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EDITORIAL

Imaging in multiple myeloma: Computed tomography or magnetic resonance imaging?

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Abstract

Multiple myeloma (MM) is the second most common type of hematological disease with its incidence rising in the elderly. In MM, the extent of the bone disease increases both morbidity and mortality. The detection of lytic bone lesions on imaging, especially computerized tomography (CT) and magnetic resonance imaging (MRI) is crucial to separate asymptomatic from symptomatic MM patients even when no clinical symptoms are present. Although radiology is essential in the staging and management of patients with MM there is still high variability in the choice between MRI and CT. In addition, there is still suboptimal agreement among readers. The potential of medical imaging in MM is largely under-evaluated: artificial intelligence, radiomics and new quantitative methods to report CT and MRI will improve imaging usage.

Key Words: Multiple myeloma; Imaging; Magnetic resonance imaging; Computed tomography; Quantitative imaging

Core Tip: Introduction of new quantitative scores and biomarkers to predict multiple myeloma (MM) prognosis, possibly outperforming current staging methods to create new reliable standards for disease prediction and monitoring is an opportunity for further research in MM imaging.

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INTRODUCTION

Multiple myeloma belongs to the so-called plasma cell dyscrasias which are pathological conditions including monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), and full-blown multiple myeloma (MM)[1]. Epidemiological studies show that, on the one hand, around 5% population over 70 is MGUS carriers and around 1% of them will turn into MM every year. On the other hand, around 10% SMM population evolves into full-blown MM[1]. Finally, the early MM mortality, *i.e.* the number of MM patients that dye within the first year after diagnosis, is nowadays around 28%, with a peak of 35% among older patients[1]. The single or, more frequently, multiple bone lesions are biologically determined by the proliferation of abnormal cells from a single clone and the excessive and unbalanced activation of osteoclasts eroding the bone starting from the medulla and then reaching the cortical bone and even the extra-osseous soft-tissues. However, MM has a heterogenous genetic architecture which is evident among different patients with the same disease. Genetic heterogenicity is evident also in the same patient where different focal bone lesions may have different genetic patterns[2-4]. MM patients are classically described and defined by the CRAB-criteria (Calcium elevation, Renal insufficiency, Anemia, Bone lesion), indeed symptoms of MM patients vary from bone pain or pathological fractures over renal failure and anemia to calcium elevation and even immune deficiency. It is not known why up to 20% of patients with SMM become symptomatic within 2 years, while one third does not progress to MM within a decade [5], therefore there are several unmet research questions that need to be addressed. In MM patients, having a single focal lesion > 5 mm in diameter identified by mean of computed tomography (CT) or magnetic resonance imaging (MRI) is currently used to identify high-risk SMM patients to upstage them to MM according to the International myeloma working group updated criteria for the diagnosis of multiple myeloma[6]. Therefore, detection of lytic bone lesions on imaging has been recognized crucial since 2003 when the international myeloma working group replaced the classical Durie-Salmon staging system with a more complex and complete revised version called Durie-Salmon plus system. This latter system replaced radiography for identifying bone involvement with the increased sensitivity of MRI, CT or Positron emission tomography (PET)[7]. Therefore, the detection of lytic bone lesions on imaging, especially CT and MRI, is becoming crucial from the clinical viewpoint to separate asymptomatic from symptomatic MM patients. According to Rajkumar *et al*[8] bone imaging in MM is relevant for diagnosis because osteolytic lesion detection justifies the beginning of a treatment. Medical imaging is required for several reasons: (1) Localization of bone pain; (2) Prevention of complications such as pathologic fractures on long bones (*i.e.* femur) and vertebral pathological fractures; (3) Identification of focal lesions with high risk of progression; (4) To identify sites of extra-medullary disease; and (5) Identification of sites at potential risk of neurologic complications (Figure 1). In spite of the pivotal role of medical imaging in MM patient care, there is still considerable heterogeneity in clinical practice regarding imaging usage in MM, essentially due to the high variability in the choice between various imaging methods and the high variability in image interpretation[9,10]. In this editorial, the unmet research questions in the usage of imaging in MM are reported and possible future directions are discussed.

POTENTIAL OF MEDICAL IMAGING IN MM

Firstly, it must be underlined that the detection of lytic bone lesions with a diameter > 5 mm can be done with both CT and MRI and no study directly compared the two modalities regarding patients' outcomes after CT or MRI. At least in theory, MRI could have some advantages, such as the possibility to introduce functional sequences such as diffusion weighted sequences, but, no clear advantage of one technique over another has been found, even when a systematic review approach was adopted[11, 12]. Regelink *et al*[12] found that there was only few additional lesions detected by both PET and MRI if CT was used as reference test (detection rate 1.00 and 1.00-1.25 respectively). In addition, the review by Regelink *et al*[12] review was limited by the suboptimal methodological quality of the involved studies due to lack of a technical details. It could be suggested that both MRI and CT have equal diagnostic value and there is no clear advantage to prefer one of the two techniques (Table 1). The scientific community is waiting for thorough comparative future studies, possibly focusing on prognostic value and follow-up. Furthermore, an analysis of multiple bone lesions

Table 1 Specific advantages and disadvantages or computed tomography and magnetic resonance imaging in multiple myeloma

	Availability	Reader expertise	Radiation dose	Repeatability among different readers	Repeatability among different scanners	Availability of reporting guidelines	Ability to detect > 5 mm focal lesions	Exam duration
CT	High	Medium	Similar to total body CT	High	Medium	Low	High	Less than 10 min
MRI	Medium	Low	None	Medium	Medium	Low	High	More than 30 min

CT: Computed tomography; MRI: Magnetic resonance imaging.

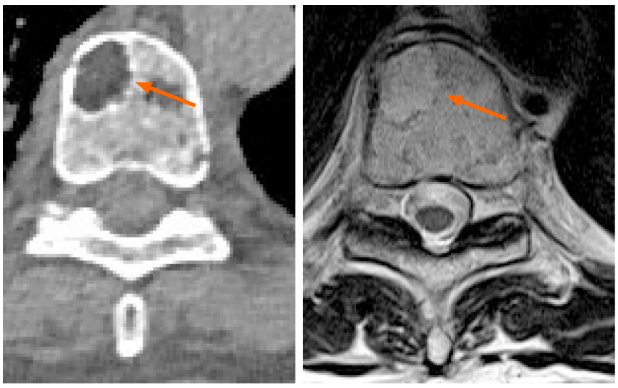

Figure 1 Computed tomography and magnetic resonance imaging of the same lytic lesion located into the vertebral body acquired in the same week for different reasons. No major differences in detection capabilities are evident.

