Imaging the COVID-19: a practical guide

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Abstract

The Coronavirus Disease 2019 (COVID-19) represents the first medical catastrophe of the new millennium. Although imaging is not a screening test for COVID-19, it plays a crucial role in evaluation and follow-up of COVID-19 patients. In this paper, we will review typical and atypical imaging findings of COVID-19.

Introduction

The Coronavirus Disease 2019 (COVID-19) represents the first medical catastrophe of the new millennium. COVID-19 initially presented in China, in the Wuhan area, Hubei province, at the end of 2019, and quickly spreads around the globe because of its easy human-to-human transmission, hospital infection, and international air travel [1-4]. At the time of this writing, more than 34 million confirmed cases, and more than one million of deaths were reported globally by the World Health Organization (WHO) [5]. COVID-19 is due to an aggressive, highly contagious, betacoronavirus that involves mainly the respiratory system. Fever, dry cough, and dyspnea are the most common symptoms, while rhinorrhea and sneezing are less frequent [6]. This suggests that the target cells are preferentially located in the lower airways [6]. Less frequently, patients present central nervous system or gastrointestinal symptoms [6]. The absence of clinical symptoms was reported in approximately 50% of patients at the time of first diagnosis [7].

Individuals with old age, obesity, or other comorbidities are at increased risk to develop pneumonia, acute respiratory distress syndrome, and multiorgan failure suggesting that COVID-19 pathogenicity can depend on patient immune response [8,9]. Because of the absence of proven drugs and vaccines, early diagnosis, timely treatment, and immediate patient isolation are the pillars for containing the infection. The gold standard for diagnosis is positive results of real-time reverse transcription–polymerase chain reaction (RT-PCR) test of swabs taken from the nasopharynx and/or oropharynx [3,10]. However, a high rate of false-negative RT-PCR results is reported due to multiple causes, such as insufficient cellular material for detection and improper extraction of nucleic acids from clinical materials [11,12]. This leads to a delay in diagnosis and treatment, and a spread of the disease. Imaging can flag suspicious cases and alert referring physicians. In this paper we review the role of imaging in COVID-19 patients.

Chest findings

Chest CT is the main imaging methodology for detecting pulmonary involvement and optimized the future treatment because of high sensitivity and speed [13-15]. Although CT is not a screening test for COVID-19, it is strongly recommended for initial evaluation and follow-up of COVID-19 positive patients and to exclude other disease conditions, which can be treated (*e.g.*, pulmonary embolism) [10,16,17]. Other imaging tests such as chest radiography (CXR) and lung ultrasound (LUS) are not routinely recommended in clinal practice.

CXR has low sensitivity for the detection of COVID-19 pneumonia in early and mild stages [8]. Currently, CXR is indicated in severe and critical COVID-19 patients, which require bedside exam, and in resource-constrained environments [18].

LUS has been proposed as an alternative tool to quickly assess lung injury. LUS can identify alteration in subpleural regions, which represents the typical COVID-19 locations [19]. Similar to CXR, LUS has some utility in bedside in critical patients [20]. Almost all COVID-19 confirmed patients show typical CT features including bilateral ground glass opacities (GGO), consolidation, vascular enlargement, and crazy-paving pattern. Most abnormalities are bilateral and involve more segments with a predomi-

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nant peripheral and posterior distribution and a slight predominance of lower lobes [21,22]. During the course of disease nodule, reversed halo sign, pleural changes, pericardial effusion, and enlargement of hilar and mediastinal lymphadenopathies can also occur. Infection control and regression of CT abnormalities can lead to tissue organization and fibrosis [23,24]. Extra-pulmonary abnormalities are absent in early stages and can occur in severe type of disease [24]. Unfortunately, CT findings of COVID-19 are not specific and overlap with those of other viral and not viral pneumonia [22,25-27]. Moreover, CT features are not always consistent with the clinical stage. Specifically, some asymptomatic patients can show typical CT features and some patients with clinically severe disease can show normal CT [28].

