The Spectrum of Presentations of Cryptogenic Organizing Pneumonia in High Resolution Computed Tomography

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Payam Mehrian[1AB], **Makhtoom Shahnazi**[2AB], **Ali Ahmadi Dahaj**[1,3ABCEF], **Sorour Bizhanzadeh**[4BF], **Mohammad Ali Karimi**[1,3CDEF]

[1] Chronic Respiratory Disaeses Research Center, National Research Institute of Tuberculosis and Lung Disease, Masih-e-Daneshvari Hospital, Shahid Beheshti Medical University, Tehran, Iran
[2] Department of Radiology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3] Department of Radiology, Masih-e-Daneshvari Hospital, Shahid Beheshti Medical University, Tehran, Iran
[4] Department of Pathology, Masih-e-Daneshvari Hospital, Shahid Beheshti Medical University, Tehran, Iran

Author's address: Ali Ahmadi Dahaj, Department of Radiology, Masih-e-Daneshvari Hospital, Shahid Beheshti Medical University, Tehran, Iran, e-mail: drahmadi78@yahoo.com

Summary

Background: Various radiologic patterns of cryptogenic organizing pneumonia (COP) in X-rays have been reported for more than 20 years, and later, in computed tomography scans. The aim of the present study was to describe the spectrum of radiologic findings on high resolution computed tomography (HRCT) scans in patients with COP.

Material/Methods: HRCT scans of 31 sequential patients (mean age: 54.3±11 years; 55% male) with biopsy-proven COP in a tertiary lung center between 2009 and 2012 were reviewed by two experienced pulmonary radiologists with almost perfect interobserver agreement (kappa=0.83). Chest HRCTs from the lung apex to the base were performed using a 16-slice multi-detector CT scanner.

Results: The most common HRCT presentation of COP was ground-glass opacity (GGO) in 83.9% of cases, followed by consolidation in 71%. Both findings were mostly asymmetric bilateral and multifocal. Other common findings were the reverse halo (48.4%), parenchymal bands (54.8%) and subpleural bands (32.3%). Pulmonary nodules were found in about one-third of patients and were frequently smaller than 5 mm in diameter. Both GGOs and consolidations were revealed more often in the lower lobes.

Conclusions: The main presentations of COP on HRCT include bilateral GGOs and consolidations in the lower lobes together with the reverse halo sign.

MeSH Keywords: Cryptogenic Organizing Pneumonia • Multidetector Computed Tomography • Pneumonia

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Background

Cryptogenic organizing pneumonia (COP) is a non-infectious pneumonia, often a complication of an existing chronic inflammatory disease [1,2]. The clinical features and radiological images resemble infectious pneumonia. However, the diagnosis is suspected if there is no response to multiple antibiotics, and blood and sputum cultures are negative for microorganisms [3–5]. As far as pathological features are concerned, the most intriguing characteristic of the disease is intra-alveolar fibrosis, resulting from organization of inflammatory exudates [6–10]. Once the diagnosis of COP is suspected, obtaining lung tissue for histopathological study is necessary [11]. However, this tool is invasive and accompanied by a high rate of patient dissatisfaction [12,13].

The diagnostic accuracy of thin-section high-resolution computed tomography (HRCT) in a series of studies on patients with COP has been shown to be high: the diagnosis

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Table 1. Frequency (%) of HRCT findigs in patints with cryptogenic organizing pneumonia.

HRCT findings		Sex		Age group		Total
		Male (n=17)	Female (n=14)	30–50 (n=9)	50–70 (n=22)	(n=31)
Ground glass opacities		82.3	85.7	88.9	90.9	83.9
Consolidation		76.4	64.3	77.8	68.2	71.0
Reverse halo		47.0	50.0	55.5	45.5	48.4
Nodules	≤5 mm	41.2	28.6	44.4	31.2	35.5
	>5 mm	17.6	28.5	22.2	22.7	22.6
Parenchymal bands		58.9	35.7	55.5	54.5	54.8
Sub-pleural bands		35.2	28.6	33.3	31.8	32.3
Bronchiectasis		5.9	0.0	0.0	4.5	3.2
Pleural thickening		5.9	7.0	11.0	4.5	3.2

of COP was correct in 79% of cases [14], suggesting that the CT imaging features are characteristic. The three main characteristic imaging patterns of COP include multiple alveolar opacities (typical COP), solitary opacity (focal COP), and infiltrative opacities (infiltrative COP) that can be accurately discriminated by HRCT [15]. However, imaging patterns of COP in HRCT varied in different studies and thus no hallmark radiologic pattern has been introduced yet [16]. On the other hand, various radiologic patterns of COP have been found in X-ray films for more than 20 years, and later, in computed tomography scans [17,18]. The aim of the present study was to describe the spectrum of findings on HRCT scans in patients with COP.