detected on CT and MRI could be performed using artificial intelligence and radiomics [13]. Up-to-date, radiomics[14] is a quantitative radiological promising technique, with the ultimate goal to improve cancer treatment by improving prognostic capabilities of medical imaging. Radiomics is a complex, quantitative feature-based tool for image analysis described as the conversion of images to higher dimensional data and the subsequent mining of these data for improved decision support[14]. In MM, a recent application of radiomics improved the radiological evaluation of focal and diffuse pattern on CT by increasing the area under the curve of radiologists[15]. Accuracy of radiologists compared to the reference standard was lower (64%) than the accuracy using a radiomics approach (79%)[15]. In addition, machine learning-based classifiers resulted a satisfactory in differentiating MM lesions from those of tumor metastasis of the spine evaluated on MRI[16]. Radiomics was also on PET/CT in MM to elaborate a prognosis model predicting outcome in transplant-eligible newly diagnosed patients [17]. Finally, radiomics has been used with MRI to correlate features with the clinical and hematological response in multiple myeloma patients undergoing systemic treatment. In detail, one textural feature (GLSZM large area low gray level emphasis), in the study by Ekert *et al*[18] resulted to be correlated also with the bioptic degree of bone marrow infiltration.

CONCLUSION

Introduction of new quantitative scores and biomarkers to refine diagnosis, to predict MM prognosis, possibly outperforming current staging methods to create new reliable standards for disease prediction and monitoring is an opportunity for further research in MM imaging.

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MINIREVIEWS

Abdominal imaging in COVID-19

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Abstract

Initially thought of as a respiratory infection, coronavirus disease-2019 (COVID-19) is now recognized as a complex disease with a wide clinical spectrum, including digestive involvement. While several studies have evaluated chest imaging findings in COVID-19, few papers have looked at the abdominal imaging features of these patients. Liver, biliary, pancreas and bowel involvement have been reported in COVID-19 infected patients. In this review, we aim to summarize currently available data related to abdominal imaging techniques in COVID-19, in accordance with relevant clinical and laboratory workup of these patients. Underlying mechanisms, indications and imaging findings related to COVID-19 are discussed based on published data. Also, practice points for clinicians are highlighted in order to adequately recognize digestive-related injuries of severe acute respiratory syndrome coronavirus 2 infection. While there's been a steady accumulation of data with respect to abdominal imaging findings in COVID-19, currently available recommendations are based on limited research. There is a wide spectrum of abdominal imaging findings in COVID-19, which includes hepato-biliary, pancreatic and luminal pathology.

Key Words: COVID-19; Gastrointestinal; Digestive; Features; Imaging; Ultrasound; Computed tomography

Core Tip: Initially being thought of as a respiratory infection, coronavirus disease-2019

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(COVID-19) is now widely recognized as a complex disease with systemic features. Gastrointestinal manifestations have been reported with high prevalence in severe acute respiratory syndrome coronavirus 2 infected patients, including gut, pancreas, liver and biliary dysfunction. In this review we summarize and analyze currently available evidence on abdominal imaging techniques, indications and findings in COVID-19, in accordance with relevant clinical and laboratory workup of these patients.

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INTRODUCTION

In late December 2019, a cluster of pneumonia cases of unknown origin was reported in Wuhan, Hubei province, China. The causative agent was identified as a novel coronavirus, linked to the severe acute respiratory syndrome (SARS). The virus was named SARS coronavirus 2 (SARS-CoV-2) and the related disease coronavirus disease-2019 (COVID-19). The novel coronavirus rapidly spread worldwide, and since March 11th 2020, the date on which COVID-19 was declared a pandemic[1], over 150 million cases and 3.2 million COVID-19 associated deaths have been reported[2].

Initially being thought of as a respiratory infection, COVID-19 is now recognized as a complex disease with a wide spectrum of presentations, from viral pneumonia and flu-like symptoms to acute hepatitis and Kawasaki-like disease[3,4]. The systemic nature of COVID-19 is related to the interaction of SARS-CoV-2 with the human body, mediated by angiotensin converting enzyme 2 (ACE2) expressed on cell surfaces[5]. ACE2 is most abundant in alveolar epithelium, but is also found in large amounts in enterocytes, vascular endothelium, liver and biliary epithelium[6]. Binding of SARS-CoV-2 at these susceptible extrapulmonary sites can generate symptoms directly related to the infected organ. Moreover, several reports have identified SARS-CoV-2 to be present in stool samples of infected patients[7-9], and there have been proposals to use anal swabs for SARS-CoV-2 detection and follow-up of infected individuals[10].

With regard to involvement of the gastrointestinal tract, several studies have shown high prevalence of digestive symptoms in COVID-19[7,11,12]. This was explained by the high density of ACE2 receptor (the cell entry point for SARS-CoV-2) in the small bowel and pancreas, but also as a side effect of COVID-19 related therapy and secondary to systemic inflammation and ischemia[13]. Not least, laboratory changes reflecting on gut or hepato-bilio-pancreatic pathology have been reported in COVID-19. In this setting, abdominal imaging has been used to define the cause of symptoms and laboratory abnormalities in these patients.

While an abundance of papers has described chest imaging findings in COVID-19, few articles have focused on abdominal imaging features of these patients. In this review we aim to summarize and analyze current evidence on abdominal imaging techniques, indications and findings in COVID-19, in accordance with relevant clinical and laboratory workup of these patients.

ABDOMINAL IMAGING

Abdominal imaging reported in COVID-19 patients include abdominal ultrasound and cross-sectional imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI). A literature search on the topic also revealed isolated reports of plain abdominal X-ray, endoscopy or positron emission tomography CT (PET-CT) findings in COVID-19 patients.

Ultrasound

Abdominal ultrasound is being routinely used in patients with abdominal complaints. With regard to COVID-19, ultrasound (US) has been mostly indicated to evaluate for

abdominal pain and abnormal liver function tests. While sometimes the abdominal pain does not reflect digestive pathology and is probably referred pain as the one seen in basilar pneumonias, the prevalence of transaminitis in COVID-19 has been estimated at 15%[14]. Sonographic examination has been also ordered for abdominal distention, suspected sepsis, increase in renal function tests or drop in hemoglobin [15]. Abdominal sonographic scanning also includes evaluation of hydration status by assessment of the inferior vena cava, presence of ascites (also pericardial or pleural effusions) or hydronephrosis[16].

In the study by Abdelmohsen *et al*[15] which aimed to characterize the sonographic abdominal imaging findings in COVID-19 intensive care patients, the most frequent sonographic finding was hepatomegaly (56.09%), followed by biliary system disease (41.4%) consisting of gallbladder wall thickening, mural hyperemia, intraluminal mud and pericholecystic fluid. Results are similar to those reported by Bhayana *et al*[17], with gallbladder sludge and distention being seen in 54% of right upper quadrant ultrasound studies. In this latter study, US also detected portal venous gas in one patient, which was confirmed by CT scan. US can also be used for guiding drainage procedures, as reported in cases of COVID-19-related acute cholecystitis[18].