Ground glass opacity

GGO represents the most common CT finding in COVID-19 patients, with a reported incidence of 49 to 94% [29]. GGO is an area of increased attenuation with the preservation of bronchial and vascular margins [30]. In the context of COVID-19, GGO results from by partial filling of airspaces and interstitial thickening [30]. Three patterns of GGO have been described: pure GGO, GGO with superimposed intra and interlobular septal thickening (“crazy paving”), and GGO with consolidation [22] (Figure 1). Different patterns can often be seen simultaneously in the same patient [22]. Pure GGO and GGO with consolidation are the most common patterns in early stage of the disease [23,24]. Of note, GGO with peripheral distribution and unilateral location is the most common abnormality in asymptomatic (so called covert transmitter), patients.

Consolidation

Consolidation is a patchy area of increased attenuation, which renders the lung solid (Figure 2) [30]. Unlike GGO, the filling of airspaces is complete and obscures totally bronchial and vascular margins [30], suggesting disease progression [22]. Air bronchograms within the consolidation can often be found. Consolidation is reported in 11 to 73% of patients [21], and is seen much more frequently in the elderly than in young patients [22]. Its presence is rare in early-stage and typically occurs in progressive and peak stages [23]. Multiple consolidations are the most common imaging features in the intensive care unit patients [31].

Crazy paving pattern

Crazy paving pattern is defined as a GGO with superimposed thickened intra- and inter-lobular septa (Figure 1C) [30]. The latter is due to lymphocyte infiltration of small interstitium [32,33]. It occurs in 5% to 43% of patients [23,24]. Crazy paving pattern is a common finding in progressive and peak stage of the disease [23].

Vascular enlargement

Vascular enlargement refers to a segmental or subsegmental pulmonary artery with a diameter >3 mm in GGO and consolidation areas (Figure 3). It is a common finding in COVID-19 patients and was reported in 70 to 90% of patients [15, 35,36]. This finding is probably related to three processes, in isolation or varying combinations: hyperemia induced by acute inflammatory reaction; small pulmonary embolism, and COVID-19 induced vasculitis [36]. Since this sign was not described in other pneumonia, it may be useful to the identify COVID-19 [36].

Reversed halo sign

The reversed halo sign (also called atollo sign) refers to a central round or half-moon shape GGO surrounded by a complete or partial ring-like area of consolidation (Figure 4) [30].

