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Organizing pneumonia-like pattern in COVID-19

Abstract

Introduction: Organizing pneumonia (OP) is a radio-histologic pattern that forms in response to lung damage in patients with focal or diffuse lung injury. OP is frequently observed subsequent to viral-induced lung damage and is associated with a diverse range of clinical outcomes.

Material and methods: We included 210 patients (mean age: 55.8 ± 16.5 years old; 61% male) with mild Coronavirus disease 2019 (COVID-19) who underwent chest computed tomography (CT) from 25 February to 22 April, 2020. The patients were divided into two groups based on the presence (n = 103) or absence of typical OP-like pattern (n =107) on initial chest CT. The extent of lung involvement and final outcome was compared across the two groups. Serial changes in imaging were also evaluated in 36 patients in the OP-group with a second CT scan.

Results: Duration from symptom onset to presentation was significantly higher in the OP group (7.07 ± 3.71 versus 6.13 ± 4.96 days, $p = 0.008$). A higher COVID-19-related mortality rate was observed among patients with OP-like pattern (17.5% vs 3.7%, $p = 0.001$).There was no significant difference in the overall involvement of the lungs ($p = 0.358$), but lower lobes were significantly more affected in the OP group ($p < 0.001$). Of the 36 patients with follow-up imaging (mean duration of follow-up = 8.3 ± 2.1 days), progression of infiltration was seen in more than 61% of patients while lesions had resolved in only 22.2% of cases.

Conclusions: Our observation indicates that physicians should carefully monitor for the presence of OP-like pattern on initial CT as it is associated with a poor outcome. Furthermore, we recommend interval CT to evaluate the progression of infiltrations in these patients.

Key words: COVID-19, computed tomography, organizing pneumonia, respiratory, lung

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Introduction

Organizing pneumonia (OP) is a radio-histologic pattern which forms in response to lung damage in patients with focal or diffuse lung injury [1]. As it has previously been documented in H1N1 influenza, SARS-CoV and MERS-CoV, viral pneumonia is one of the many etiologies of secondary OP [2–4]. A diverse entity of clinical outcomes is seen in patients with OP-like pattern, ranging from complete clearance of lesions without any sequela to severe and progressive conditions such as pulmonary fibrosis [5]. Here, we briefly report the imaging findings and prognosis of Coronavirus disease 2019 (COVID-19) in patients with and without OP-like pattern on initial computed tomography (CT). Also, the serial changes of imaging findings are reported in a subset of patients with OP-like pattern.

Materials and methods

We retrospectively enrolled 210 adult patients (> 18 years old) with PCR-confirmed diagnosis of COVID-19 who underwent CT in a single institution from 25 February to 22 April,

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2020. All subjects had mild disease at presentation and did not require ventilation support. Demographic and clinical data and final outcome was collected. All patients had undergone at least one non-contrast CT with reconstructions of the volume at 3 mm to 5 mm slice thickness. OP pattern was defined as: 1) peripheral, bilateral, lower lung predominant multifocal consolidation or even a frequent appearance in all lungs zones and/or 2) peribronchovascular consolidation, which could extend to the subpleural regions in the lower lobes associated with patchy ground-glass opacities (GGO) [6]. Based on the presence or absence of typical OP-like pattern on the initial CT, the patients were divided into two groups: OP group (n = 103) and non-OP group (n = 107). CT images were reviewed by two radiologists blinded to the patients' final outcome. Imaging findings were first interpreted independently based on the Fleischner society nomenclature [7]. Final decision was reached by consensus. To assess the extent of lobar involvement, a score was given based on the percentage of infiltration: 0 (none), 1 (1–5%), 2 (6–25%), 3 (26–49%), 4 (50–75%), and 5 (> 75%). Total lung score was obtained by summing the individual scores of each specific lobe. Temporal changes of imaging on follow-up CT were defined as follows: 1) disease resolution: complete or near-complete resolution of radiologic opacities; 2) disease progression: increased extent of lung infiltration; 3) no change.

Normality tests were used to assess distribution. Categorical variables are reported as frequency (percentages) and continuous variables are expressed as mean (standard deviation (SD)). Continuous data were compared between the groups by using t-test and categorical variables were compared using Chi-square or Fisher's exact test. Statistical tests were performed by SPSS v.23 (IBM Inc., Chicago, IL, USA). P-value < 0.05 was considered statistically significant.

The ethical review board of our institution approved the study (ethics code:IR.SBMU.MSP.REC.1399.083).