A rather high prevalence of fatty liver has been reported in COVID-19 patients who underwent US examination, likely attributable to the established association between SARS-CoV-2 infection and obesity[17,19].

Taking into account the altered coagulation in COVID-19 and the potential thrombotic complications, US can be of value in evaluating the abdominal vasculature. Doppler US can be used to assess for venous or arterial thrombosis. Decreased vascularity at Doppler examination can indicate infarction and needs further studies. Contrast-enhanced US has been reported to adequately detect abdominal microcirculatory disorders by assessing mesenteric blood flow, liver and kidney perfusion[20].

A concern regarding US in COVID-19 patients was related to sonographer exposure while performing the examination. In order to minimize the scanning time, there have been proposals to capture cine clips and proceed with postprocessing of images after the examination[21].

CT

Several papers have looked at abdominal CT findings in COVID-19. Most frequent features seen on abdominal CT in COVID-19 patients were bowel wall thickening, fluid-filled colon, pneumatosis, pneumoperitoneum, intussusception, and ascites[22]. Abdominal findings in COVID-19 are detected either by ordering an abdominal scan in a SARS-CoV-2 positive patient, or by incidentally detecting ground-glass opacities in lung bases during an abdominal scan ordered for non-COVID related reasons.

CT scan has been usually indicated for prominent, otherwise unexplained digestive pain or for suspected complications such as mesenteric thrombosis or bowel ischemia [12,17]. Also, elevations in serum amylase and lipase have been reported in COVID-19; while the increased values of pancreatic enzymes did not usually reflect pancreatitis, there are reports of COVID-19 associated acute pancreatitis documented by CT[23-29]. Others, however, have considered inappropriate to define a causal relationship between SARS-CoV-2 and acute pancreatitis, due to insufficient etiological workup [30].

MRI

MRI has been rarely reported in COVID-19 patients, significantly less than US and CT [17]. In a study by Shiralkar *et al*[31], MRI was indicated for liver dysfunction; no acute findings were seen. A potential limitation of abdominal MRI studies in COVID-19 is the prolonged examination time in patients suffering from respiratory failure. Although MRI is an excellent modality for the evaluation of biliary disease, findings are usually non-specific as cholestasis is related to the high expression of ACE2 receptor in cholangiocytes.

DISCUSSIONS

In front of this novel threat for humanity, knowledge is continuously evolving with unprecedented efforts from the academic community. Despite good evidence on gastrointestinal involvement in COVID-19, related to the abundant expression of ACE2 receptors in the gut and biliary endothelium, there is a paucity of data regarding the imaging approach of digestive-related symptoms or laboratory test abnormalities of these patients. Moreover, currently available data on abdominal imaging in COVID-

Table 1 Summary of proposed mechanisms and abdominal imaging techniques recommended for gastrointestinal involvement in coronavirus disease-2019[13,34,35]

	Proposed mechanism	Abdominal imaging
Hepato-biliary	Direct viral cytopathic injury; Congestive hepatopathy; Drug-induced liver injury; Systemic inflammatory response; Exacerbation of preexistent chronic liver disease	Ultrasound to check gallbladder and biliary tree; CT/MRI to asses for perfusion injury and complications
Pancreas	Direct viral cytopathic injury; Systemic inflammation; Dehydration	CT scan to assess severity and complications of pancreatitis, and evaluate for alternative diagnosis; Ultrasound to check for biliary etiology or alternative diagnosis, also for diagnosis and follow-up of complications in pancreatitis
Gastrointestinal tract	Direct viral cytopathic injury; Systemic inflammation; Thrombosis; Adverse effects of COVID-19-related drugs	CT scan to assess for clinically similar alternative diagnosis, to detect extension and severity of bowel inflammation and to check the vascular patency

COVID-19: Coronavirus disease-2019; CT: Computed tomography; MRI: Magnetic resonance imaging.

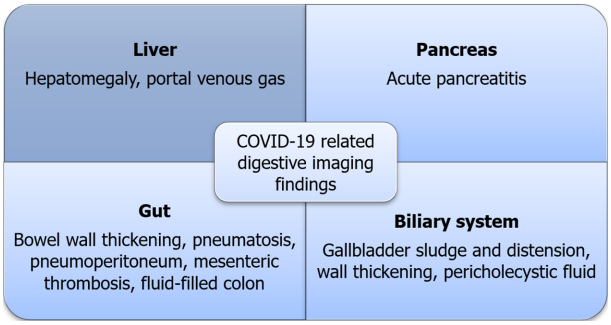

Figure 1 Summary of coronavirus disease-2019 related abdominal imaging findings.

19 is retrospective in nature and limited by significant heterogeneity with respect to indications, protocol and follow-up of pathological findings.

Most frequent indications for US examination in SARS-CoV-2 positive patients were upper abdominal pain and altered liver function tests. COVID-19-related liver injury is usually mild and transient, but liver failure can occur in the setting of sepsis or coagulopathy with microthrombosis[21]. While Doppler examination might be limited in detecting small vessel thrombosis, assessment of mesenteric and liver vasculature patency is well done by contrast-enhanced CT scan or gadolinium-enhanced MRI. Usually, abdominal CT scan is indicated in cases of suspected bowel ischemia/perforation, solid organ infarction (spleen, kidney), sepsis or cholestasis-related complications[21]. Segmental or diffuse thickening of the gut wall, along with distended intestinal lumen is a frequent finding in COVID-19 and can present as gastritis, enteritis, colitis or combination of these[21]. Bowel findings in COVID-19 are supposed to be caused be either direct viral infection of gut epithelium or by small-vessel thrombosis with consecutive ischemia[17].

Along with ischemic complications, CT scan can also depict hemorrhagic complications such as hematomas or hemorrhagic transformation of bowel ischemia[21]. Besides its diagnostic role, abdominal imaging has also demonstrated prognostic value upon detection of ischemic gastrointestinal complications in COVID-19, which has been shown to be associated with higher mortality[32,33]. The most frequent findings on abdominal imaging in COVID-19 are summarized in Figure 1.

Not least, cross-sectional abdominal imaging performed in symptomatic individuals not suspected of having COVID-19 can alert clinicians of the possibility of SARS-CoV-2 infection by detection of ground-glass opacities on sections of the upper abdomen which are also capturing the lung bases. Thus, a CT scan ordered for a non-pulmonary indication can incidentally detect COVID-19 patients, before occurrence of respiratory manifestations.