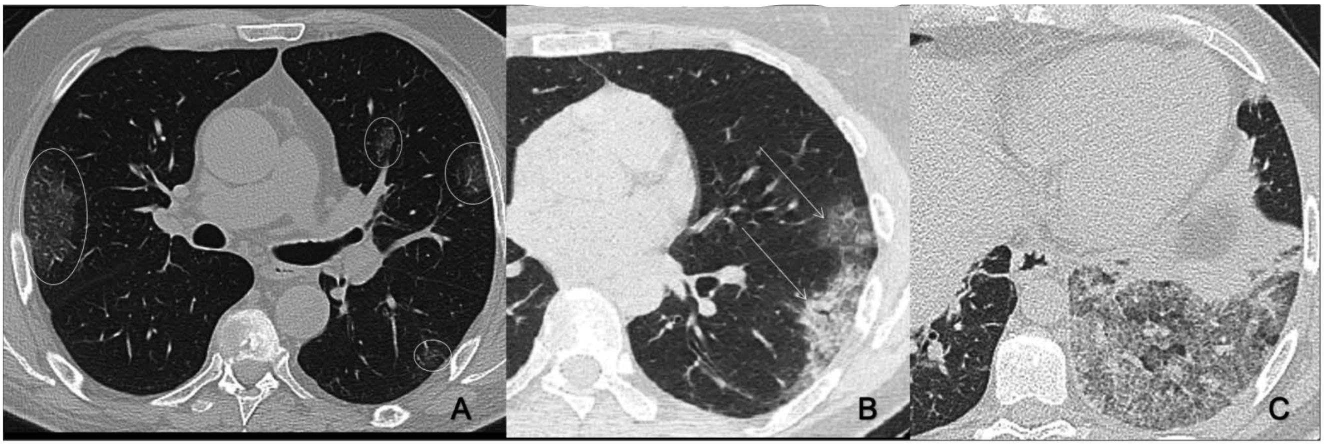

Figure 1. GGO patterns. A) Axial unenhanced CT image obtained in a 66-year-old male shows multiple bilateral patchy ground glass opacities (circles) with predominantly peripheral distribution. B) Axial unenhanced CT image obtained in a 50-year-old female shows ground glass opacities with consolidation in the lower left lung lobe and in the lingula. C) Axial CT image obtained in a 68-year-old female shows a marked crazy paving in the left lower lung lobe.

The pathological responsible mechanism is the inflammatory reaction, which leads to alveolar septal thickening and cellular debris in the alveoli [37]. This sign is extremely rare in COVID-19 patients. Bernheim *et al.* reported its presence in approximately 2% in a series of 121 patients [34]. The detection of this sign can suggest a progression from GGO to consolidation or an inflammatory repair [34,38].

Nodule

A discrete nodule is a rounded opacity, measuring less than 3 cm in diameter (Figure 5A) [30]. A pure solid nodule is a rare finding in COVID-19 patients. More frequently, a nodule is surrounded by a peripheral halo of GGO, due to diffuse progressive alveolar damage ("halo sign") (Figure 5B) [33,39,40]. The halo sign is typically described in early-stage of disease [15,33-40].

Fibrosis

Fibrosis is a dysregulated repair process to an inflammatory reaction [41]. In case of COVID-19 pneumonia, alveolar epithelial injury can activate fibroblasts and myofibroblasts to repair the damage resulting in lung fibrosis and irreversible injury [32,41]. Fibrosis and strip-like lesions can cause bronchial traction and consequent bronchus irreversible distortion (*i.e.*, bronchiectasis) (Figure 6) [42].

Subpleural curvilinear line

A subpleural curvilinear line is a curvilinear opacity, 1-3 mm in thickness, parallel to the pleural surface (Figure 7). It may occur for a supine position or may reflect edema or fibrosis process [30].

This finding is reported in approximately 10% of asymptomatic patients and probably is due to edema or fibrosis [42,43]. When it is found in the dependent, posteroinferior portion of the lung, atelectasis is the most likely cause [30].

Pleural changes

Pleural effusion and pleural thickening more frequently occur in severe COVID-19 patients (Figure 8) [43,44]. In a large meta-analysis, Zhu *et al.* have reported pleural thickening in 27.1% of patients and pleural effusion in 5.3% of patients [45]. Pleural inflammatory reaction can be due to inflammation spread from subpleural lesions and septa [46]. Pleural effusion can also be related to fluid overload due to prior cardiac or renal disease [44].

Hilar and mediastinal lymphadenopathy

Hilar or mediastinal lymphadenopathy is a lymph node with a short axis greater than 1 cm (Figure 9) [30]. It is a rare finding and occurs in severe disease [35,43].