Material and Methods

In this case series, HRCT scans of 31 sequential patients (mean age: 54.3±11 years; 55% male) with open-biopsy-proven COP in a tertiary lung center between 2009 and 2012 were reviewed by two experienced pulmonary radiologists with almost perfect inter-observer agreement (kappa=.83). The radiologists were blinded to the medical history and clinical status of the patients. None of the patients had co-infections or primary or metastatic lung cancer.

Chest HRCTs were performed using a 16-slice multidetector CT scanner (SOMATOM Definition Flash, Siemens Healthcare, Forchheim, Germany). The image acquisition was spaced from the lung apex to the base (1.25-mm collimation at 10-mm intervals) with scan parameters of 120 kVp, 200 mA and scan duration of 3 seconds.

Pathological examinations were performed by an experienced pathologist in all cases. The study was conducted under the approval of the hospital ethics committee.

The results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. For the statistical analysis, the statistical software SPSS version 19.0 for windows (SPSS Inc., Chicago, IL) was used and the comparisons of HRCT findings between subgroups were performed with the use of Chi^2 and Fisher's exact test as appropriate. P values less than 0.05 were considered significant.

Results

The results are summarized in Table 1. The ground-glass opacity (GGO) was found in 83.9% of cases, being the most common imaging finding. That opacity was subpleural in 88.5%, peribronchovascular in 50%, and random in only 3.8% of study subjects. Also, GGO was commonly found in the right lower lobe in 53.8%, followed by the right middle lobe in 50%, left lower lobe in 42.3%, lingula in 42.3%, left upper lobe in 34.6%, and right upper lobe in 15.4% of cases; while in 26.9% it had also a diffuse pattern.

Consolidation was found in 22 patients (71%) and among them: 22 had a subpleural pattern, 10 had a peribronchovascular pattern, and 10 had a halo pattern. Regarding the distribution of consolidation, that feature was more often revealed in the left lower lobe (72.7%) followed by the right lower lobe (68.2%), left upper lobe (45.5%), right middle lobe (31.8%), lingula (31.8%), and right upper lobe (13.6%). Both GGOs and consolidations were bilateral multifocal opacities distributed in an asymmetric pattern.

Other common imaging findings included the reverse halo sign (central lucency or GGO surrounded by a crescent or ring-shaped denser opacity) in 15 patients (48.4%), parenchymal bands in 17 patients (54.8%), and subpleural band in 10 patients (32.3%).

Pulmonary nodules were detected in 35.5% of cases and the nodules were smaller than 5 mm in all 11 patients; associated larger nodules were observed in 7 of those patients, with the following pattern: pleural tag in 2 patients, with a smooth margin in 2 patients, halo margin in 2 patients, and speculated pattern in one of them. Tractional bronchiectasis was revealed in one patient only. Pleural involvement was found in only two patient and it appeared as pleural thickening. Some HRCT findings of COP are shown in Figures 1–3.