To sum up, abdominal ultrasound and cross-sectional imaging techniques such as CT scan can accurately assess for gastrointestinal involvement in SARS-CoV-2 infected patients, particularly in a clinically significant setting; knowledge of the underlying mechanisms of hepatobiliary, pancreatic and gut alterations in COVID-19 and a high

index of suspicion is mandatory for prompt detection of digestive-related injuries of SARS-CoV-2 infection (Table 1). Further studies looking at abdominal microvasculature and follow-up of patients with abdominal features related to COVID-19 are warranted to better depict the imaging features of this infection.

CONCLUSION

While there's been a steady accumulation of data with respect to abdominal imaging findings in COVID-19, currently available recommendations are based on limited research. There is a wide spectrum of abdominal imaging findings in COVID-19, which includes hepato-biliary, pancreatic and luminal pathology. Underlying mechanisms behind the wide spectrum of digestive involvement in COVID-19 include direct viral infection, small-vessel thrombosis and systemic inflammation. Prompt recognition of abdominal imaging findings in COVID-19 is mandatory to adequately guide management and improve prognosis of these patients. Also, abdominal imaging in patients with primarily digestive symptoms not initially suspected of COVID-19 can alert clinicians about the possibility of SARS-CoV-2 infection if typical lesions are found on evaluation of lung bases.

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ORIGINAL ARTICLE

Retrospective Study

"Pulmonary target sign" as a diagnostic feature in chest computed tomography of COVID-19

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Abstract

BACKGROUND

In chest computed tomography (CT) scan, bilateral peripheral multifocal ground-glass opacities, linear opacities, reversed halo sign, and crazy-paving pattern are suggestive for coronavirus disease 2019 (COVID-19) in clinically suspicious cases, but they are not specific for the diagnosis, as other viral pneumonias, like influenza and some viral pneumonia may show similar imaging findings.

AIM

To find a specific imaging feature of the disease would be a welcome guide in diagnosis and management of challenging cases.

METHODS

Chest CT imaging findings of 650 patients admitted to a university Hospital in Tehran, Iran between January 2020 and July 2020 with confirmed COVID-19 infection by RT-PCR were reviewed by two expert radiologists. In addition to common non-specific imaging findings of COVID-19 pneumonia, radiologic characteristics of "pulmonary target sign" (PTS) were assessed. PTS is defined as a

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circular appearance of non-involved pulmonary parenchyma, which encompass a central hyperdense dot surrounded by ground-glass or alveolar opacities.

RESULTS

PTS were presented in 32 cases (frequency 4.9%). The location of the lesions in 31 of the 32 cases (96.8%) was peripheral, while 4 of the 31 cases had lesions both peripherally and centrally. In 25 cases, the lesions were located near the pleural surface and considered pleural based and half of the lesions (at least one lesion) were in the lower segments and lobes of the lungs. 22 cases had multiple lesions with a > 68% frequency. More than 87% of cases had an adjacent bronchovascular bundle. Ground-glass opacities were detectable adjacent or close to the lesions in 30 cases (93%) and only in 7 cases (21%) was consolidation adjacent to the lesions.

CONCLUSION

Although it is not frequent in COVID-19, familiarity with this feature may help radiologists and physicians distinguish the disease from other viral and non-infectious pneumonias in challenging cases.

Key Words: Chest computed tomography; Diagnosis; Viral pneumonia; COVID-19; Pulmonary target sign; Case report

Core Tip: In this report, a new diagnostic imaging sign in chest computed tomography of coronavirus disease 2019 cases, the "pulmonary target sign", is reported and its characteristics are described. Previous reports are limited to a small number of case reports and this appearance is not fully described.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is the seventh member of the non-segmented, enveloped, and positive-sense-RNA Coronaviridae family, which causes acute respiratory illness. This new coronavirus was first detected in Wuhan, China, in December 2019. It has since rapidly spread throughout the world and was recognized as a global health emergency[1,2]. COVID-19 presents as a wide spectrum of clinical pictures, from asymptomatic or mild flu-like illness to severe respiratory infection and even death[3,4].

A definitive diagnosis of COVID-19 mainly relies on RT-PCR testing in suspected cases. Chest computed tomography (CT) also has an undeniable importance in the diagnostic management of COVID-19 due to its high sensitivity and widespread availability[5]. The most common radiologic findings of COVID-19 are bilateral, peripheral, multifocal ground-glass opacities (GGO) and consolidations, linear opacities, reversed halo sign, and crazy-paving pattern[4,6]. These findings are highly suggestive, but not specific, for the diagnosis of COVID-19 infection, as other viral pneumonias, like influenza, severe acute respiratory syndrome and middle east respiratory syndrome, may show similar imaging findings[7,8]. Therefore, finding a specific and unique imaging feature of the disease in chest CT of patients with COVID-19 could be extremely helpful in the diagnostic work-up of these patients by limiting the differential diagnosis.

Some relatively specific features of the disease in chest CT have been discussed in the literature, including the "parallel pleural sign", "rings of Saturn appearance" and, recently, the "pulmonary target sign (PTS)"[9,10]. The latter imaging finding seems to be more specific for the disease. It was initially reported by Jafari *et al*[11] and

Shaghaghi *et al*[12] as a hyperattenuating ring surrounding a dense central dot, mimicking a target sign. This was termed a "target-shaped combined halo and reversed-halo sign" and "rings of Saturn"[11,12]. One month later, a similar pattern, named "chest target sign", was reported by McLaren *et al*[13] called "Bulls eye sign". Subsequently, de Farias *et al*[14] and Müller *et al*[15] also reported this imaging feature and its variants. Recently, Jafari *et al*[16] reported four cases of "PTS". In this contribution, we review chest CT images of 32 cases of PTS.

MATERIALS AND METHODS

Study design

Chest CT imaging findings of 650 patients admitted to a university Hospital in Tehran, Iran with confirmed COVID-19 infection by RT-PCR between January 2020 and July 2020 were reviewed by two expert radiologists.

Imaging protocol

All chest CT scan were obtained using a 16-row detector CT scanner (GE, optima, United States). Based on protocol of COVID-19 low-dose thoracic CT scan, the following items were considered: Tube voltage, 120 kVp; mAs, 30; slice thickness, 2.5 mm; reconstruction interval, 1.25 mm; rotation time, 0.5 s; pitch, 0.984; beam collimation, 40.

Chest CT interpretation

In addition to common non-specific imaging findings of COVID-19 pneumonia, radiologic characteristics of PTS will be presented. This chest CT sign of the disease as a circular appearance of non-involved pulmonary parenchyma with a central hyperdense dot, which is surrounded by ground glass or alveolar opacities, resembling a shooting target.