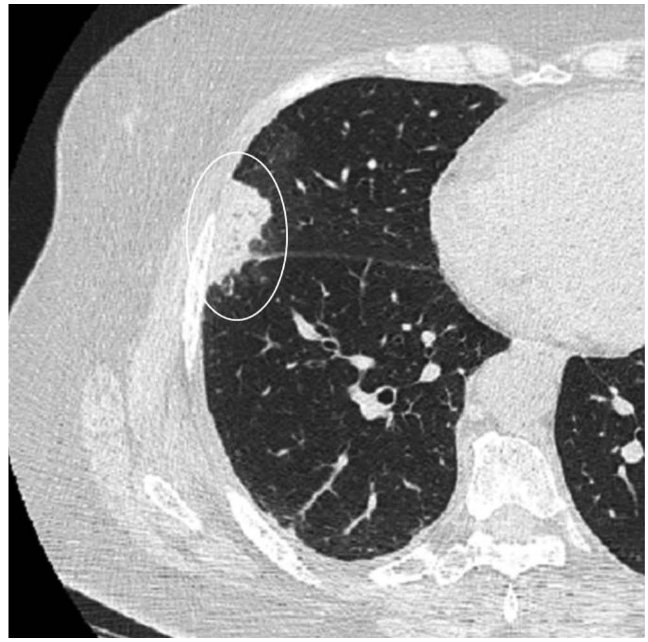

Figure 2. Axial CT image obtained in a 50-year-old female COVID-19 patient shows a subpleural consolidation area (circle) in middle and lower lung lobes.

Figure 3. Axial contrast-enhanced CT image obtained in a 33-year-old female COVID-19 patient shows vascular enlargement due to a thrombus (arrow) in a large consolidation area (asterisk).

Figure 4. Axial CT image obtained in a 23-year-old female COVID-19 patient shows a ground glass area surrounded by a ring-like consolidation area (circle) in the peripheral right lower lobe (reversed halo sign).

Pericardial effusion

Pericardial effusion is rare and suggests a severe condition (Figure 8) [35,43]. Of note, the concomitant presence of lymphadenopathies, pleural effusion, and extensive tiny lung nodules raise suspicion of bacterial superinfection [47].

Abdominal findings

Abdominal manifestations, including gastrointestinal (GI) symptoms (*e.g.*, diarrhea and vomiting) and abnormal liver function are not uncommon and usually occur in severe stage of COVID-19 [48]. Isolated abdominal manifestations at presentation (*i.e.,* without respiratory symptoms) are less frequent [48]. In a meta-analysis including 6064 patients, Mao *et al.* have found GI symptoms in 15% of patients, abnormal liver function in 19% of patients, and isolated GI symptoms in 10% of patients [48]. The latter has an increased risk of delayed diagnosis of COVID-19 with