Results

The mean age of patients was 55.85 ± 16.52 years old (range: 26–97); 61% were male. Death had occurred in 22/210 patients (10.5%) and the rest were discharged; the COVID-19-related mortality rate was significantly higher in the OP group compared with the non-OP group (17.5% vs 3.7%, p = 0.001). The mean presentation time for the entire cohort was 6.6 ± 4.3 days after symptom onset. This duration was significantly higher in the OP group (p=0.008). Non-adjusted mortality rate was approximately 5.5 times higher in the OP group compared with the non-OP group (Table 1). Peripheral and bilateral lesion distribution was the predominant finding in both groups. The extent of right middle lobe (RML), right lower lobe (RLL) and left lower lobe involvement was significantly different between the two groups (p = 0.001, p < 0.001, p < 0.001, respectively); however, total lung involvement did not differ across the two groups. In both groups, the least amount of involvement was seen in the RML while the RLL and the right upper lobe had the most involvement in the OP and non-OP groups, respectively (Table 1).

Table 2 shows in detail the imaging findings of patients with OP. Sixty-nine percent of patients demonstrated involvement of more than three lobes; higher number of involved lobes was not related to worse prognosis (p = 0.394). Subpleural band-like consolidation (72.8%), GGO (62.3%) and peripheral consolidation (39.8%) were the predominant patterns. Bronchial dilatation (29.1%), peribronchovascular opacities (25.2%) and air space nodules (23.3%) were also common; however, halo sign, bronchiectasis, crazy paving and honeycomb sign were infrequent. In a subset of 36 patients in the OP group who had follow-up CT (mean duration of 8.3 ± 2.1 days; range: 4–50), progression of infiltrations, mostly seen as lower-lobe GGO, was found in more than 61% of patients (Figure 1) and in 22.2% of patients, lesions had obviously resolved (Figure 2).

Discussion

We observed that the mean interval from symptom onset to admission in patients presenting with radiologic OP-like pattern was approximately a week (7.1 ± 3.7 days), and this duration was significantly higher compared with the non-OP group. More importantly, we found that in patients who manifest OP-like pattern at initial imaging, the mortality rate was significantly higher than others, suggesting a possible worse prognosis for these cases. Identifying imaging patterns that reflect more advanced stage of COVID-19 is helpful for selecting the most appropriate therapy and avoiding acute-phase treatments that most probably do not bring benefit to patients [8]. Our study showed that subpleural band-like consolidation, GGO and peripheral consolidation were the most common imaging findings of patients with OP-like pattern. GGO was mostly seen in

Table 1. Comparison of demographic, clinical and radiologic findings across organizing pneumonia (OP) and non-OP groups

	OP group (n = 103)	Non-OP group (n = 107)	P-value
Age, years	61.94 ± 15.98 (29–97)	49.98 ± 15.17 (26–92)	< 0.001
Sex			
Male	63 (61.2)	65 (60.7)	0.532
Female	40 (38.8)	42 (39.3)	
Symptom onset to presentation, days	7.07 ± 3.71 (1–20)	6.13 ± 4.96 (1–30)	0.008
Disease outcome			
Discharged	85 (82.5)	103 (96.3)	0.001
Death	18 (17.5)	4 (3.7)	
Positive smoking history*	3 (2.9)	5 (4.7)	0.382
Comorbidities			
Cardiovascular disease	14 (13.6)	16 (15)	0.845
Hypertension	19 (18.4)	13 (12.1)	0.250
Diabetes	25 (24.3)	20 (18.7)	0.327
Respiratory disease	3 (2.9)	7 (6.5)	0.333
Renal disease	2 (1.9)	2 (1.9)	0.969
Liver disease	2 (1.9)	2 (1.9)	0.969
Malignancy	3 (2.9)	6 (5.6)	0.268
Obesity	5 (4.8)	13 (12.1)	0.058
Other	2 (1.9)	7 (6.5)	0.054
Any comorbidity	47 (45.6)	48 (44.8)	0.911
Lobar score			
Right upper lobe	2.17 ± 0.99 (0–5)	2.06 ± 1.03 (0–4)	0.524
Right middle lobe	1.77 ± 0.98 (0–4)	1.31 ± 1.02 (0–4)	0.001
Right lower lobe	2.89 ± 1.02 (0–5)	1.48 ± 1.05 (0–4)	< 0.001
Left upper lobe	2.17 ± 1.03 (0–5)	1.90 ± 1.03 (0–4)	0.54
Left lower lobe	2.67 ± 1.05 (0–5)	1.76 ± 1.07 (0–4)	< 0.001
Total score	11.72 ± 3.67 (4–22)	10.17 ± 3.16 (3–20)	0.358
Pattern of involvement			
Predominant ground-glass opacification	44 (42.7)	64 (59.8)	0.003
Predominant consolidation	33 (32.1)	34 (31.7)	
Mixed pattern	26 (25.2)	9 (8.4)	
Lesion distribution			
Axial			< 0.001
Central	5 (4.9)	7 (6.5)	
Peripheral	94 (91.3)	53 (49.5)	
Diffuse	4 (3.9)	47 (43.9)	
Bilateral	100 (97.1%)	97 (90.6%)	0.872

