The Reversed Halo Sign in COVID-19 Pneumonia

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Abstract

Objectives

To evaluate the frequency and time course of RHS on CT in patient with COVID-19 pneumonia.

Materials and methods

A total of 147 patients with COVID-19 pneumonia were divided into mild, moderate, severe and critical categories. The number, location, shape, wall appearance of RHS on CT were analyzed. Other parenchymal abnormalities include GGO, consolidation and linear opacity were also recorded.

Results

RHS was observed in 37 (25.2%) of 147 patients and it was more common in patients with moderate disease than severe or critical disease (31.3% vs. 13.0%, $P = 0.019$). Time from symptom onset to appearance of RHS was 9 ± 5 days in moderate patients and 14 ± 8 days in severe/critical patients. A total of 64 RHS lesions were identified and the majority of lesions were located in peripheral aspect of lungs (55, 85.9%) and lower lobes (52, 81.2%). All lesions with RHS were round or oval-shaped. The rim of RHS were smooth in 54 (84.4%) and irregular in 10 (15.6%). Follow-up CT scans of 27 patients (50 lesions) showed 43(86%) lesions gradually resolved or developed into GGO and linear opacities and 7(14%) lesions remained unchanged appearance.

Conclusions

RHS occurred sooner after symptom onset and with higher frequency in patients with moderate compared to those with severe or critical disease. RHS may represent a favorable prognostic sign in COVID-19 pneumonia.

Key Points

- 37 (25.2%) of 147 patients with COVID-19 pneumonia had RHS on at least one CT
- RHS was more prevalent in patients with moderate disease than those with severe or critical disease
- RHSs (78.4%) mostly occurred within 2 weeks after symptom onset

Introduction

In December 2019, an outbreak of respiratory disease caused by a novel coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), began in Wuhan (Hubei Province, China) and rapidly spread throughout China and the globe [1]. The main features of coronavirus disease 2019 (COVID-19) pneumonia on chest CT are multifocal, peripheral and basal predominant ground-glass opacities (GGO), consolidation, or both [2,3]. These CT findings may indicate an organizing pneumonia (OP) pattern in

response to idiopathic or secondary lung injury [4,5]. The reversed halo sign (RHS), focal area of GGO surrounded by a ring-shaped consolidation, has been described in association with OP [6].

RHS is a CT finding strongly suggestive but not specific for OP, and it can be found in various infectious and noninfectious pulmonary diseases [7]. Although previous studies have reported the presence of the RHS in COVID-19 pneumonia [5,8], its characteristics and significance in this disease remains unclear. We evaluated serial CT scans in patients with confirmed COVID-19 pneumonia to describe the frequency and features of RHS to improve understanding of the potential significance of this CT finding.

Materials And Methods

This study was approved by our institutional review board and the need for informed consent was waived.

Patients

We retrospectively reviewed the CT images obtained between January 22 to March 7, 2020 of 147 patients with confirmed COVID-19 pneumonia from eight institutions in Shannxi and Hubei provinces in China. A total of 437 chest CT scans were performed, and each patient underwent an average of 3 ± 2 CT scans (range: 1-8). Laboratory investigations, clinical history and epidemiologic characteristics were collected. According to the Chinese Guideline of 2019-nCoV (Trial Version 7), the patients were divided into mild, moderate, severe and critical categories [9].

Image acquisition and evaluation

Chest CT scans were performed on 16- to 64-multidetector CT scanners without intravenous contrast (Philips Brilliant 16, Philips Healthcare, Netherlands; GE LightSpeed 16, GE VCT LightSpeed 64, GE Optima 680, GE Healthcare, USA; Somatom Sensation 64, Somatom AS, Somatom Spirit, Siemens Healthcare, Germany). The CT parameters were as follows: tube voltage 120kVp, automatic tube current modulation 30-300 mA, and slice thickness reconstructions 0.6–3.0 mm.

Image analysis was performed by two cardiothoracic radiologists with approximately 10 years of experience each and final decisions were determined by consensus. For RHS, the number, location, shape, wall appearance were analyzed. Wall appearance was classified as smooth, nodular, or irregular based on the publication of Menna et al [10]. Other parenchymal abnormalities include GGO, consolidation and linear opacity were also recorded.

Statistical Analysis

Continuous variables were expressed as means and standard deviations, while categorical variables were expressed as frequency and percentages. Differences between groups were analyzed by Chi-square test (for categorical data) or independent t-test (for continuous data). SPSS 18.0 was used for the statistical analyses and the results were considered significant at $p<0.05$.

Results

Patient demographics

Demographic information and clinical characteristics were demonstrated in Table 1 and no significant differences were found between groups were identified. RHS was observed in 37 (25.2%) of 147 patients. According to the guideline of 2019-nCoV, all patients were divided into four groups: mild (n=2), moderate (n=99), severe (n=40) and critical (n=6).