RESULTS

Of the 650 patients reviewed, 32 cases of PTS were found (4.9% prevalence). The location of the lesions in 31 of the 32 cases was peripheral, while 4 of the 31 cases had lesions both peripherally and centrally. Only one case had an isolated central lesion mimicking a solitary pulmonary nodule (Figures 1 and 2A).

The typical shape of PTS was seen in 31 cases, while 1 case had a PTS variant with double peripheral dense rings, which was previously named "rings of Saturn" (see Figure 2).

In 25 cases, the lesions (at least one if there were multiple) were located near the pleural surface and considered pleural based (see Figure 3). Half of the lesions (at least one lesion) were in the lower segments and lobes of the lungs (see Figure 4).

More than 87% of cases had an adjacent bronchovascular bundle (BVB). This characteristic was reported when a dense branching linear structure was approaching the lesion (see Figure 5).

Of the 32 cases, 22 had multiple lesions with a > 68% frequency (see Figure 6). GGOs were detectable adjacent or close to the lesions in 30 cases (93%) and only in 7 cases (21%) was consolidation adjacent to the lesions, Figure 7.

8 cases showed pulmonary complications of COVID-19, including pneumothorax (1 case) and pleural effusion (7 cases/21%). Three cases (9%) showed parallel pleural sign and 6 cases (18%) showed fibrotic bands (see Figure 8). The characteristics are summarized in Table 1.

DISCUSSION

Regarding the descriptive findings and characteristics of PTS lesions, they tend to be multiple lesions, located in the periphery, and located adjacent to a BVB and GGOs. They are uncommonly seen centrally or basally or with adjoining consolidation. Due to a low frequency of fibrotic bands as a marker of healing and concomitant complications, such as pleural effusion, it seems that PTS appear at early phases.

Table 1 Cases characteristics

Characteristics of PTS	Number (32 cases)	Frequency (4.9%)
Only peripheral	31	96.8%
Both central and peripheral	4	12.5%
Age (mean ± SD)	53.1 ± 13.4	-
Gender (male)	28	87.5%
Along with BVB	28	87.5%
Pleura-based[1]	25	78.1%
Adjacent GGO	30	93.7%
Adjacent consolidation	7	21.8%
Basal lobes and segments[2]	16	50.0%
Multiple	22	68.7%

[1]Pleura based or close to pleural surface.
[2]If only one of multiple lesions present at lower segments and lobes, considered positive.
BVB: Bronchovascular bundle; GGO: Ground-glass opacities; PTS: Pulmonary target sign.

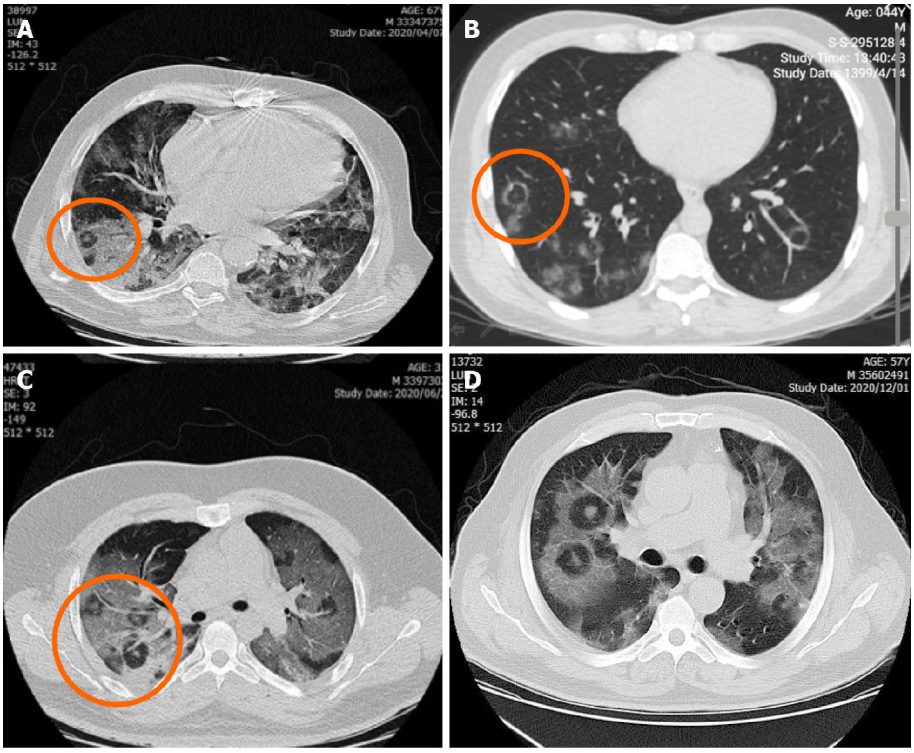

Figure 1 "Pulmonary target sign" in 4 different cases varies according to the location of the lesions. A and B: Peripheral location; C and D: Central location.

In such contagious and life-threatening infections as COVID-19, having a consistent and reliable diagnostic and screening tool is vital. Currently, CT, with its high sensitivity and specificity, is one of the most valuable screening and diagnostic tools [17,18]. Although commonly reported findings in COVID-19 CT scans are not specific for a diagnosis of COVID-19 *vs* other viral pneumonias, some recently reported specific features of the disease, like PTS, can be helpful for this aim.

It is important to know the difference between PTS and the Atoll sign. An Atoll sign has central opacities consisting of GGO, while PTS has a central dot which can represent a filled bronchiole or vessel. Moreover, it was previously noted that "the crescentic appearance of the reversed halo sign is typical on CT whereas the target sign has a polygonal appearance peripherally"[19]. This feature has been frequently re-