Continuous data is represented as mean ± SD (range) and categorical data is reported as frequency (percentage); *Positive smoking history was defined as former or current smoker with ≥ 20 pack/year history of smoking

the upper lobes and was not a common finding of the lower lobes. In fact, lower-lobe GGO was seen in less than 5% of subjects with OP-like pattern. When comparing with the non-OP group, mixed pattern was more frequently observed in patients with OP-like pattern. A previous study investigating temporal CT findings of COVID-19 reported that mixed pattern becomes more frequent at later stages, usually during day 12–17 of the disease course. They also noted that mixed pattern probably suggests the presence of secondary OP [9].

A notable finding of our study was that in more than 90% of patients with OP-like pattern, lesions were distributed peripherally, while in the non-OP group, less than half of cases demonstrated predominant peripheral lesions. This observation is consistent with that of previous studies, reporting peripheral or peribronchial infiltrations as a characteristic finding of OP [10]. Also, single-lobe involvement was seen in about 10% of patients with OP-like pattern, which is relatively similar to the results of a similar study (6.9%) [11].

In general, OP is associated with a relatively good prognosis. In most cases, the damage is mild and the lung undergoes repair without any permanent sequela; however, relapse rates

Table 2. Imaging findings in patients with organizing pneumonia-like pattern

	OP group (n = 103)
Involvement pattern	
Ground-glass opacification	64 (62.3)
Peripheral consolidation	41 (39.8)
Subpleural band-like consolidation	75 (72.8)
Honeycombing	1(0.9)
Crazy paving	1(0.9)
Interstitial fibrosing pneumonitis	15 (14.5)
Traction bronchiectasis	1 (0.9)
Bronchial dilatation	30 (29.1)
Air space nodule	24 (23.3)
Perilobular pattern	3 (2.9)
Halo sign	—
Reversedhalo sign	18 (17.5)
Reticulation	14 (13.6)
Peribronchovascular opacification	26 (25.2)
Number of involved lobes	
1	11 (10.6)
2	21 (20.3)
3	39 (37.9)
4	18 (17.5)
5	14 (13.6)
Findings on follow-up CT imaging (n = 36)	
Lesion resolution	8 (22.2)
Progression of lung infiltration	22 (61.1)
No change	6 (16.6)

Data are represented as frequency (percentage)

can be seen in 13% to 58% of patients [10, 12, 13]. In a recent study on 77 patients with mild COVID-19, OP-pattern was found to be predictive of short-term evolution to severe disease [14]. In our study, after a mean duration of eight days from presentation, progression of lung infiltrations was seen in 61.1% of patients and in less than one-fourth, lesions resolution had occurred. A recent study showed that 60% of cases with COVID-19 displayed improvement on follow-up CT while 40% presented with exacerbation of lesions [11]. Another study reported complete radiological resolution to be 53% at three-week post-discharge [15]. Reports from previous viral pandemics indicate that few months to several years might be needed for pulmonary imaging abnormalities to resolve [16, 17].

Our study was associated with some limitations. First, we did not adjust the mortality rate for other parameters that could possibly affect survival such as the presence of comorbidities or disease severity; thus, the difference in mortality rate between the two groups should be interpreted with caution. Also, we included a small sample size that might bias the results.