CT imaging findings

31 (31.3%) of 99 patients had RHS in moderate group and 6 (13.0%) of 46 patients had RHS in the severe and critical group. There was significant difference between the two groups ($P=0.019$). The average duration from symptom onset to appearance of RHS on CT was 10 ± 6 days, ranging from 2 to 24 days. Time from symptom onset to appearance of RHS in patients with moderate disease was 9 ± 5 days, earlier than in those with severe/critical disease (14 ± 8 days). Although that difference did not reach statistical significance ($P=0.074$), a trend was noted (Figure 1). In most patients (29, 78.4%), RHS appeared within 2 weeks of disease onset.

In total, 64 RHSs were identified (22 patients had one lesion; 14 patients had two lesions and 1 patient presented with multiple lesions). RHS was found mainly in the lower lobe (52, 81.2%). The majority of the lesions with RHS (55, 85.9%) were in the peripheral zone with a round or oval shape. The ring of RHSs were smooth in 54 (84.4%), irregular in 10 (15.6%) and no case had a nodular borders. The follow-up CT scans of 27 patients (50 lesions) showed resolution in 4 patients (5 lesions) within 12-26 days. In addition, follow-up CT scans 2-36 days later showed 26 lesions in 9 patients evolved into pure GGO (Figure 2 and 3), 11 lesions in 8 patients evolved into linear opacity and 1 lesion evolved into GGO and linear opacity. However, 7 lesions in 5 patients were unchanged after 2-11 days on follow-up CT. Other major image features include GGO, consolidation, and linear opacity are detailed in table 3.

Discussion

In our study, the CT RHS was recognized in 37 (25.2%) of 147 patients with confirmed COVID-19 pneumonia. The majority of lesions appeared within two weeks after symptom onset and RHS is more common in patients with moderate disease than severe or critical disease. The lesions were more common in the peripheral aspect of lungs in lower lobes. This distribution is similar to the distribution of ground glass and consolidative opacities in patients with COVID-19 pneumonia [2]. All the RHSs were round or oval shaped. Associated major parenchymal abnormalities included consolidation and GGO and linear opacities. Our data demonstrated the frequency and morphological characteristics of the RHS in the COVID-19 pneumonia.

Although RHS has been described in many pulmonary diseases, previous studies have proposed some useful RHS imaging features for differential diagnosis. For example, triangular shape of RHS was

described in pulmonary infarction [11], and nodular walls or nodules inside the halo often indicates granulomatous diseases [12]. Similarly, the presence of reticulation inside the lesion, a thicker rim, and associated pleural effusion strongly suggest the diagnosis of fungal pneumonia [13]. However, these characteristics were not observed in our case series. The RHS observed in COVID-19 pneumonia seem to be associated with organizing pneumonia pattern with associated GGO or consolidation as described in other studies [5]. It is noteworthy to mention that organizing pneumonia pattern has also been reported in the chest CT findings of patients with influenza A (H1N1) and Middle East Respiratory Syndrome (MERS-CoV) respectively [14,15].

In our study, RHS mostly appeared within 5-9 days after symptom onset in patients with moderate disease, earlier than those reported by Bernheim et al., who observed the sign in the late stage of 6-12 days [8]. Moreover, we have observed more RHSs in the moderate group than severe and critical group. As severe patients are more likely to demonstrate diffuse heterogeneous consolidation with GGOs in both lungs, and even with a white lung appearance [16]. Furthermore, follow-up CT scans showed 86% of RHS lesions gradually resolved or developed into GGO and linear opacities which reflect a similar process of evolution in radiographic improvement reported by Shi, et al [17]. All of these findings suggest that RHS may be a favorable prognostic sign. The other 14% of lesions remained unchanged, which may be related to a shorter time interval between CT scans. Given that RHS appeared several days after disease onset, it may not be due to direct lung injury from SARS-CoV-2 but instead signals the reparative process.

Our study does have limitations. First, our sample size is small, particularly for patients in severe and critical groups. CT images were difficult to obtain in patients in intensive care unit due to their reliance on mechanical ventilation therapy and unstable clinical condition. Second, longer term CT follow up would be required to monitor evolution of CT findings in patients with more severe disease, assess for possible evolution into fibrosis, and to clarify relationship of RHS with eventual clinical outcome.

In conclusion, RHS has been considered a valuable imaging finding in several infectious and non-infectious pulmonary diseases. Our study demonstrated that RHS occurred sooner after symptom onset and with higher frequency in patients with moderate disease compared to those with severe or critical disease. Majority of RHS lesions resolved or significantly improved on subsequent CT. Hence, RHS may signal a reparative process and represent a favorable imaging marker in COVID-19 pneumonia.

