographics 2018;38(3):719–39 PMID: 29757717. doi:10.1148/rg.2018170048.
- [4] Franquet T. Imaging of pulmonary viral pneumonia. Radiology 2011;260(1):18–39 PMID: 21697307. doi:10.1148/radiol.11092149.
- [5] Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH, Chung M, et al. Radiological Society of North America Expert Consensus Statement on reporting chest CT findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA - Secondary Publication. J Thorac Imaging 2020;35(4):219–27 PMID: 32324653; PMCID: PMC7255403. doi:10.1097/RTI.00000000000524.
- [6] Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. AJR Am J Roentgenol 2020;215(1):87–93 Epub 2020 Mar 14. PMID: 32174129. doi:10.2214/AJR.20.23034.
- [7] Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020;20(4):425–34 doi: 10.1016/S1473-3099(20)30086-4. Epub 2020 Feb 24. PMID: 32105637; PMCID: PMC7159053.
- [8] Rodrigues JCL, Hare SS, Edey A, Devaraj A, Jacob J, Johnstone A, et al. An update on COVID-19 for the radiologist—a British Society of Thoracic Imaging statement. Clin Radiol 2020;75(5):323–5 Epub 2020 Mar 23. PMID: 32216962; PMCID: PMC7138157. doi:10.1016/j.crad.2020.03.003.
- Kong W, Agarwal PP. Chest imaging appearance of COVID-19 infection. Radiol Cardiothorac Imaging 2020;2(1):e200028. doi:10.1148/ryct.2020200028.
- [10] Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol 2020;30(8):4381–9 doi: 10.1007/s00330-020-06801-0. Epub 2020 Mar 19. PMID: 32193638; PMCID: PMC7088323.

- Zhou S, Wang Y, Zhu T, Xia L. CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. AJR Am J Roentgenol 2020;214(6):1287–94 Epub 2020 Mar 5. PMID: 32134681. doi:10.2214/AJR.20.22975.
- [12] Zhang L, Kong X, Li X, Zhu J, Liu S, Li W, et al. CT imaging features of 34 patients infected with COVID-19. Clin Imaging 2020 Epub ahead of print. PMID: 32425337; PMCID: PMC7229931. doi:10.1016/j.clinimag.2020.05.016.
- [13] Yang W, Cao Q, Qin L, Wang X, Cheng Z, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. J Infect 2020;80(4):388–93. doi:10.1016/j.jinf.2020.02.016.
- [14] Cheng Z, Lu Y, Cao Q, Qin L, Pan Z, Yan F, et al. Clinical features and chest CT manifestations of coronavirus disease 2019 (COVID-19) in a single-center study in Shanghai, China. AJR Am J Roentgenol 2020;215(1):121–6 Epub 2020 Mar 14. PMID: 32174128. doi:10.2214/AJR.20.22959.
- [15] Wang J, Xu Z, Wang J, Feng R, An Y, Ao W, et al. CT characteristics of patients infected with 2019 novel coronavirus: association with clinical type. Clin Radiol 2020;75(6):408–14 Epub 2020 Apr 7. PMID: 32327229; PMCID: PMC7138387. doi:10.1016/j.crad.2020.04.001.
- [16] Lomoro P, Verde F, Zerboni F, Simonetti I, Borghi C, Fachinetti C, et al. COVID-19 pneumonia manifestations at the admission on chest ultrasound, radiographs, and CT: single-center study and comprehensive radiologic literature review. Eur J Radiol Open 2020;7:100231 Epub 2020 Apr 4. PMID: 32289051; PMCID: PMC7129441. doi:10.1016/j.ejro.2020.100231.
- [17] Zhu T, Wang Y, Zhou S, Zhang N, Xia L. A comparative study of chest computed tomography features in young and older adults with coronavirus disease (COVID-19). J Thorac Imaging 2020;35(4):W97–W101 PMID: 32235187; PMCID: PMC7253040. doi:10.1097/RTI.00000000000513.

- [18] Çinkooğlu A, Hepdurgun C, Bayraktaroğlu S, Ceylan N, Savaş R. CT imaging features of COVID-19 pneumonia: initial experience from Turkey. Diagn Interv Radiol 2020;26(4):308–14 PMID: 32558645; PMCID: PMC7360080. doi:10.5152/dir.2020.20307.
- [19] Tekcan Şanlı DE, Yıldırım D. A new imaging sign in COVID-19 pneumonia: vascular changes and their correlation with clinical severity of the disease. Diagn Interv Radiol 2021;27(2):172–80 PMID: 33044171; PMCID: PMC7963372. doi:10.5152/dir.2020.20346.
- [20] Zhou S, Zhu T, Wang Y, Xia L. Imaging features and evolution on CT in 100 COVID-19 pneumonia patients in Wuhan, China. Eur Radiol 2020;30(10):5446–54 Epub 2020 May 4.
 PMID: 32367418; PMCID: PMC7197364.
 doi:10.1007/s00330-020-06879-6.
- [21] Rodrigues RS, Barreto MM, Werberich GM, Marchiori E. Cystic airspaces associated with COVID-19 pneumonia. Lung India 2020;37(6):551–3 PMID: 33154225; PMCID: PMC7879870. doi:10.4103/lungindia.lungindia_551_20.
- [22] Urciuoli L, Guerriero E. Chest CT findings after 4 months from the onset of COVID-19 pneumonia: a case series. Diagnostics (Basel) 2020;10(11):899 PMID: 33152991; PMCID: PMC7693123. doi:10.3390/diagnostics10110899.
- [23] Hansell DM, Bankier AA, MacMahon H, McLoud TC, Müller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology 2008;246(3):697–722 Epub 2008 Jan 14. PMID: 18195376. doi:10.1148/radiol.2462070712.
- [24] Qureshi NR, Hien TT, Farrar J, Gleeson FV. The radiologic manifestations of H5N1 avian influenza. J Thorac Imaging 2006;21(4):259–64 PMID: 17110849. doi:10.1097/01.rti.0000213573.94032.53.
- [25] Baque-Juston M, Pellegrin A, Leroy S, Marquette CH, Padovani B. Organizing pneumonia: what is it? A conceptual approach and pictorial review. Diagn Interv Imaging 2014;95(9):771–7 Epub 2014 Feb 18. PMID: 24559802. doi:10.1016/j.diii.2014.01.004.