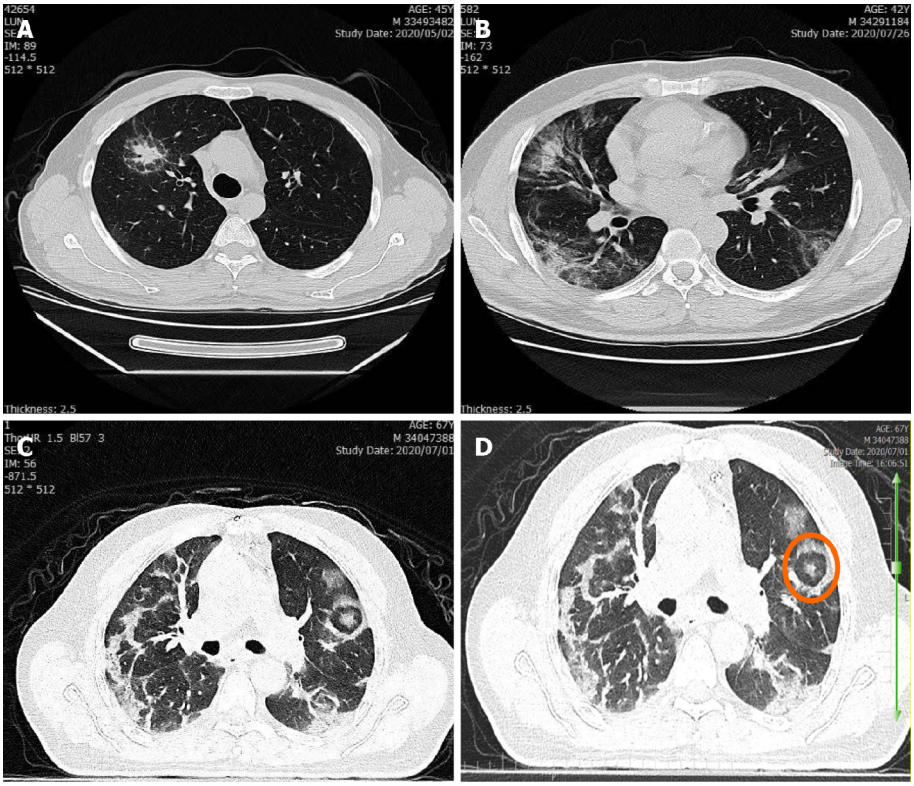

Figure 2 Variants of "pulmonary target sign" in 4 different cases. A: "Pulmonary target sign" (PTS) similar to a solitary pulmonary nodule; B: "Rings of Saturn" as a variant of PTS; C and D: PTS with parallel pleural sign.

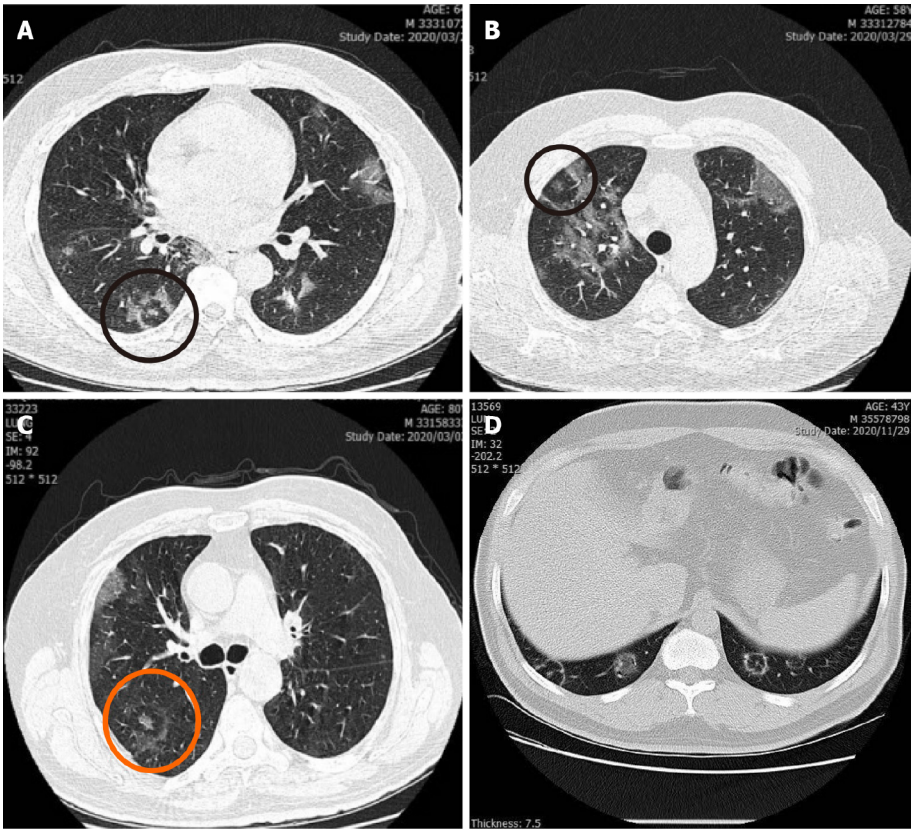

Figure 3 "Pulmonary target sign" in 4 different patients. A and B: "Pulmonary target sign" (PTS) as a pleural based lesion; C: PTS with incomplete peripheral ring; D: Complete peripheral ring.

ported as Atoll sign, which may be due to the unfamiliarity with this sign among

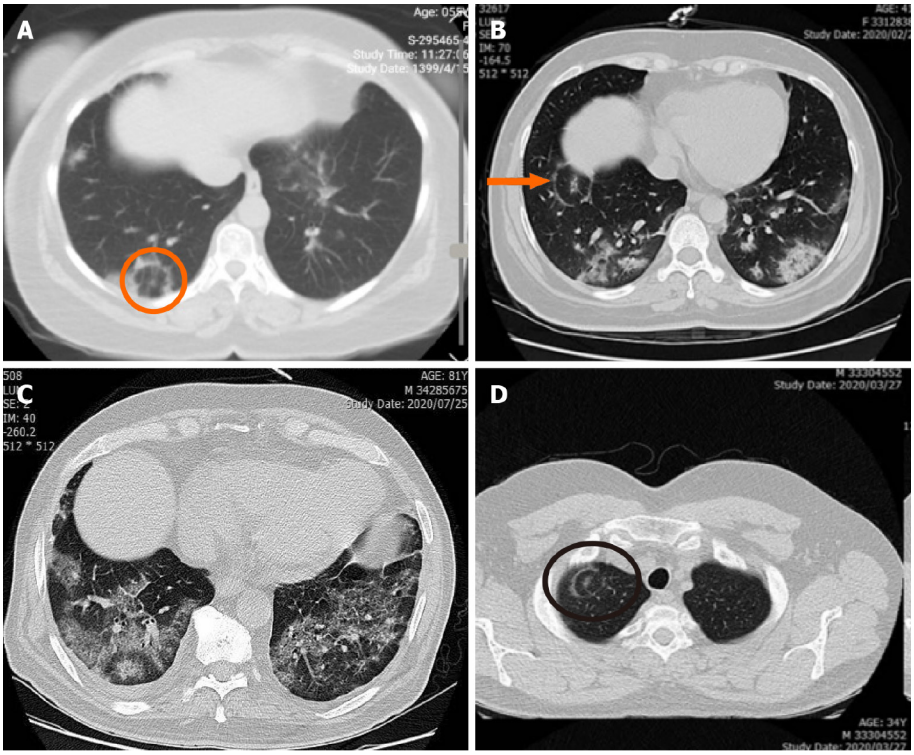

Figure 4 "Pulmonary target sign" in 4 different individuals. A, B and C: Basal location of "pulmonary target sign"; D: Apical location.