Abbreviations

RHS Reversed halo sign

OP Organizing pneumonia

GGO Ground glass opacities

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Tables

Table 1 Patient demographics

Characteristic	Patients with RHS(n=37)	Patients without RHS(n=110)	P value
Age(yr)^a	45.7±16.9	50.0±15.0	0.150
Exposure history			
Recent travel to Wuhan	24(64.9)	67(60.9)	0.271
Contact with infected patient	7(18.9)	33(30)	
Unknown exposure	6(16.2)	10(9.1)	
Initial symptoms			
Fever	33(89.2)	91(82.7)	0.349
Cough	21(56.8)	64(58.2)	0.879
Expectoration	8(21.6)	26(23.6)	0.801
Fatigue	8(21.6)	15(13.6)	0.247
Chest distress and/or shortness of breath	8(21.6)	22(20)	0.832
Muscle soreness	2(5.4)	6(5.5)	0.991
Headache	3(8.1)	4(3.6)	0.510
Nausea and/or vomiting	0(0.0)	1(0.9)	1.000
Diarrhea	1(2.7)	4(3.6)	1.000
No obvious symptoms	1(2.7)	4(3.6)	1.000
Laboratory testing on admission ^b			
White blood cell count (-,↑,↓)	26(70.3),1(2.7),10(27.0)	74(67.3),9(8.1),27(24.5)	0.515
Lymphocyte count (-,↑,↓)	26(70.3),1(2.7),10(27.0)	62(56.4),2(1.8),46(41.8)	0.274
Percent lymphocytes (-,↑,↓)	21(56.8),2(5.4),14(37.8)	60(54.5),5(4.5),45(41.0)	0.936
Percent neutrophilic granulocyte (-,↑,↓)	24(64.9),10(27.0),3(8.1)	65(59.1),34(30.9),11(10)	0.820
Percent monocytes (-,↑,↓)	25(67.6),10(27.0),2(5.4)	80(72.7),26(23.6),4(3.6)	0.800
Hemoglobin (-,↑,↓)	26(70.3),4(10.8),7(18.9)	80(72.7),7(6.4),23(20.9)	0.667
Creatine kinase (-,↑,↓)	31(83.8),2(5.4),4(10.8)	89(80.9),10(9.1),11(10)	0.776
C-reactive protein (-,↑,↓)	16(43.2),21(56.8),0(0.0)	47(42.7),63(57.3),0(0)	0.956

Note: Unless otherwise indicated, data are reported as the number of patients, with percentages in parentheses.

a, data are reported as the mean±standard derivation.

b, -, ↑, ↓ represent within, above, and below normal ranges of laboratory results, respectively. Normal ranges of white blood cell count, lymphocyte count, percent lymphocytes, percent

neutrophilic granulocyte, percent monocytes, creatine kinase, and hemoglobin, C-reactive protein were 3.5-9.5×10⁹/L, 1.10-3.20×10⁹/L, 20-50%, 3.0-10.0%, 40-75%, 13-35 U/L, 40-200 U/L, 0-10 mg/L, respectively.

Table 2 RHS characteristic of 37 patients with COVID-19 pneumonia

RHS characteristic	Number (%) of RHSs (n=64)
Distribution of lesions	
Peripheral	55(85.9%)
Central	9(14.1%)
Involved lung lobes	
Right upper lobe	6(9.4%)
Right middle lobe	2(3.1%)
Right lower lobe	26(40.6%)
Left upper lobe	4(6.3%)
Left lower lobe	26(40.6%)
Shape	
Round	45(70.3%)
Oval	19(29.7%)
RHS ring	
Smooth walls	54(84.4%)
Nodular walls	0(0%)
Irregular	10(15.6%)

Abbreviations: RHS = reversed halo sign.

Table 3. CT findings of other parenchymal abnormalities

Other CT findings	Number (%) of patients (n=37)
GGO, consolidation and linear opacity	17(45.9%)
GGO and consolidation	10(27.0%)
GGO and linear Opacity	4(10.8%)
Consolidation and linear opacity	4(10.8%)
Consolidation	2(5.4%)
Air bronchogram	23(62.2%)
Crazy-paving	6(16.2%)
Discrete pulmonary nodules	2(5.4%)
Pleural thickening	2(5.4%)

Figures

Figure 1

Time from symptom onset to appearance of RHS on CT in different disease severity groups. n=number of patients in each disease severity group.

Figure 2

32-year-old woman with moderate COVID-19 pneumonia. A, B initial CT obtained on day 1 after symptom onset shows small foci of consolidation in the left lower lobe (curved and straight arrows) . C, D CT on day 10 after symptom onset shows subtle GGO surrounded by a ring of consolidation consistent with reverse halo sign (curved and straight arrows). E, F CT obtained on day 25 shows significant decrease in density of both lesions into faint GGO.

Figure 3

32-year-old man with severe COVID-19 pneumonia. A, B, C initial CT on day 4 after symptom onset shows multiple lesions with reversed halo sign (arrows). D, E, F CT obtained on day 42 after symptom onset shows near complete resolution of all lesions.