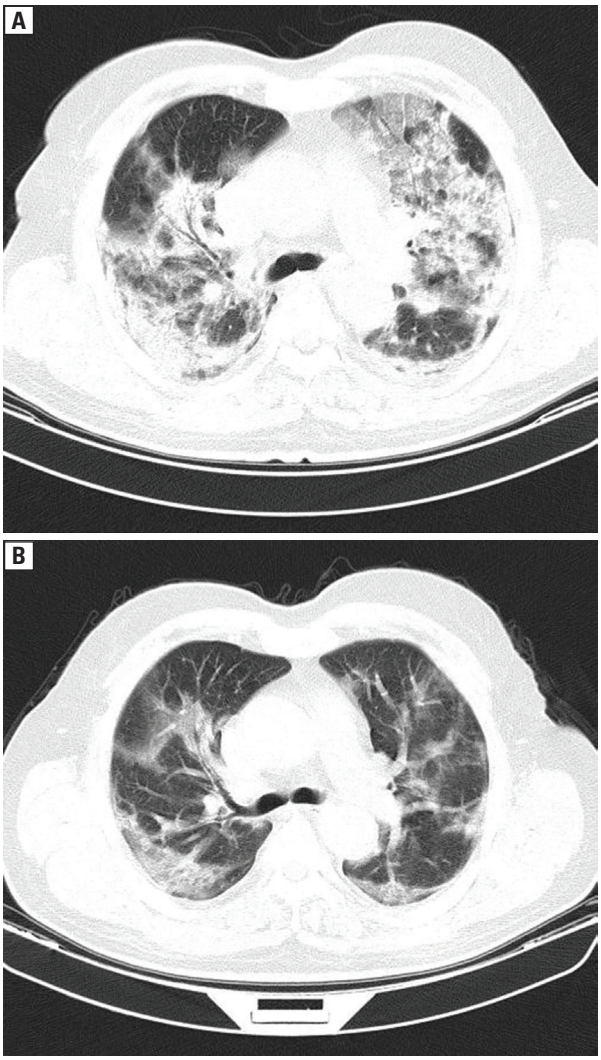

Figure 1. A. Early imaging (at admission) of a 73-year-old man without a positive history for any comorbidity, presenting about 7 days after the onset of respiratory symptoms. Non-enhanced chest CT shows sub-pleural mixed pattern of infiltration. **B.** Follow-up CT scan performed after 8 days shows extensive consolidation and bronchial dilation. The patient recovered after 10 days from admission and was discharged in good clinical condition

Clinical implications and future directions

In the appropriate clinical setting, radiologists should be aware to consider COVID-19 as a differential diagnosis of OP. This is particularly important as we observed a higher mortality rate among patients presenting with OP-like pattern on their initial CT. Also, progression of infiltrations was observed in more than half of these patients on follow-up. Thus, we recommend interval imaging to monitor for progression of pulmonary involvement. Also, increasing recognition of OP diagnosis in patients with COVID-19 will

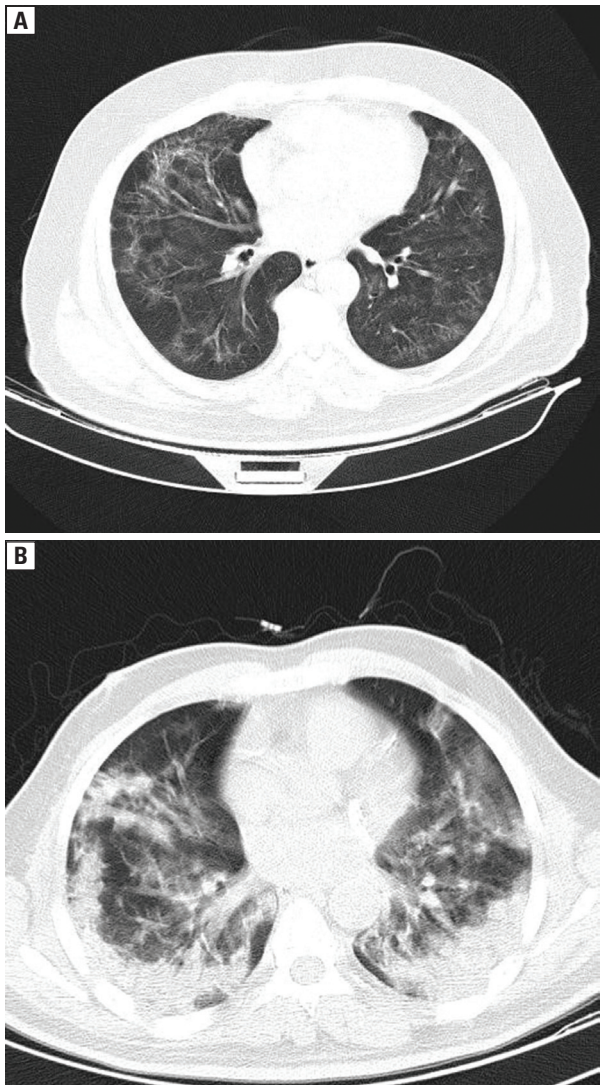

Figure 2. A. Subpleural band-like consolidation in the lung base of a 54-year-old man presenting with acute onset of respiratory symptoms. **B.** Follow-up CT scan performed 50 days later showed ground-glass opacification and innumerable small linear opacities that, by summation, resembled a net-like reticulation pattern appearance

lead to more appropriate and effective treatment approaches, subsequently reducing the need for ventilation support and improving survival.

Conflicts of interest

None declared.

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