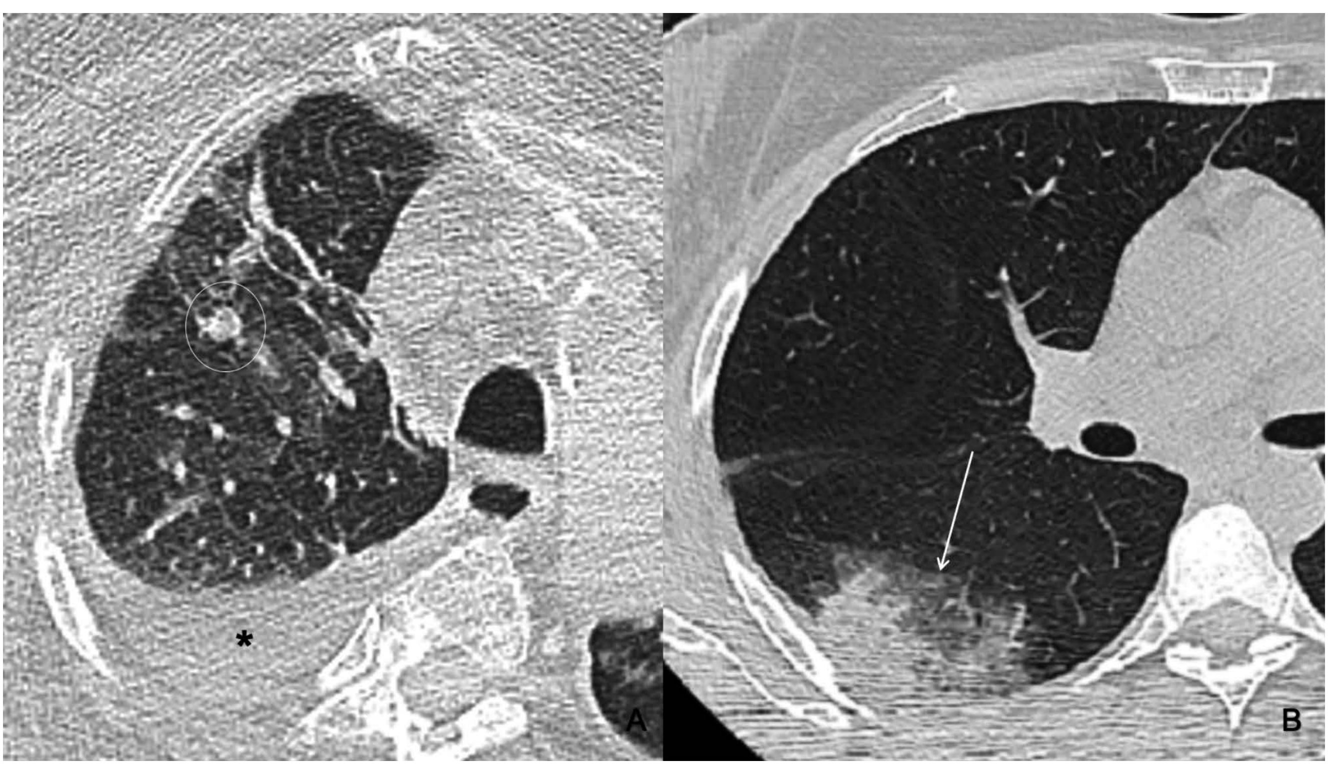

Figure 5. Lung nodule. A) Axial unenhanced CT image obtained in a 61-year-old female shows a nodule (circle) in the right upper lobe. Also note pleural effusion (asterisk). B) Axial CT image obtained in a 61-year-old female COVID-19 patient shows a nodule surrounded by a ground glass halo (arrow) in the peripheral right lower lobe (halo sign).

the risk of virus-spreading [48]. In this case, the detection of typical findings of COVID-19 pneumonia on the lung bases of abdomen CT scan, can raise the suspicion of COVID-19, despite the absence of respiratory symptoms [49].

Figure 6. Axial unenhanced CT image obtained in a 68-year-old male COVID-19 patient shows extensive fibrosis and traction bronchiectasis, involving the entire lung parenchyma.

Figure 7. Axial CT image obtained in a 60-year-old male COVID-19 patient shows subpleural lines (arrow) in the lower right lobe.

GI and liver involvement can be due to the expression of angiotensin converting enzyme 2 (ACE2), the major receptor of coronavirus or microvascular injury due to inflammation response, that leads to arterial and venous thrombi [50-52].

GI abnormalities are preferentially evaluated at CT and include bowel wall thickening, pneumatosis, portal venous gas, thrombosis of the portal vein (Figure 10) and upper mesenteric vessels and bowel ischemia [50,53,54].

Ultrasound is most commonly performed for elevated liver enzymes, and can show gallbladder sludge and distension, suggestive of cholestasis [50].

Neurologic findings

Neurologic symptoms are not uncommon in COVID-19 patients, especially in severe stage of the disease [55-59]. Rarely, they are the only presenting symptoms of COVID-19 [55]. As with abdominal manifestations, the cause of neurologic impairment is

Figure 8. Axial unenhanced CT image obtained in a 40-year-old male COVID-19 patient shows bilateral pleural effusion (arrows) and pericardial effusion (arrowhead).

Figure 9. Axial unenhanced CT image obtained in a 69-year-old female COVID-19 patient shows multiple mediastinal lymphadenopathies (arrows).