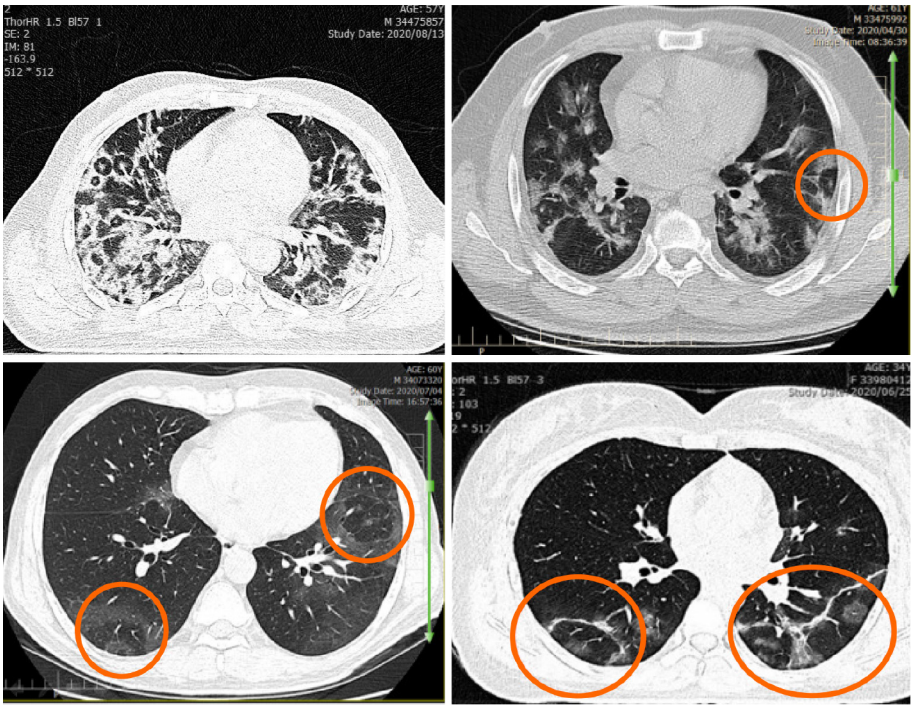

Figure 5 "Pulmonary target sign" in 4 different cases. "Pulmonary target sign" along with a broncho-vascular bundle.

physicians and radiologists[20-22]. For differentiation, it was described that "the peripheral wall of the CT target sign has a polygonal appearance in most patients", in contrast to the constellation of the reverse halo sign[19].

Generally, diffuse subpleural and peripheral ill-defined GGO with air-bronchograms, adjacent pleural thickening and septal or interlobular thickening were reported as the imaging hallmark of the novel coronavirus, while hilar or mediastinal lymphadenopathy, pleural effusion, pulmonary nodules and cavitations are unusual findings[2].

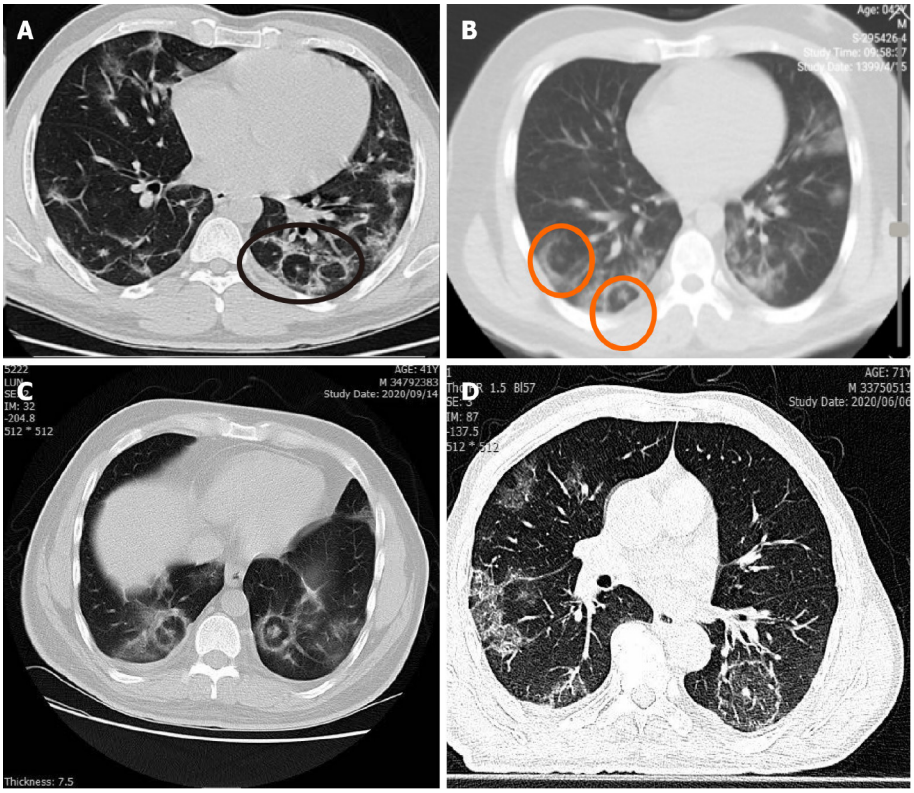

Figure 6 Laterality of "pulmonary target sign" in 4 different cases. A and B: Multiple unilateral "pulmonary target sign"; C: bilateral lesions; D: Solitary lesion.