ACE2 expression [55]. Main neurological findings are polyneuropathy, encephalopathy, demyelinating lesions, brain microhemorrhage, and ischemic stroke (Figure 11) [55-59]. The latter can be related to increased thrombosis rates in coronavirus infection [56]. Although imaging findings are not specific of COVID-19, CT and MRI are strongly recommended for the evaluation of neurologic involvement.

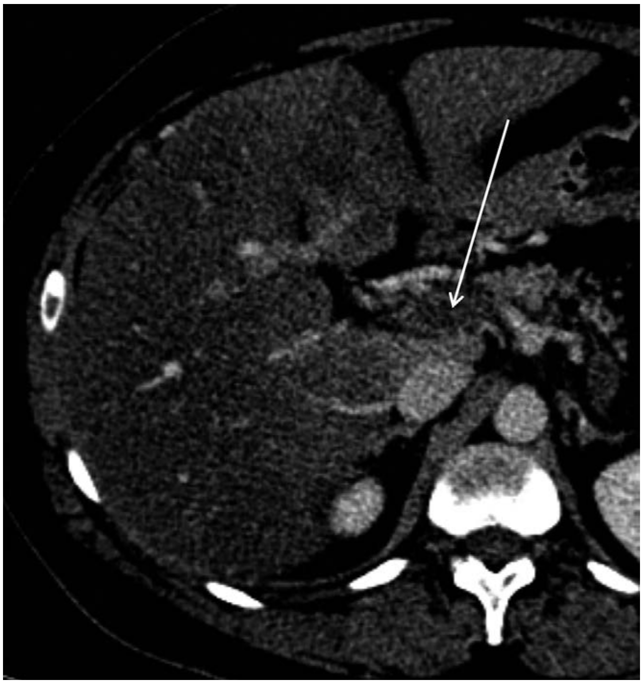

Figure 10. Axial portal venous phase contrast-enhanced CT image obtained in a 40-year-old male COVID-19 patient shows hypoattenuation within mildly dilated thrombosed main portal vein (arrow).

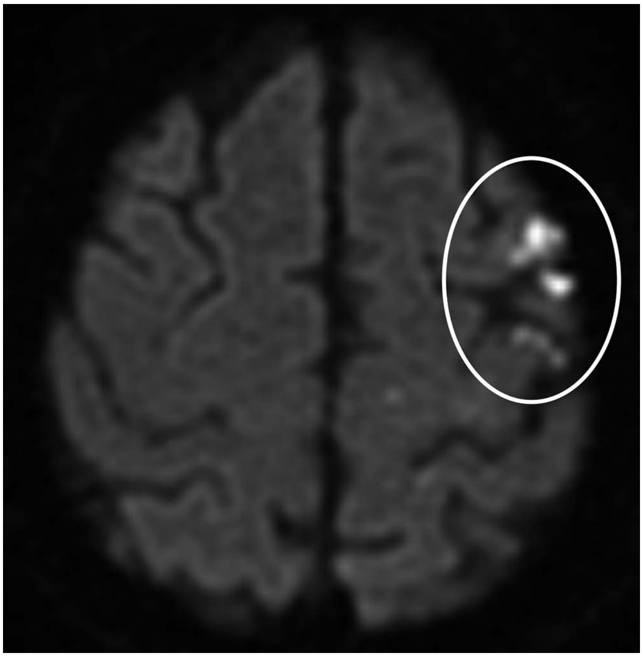

Figure 11. Brain MRI obtained in a 65-year-old male COVID-19 patient shows show multiple acute lacunar ischemic strokes in the left frontal and left parietal lobe (circle) visible as hyperintense areas on diffusion-weighted sequence (b = 1000 s/mm^2).

Conclusions

Although RT-PCR is the reference assessment for the diagnosis of COVID-19 infection, imaging plays a crucial role for initial evaluation and follow-up of COVID-19 positive patients and to exclude other disease conditions, which can be treated. Physicians should be familiar with typical and atypical COVID-19 imaging findings.

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