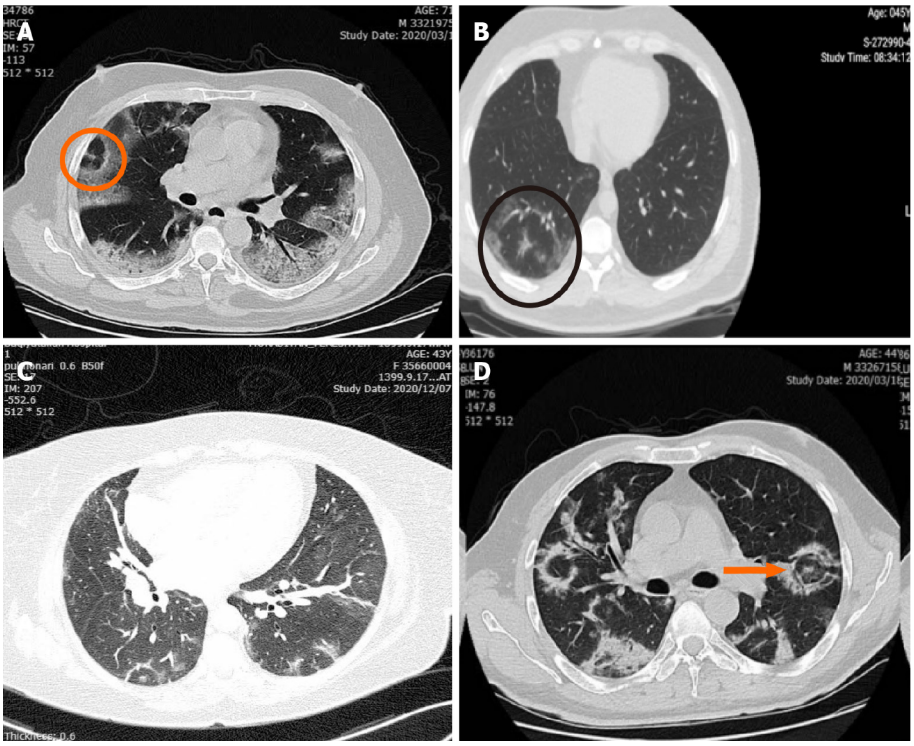

Figure 7 Correlation of "pulmonary target sign" with adjacent ground-glass opacities or consolidation. A: Circular adjacent ground-glass opacities (GGO); B and C: Patchy adjacent GGO; D: adjacent patchy consolidation.

In our contribution, we present 32 PCR confirmed cases of COVID-19 infection with specific findings on their chest CT. As mentioned previously, in addition to common findings of COVID-19 infection, their chest CT revealed a circular appearance of non-involved pulmonary parenchyma, which encompassed a central hyperdense dot

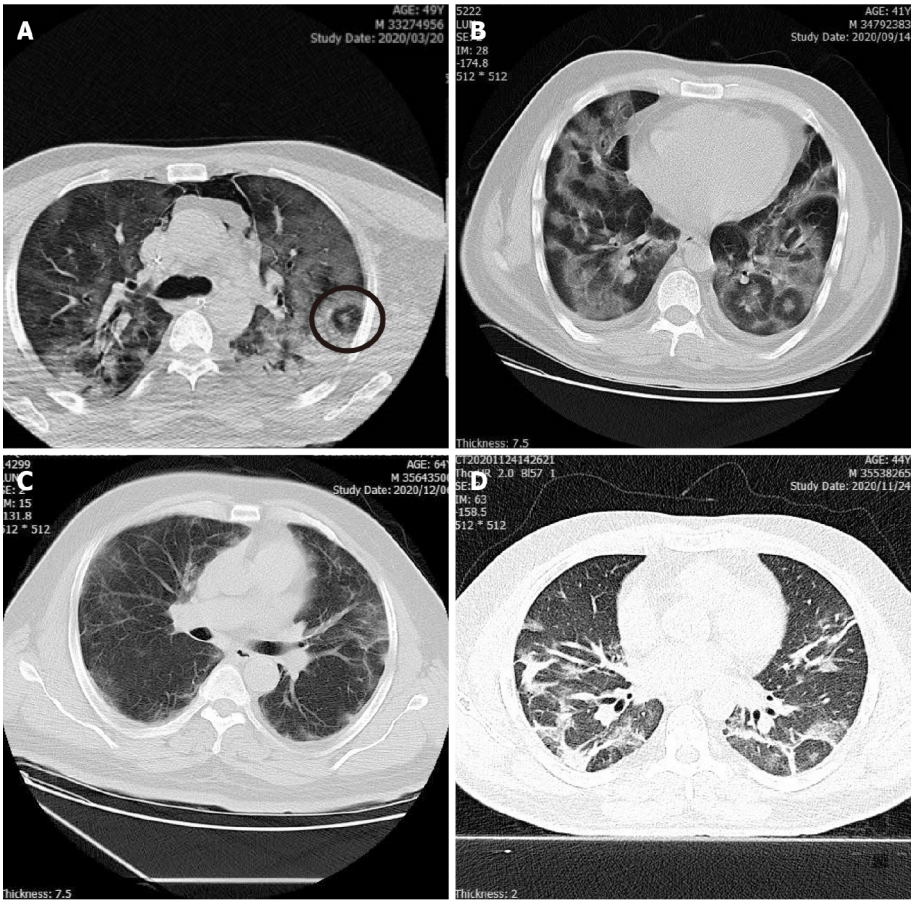

Figure 8 "Pulmonary target sign" with coronavirus disease 2019 complications. A: Pneumothorax and pneumomediastinum; B: Pleural effusion; C: Pleural thickening; D: Fibrotic band.

surrounded by ground-glass or alveolar opacities. This represents a unique finding that has never been reported in any other disease. We hypothesize that this appearance is due to a pattern of lobar involvement of COVID-19 *via* bronchiolar and venolymphaticdrainage[11,23]. Interstitial pneumonitis and subsequent organizing pneumonia with diffuse alveolar damage were reported in the advanced phase of the disease[19,24]. Therefore, the PTS feature will likely develop when the venolymphatic drainage system is subject to a considerable load of fluid entrapment, as in the case of alveolar wall injury and bronchial occlusion by this secretion (central dot) secondary to COVID-19.

CONCLUSION

We present specific, unique chest CT imaging features in 32 confirmed cases of COVID-19 infection. Although these findings are not observed in all patients with this disease and it is uncommon (about 5% frequency), we believe PTS to be a specific finding which can distinguish COVID-19 pneumonia from other similar viral pneumonias. However, due to the only recent recognition of this feature and the scarcity of reported cases, it is not yet clear whether PTS is seen only in COVID-19 or will also be observed in other viral pneumonias with similar pathophysiology.

ARTICLE HIGHLIGHTS

Research background

Chest computed tomography scan findings like bilateral ground glass opacities and consolidations are commonly used as distinguishing features in the differential diagnosis of coronavirus disease 2019 (COVID-19). However, a problem in diagnosis

arises when other viral or atypical pneumonia infections are suspected, as they may present similarly.

Research motivation

Pulmonary target sign (PTS) is a feature of COVID-19 that has been recently suggested as an atypical presentation of pulmonary involvement and may be used to distinguish COVID-19 from other similar pneumonia infections.

Research objectives

In this paper, the PTS and its characteristics were assessed among COVID-19 confirmed patients.

Research methods

Among all cases of COVID-19 that were referred to a tertiary medical center in Tehran, Iran, chest CT scan findings of 650 serologically positive cases of COVID-19 were evaluated for PTS and its characteristics.

Research results

32 individuals with at least one PTS in their CT scan were identified in which most of the PTSs were multiple in number, in a peripheral location, and near a bronchovascular bundle.

Research conclusions

The PTS has a frequency of about 5% and specific characteristics that may make it useful in the prompt diagnosis of COVID-19.

Research perspectives

The relationship between the presence of the PTS and the prognosis of COVID-19 still needs to be elucidated. Additionally, the mechanisms behind the pathogenesis and the timeline of PTS progression are suggested areas of research for future studies.

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