Intrathoracic (mediastinal and/or hilar) lymphadenopathy was not found in any patient.
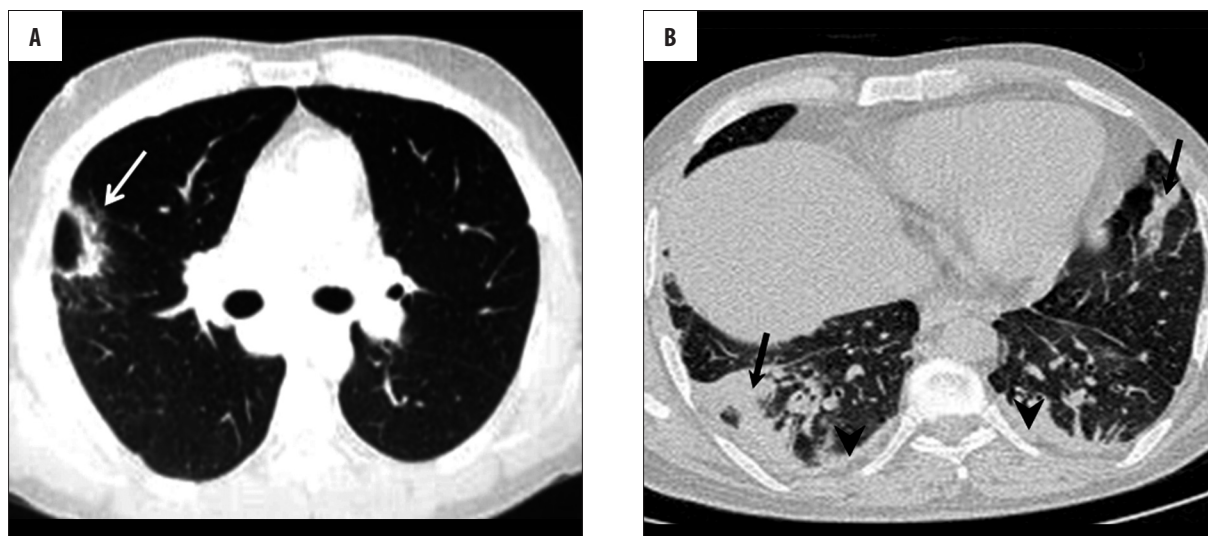
Figure 1. Chest HRCT of a 54-year-old man with COP. (**A**) The reverse halo sign is seen in the right upper lobe as central lucency with a surrounding rim of consolidation and GGO. (**B**) Bilateral focal consolidation in the base of the lungs (arrows) and pleural thickening (arrowheads).
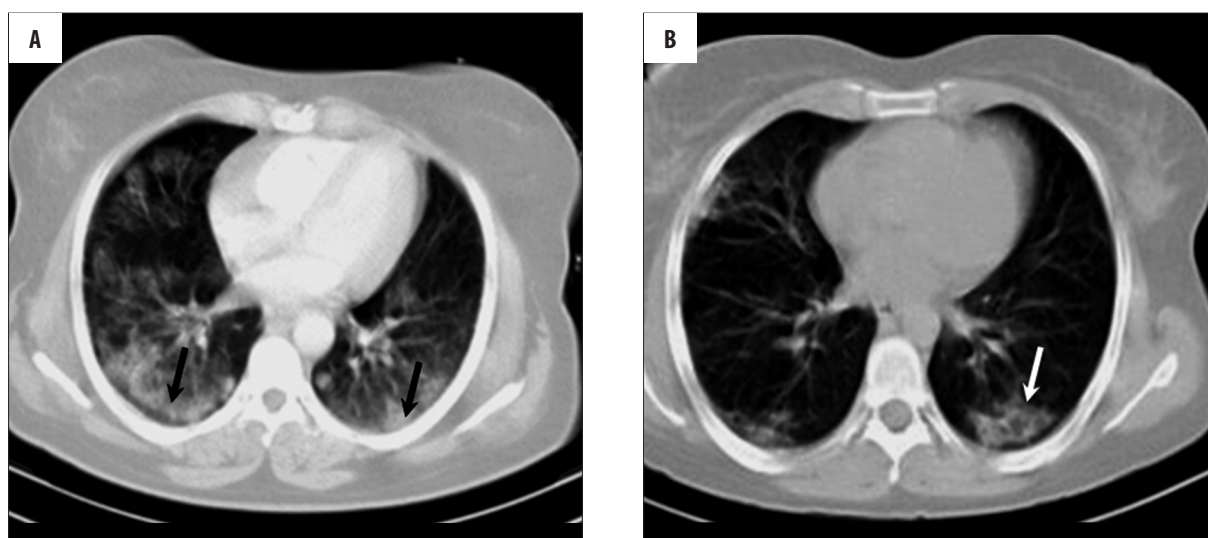

Figure 2. Chest HRCT of two female patients with COP. Bilateral asymmetric ground-glass opacities are seen along with subpleural bands (arrows) in (**A**) and the halo sign is evident in the left lung in (**B**).

There was no statistically significant difference between subgroups divided by age and gender.

Discussion

Since COP may mimic other pulmonary diseases, mostly pneumonia, a correct diagnosis is crucial for patient management; misdiagnosis of pneumonia as COP may result in unnecessary corticosteroid therapy and deterioration of pneumonia. On the other hand, misdiagnosis of COP as pneumonia results in unnecessary antibiotic therapy without any therapeutic effect. We attempted to find a specific HRCT pattern for COP. We revealed that the most common imaging patterns of COP in HRCT were GGO and consolidation. Other common findings were the presence of reverse halo, and parenchymal and subpleural bands; nodules were found in about one-third of patients and were frequently smaller than 5 mm in diameter. The lungs were mostly involved in the lower lobes. Reviewing previous studies

showed controversial findings with respect to HRCT patterns. In a study by Bouchardy et al. [19], consolidation was a prominent finding in 33%, subpleural reticular opacities in 25%, and GGO in only 8% of cases. In the study by Lee et al. [20], the most frequent pattern was consolidation (in 79%), followed by GGO in 60%, and nodules in 30% of cases (they were all distributed diffusely and irregularly). Lamont et al. [21] also found patchy consolidation with linear opacities in 81.8% of patients and GGO in 36.4%. In the study by Greenberg et al. [22], all patients had bilateral airspace consolidation, 75% had small nodules and 37.5% had larger nodules. Xu et al. [23] found consolidation in 80%, GGO in 60%, and nodules in 40% of patients. In another study by Lee et al. [24], two most common abnormal lung patterns on initial scans were ground-glass opacification in 86% of patients followed by consolidation in 77% of patients, distributed along the bronchovascular bundles or subpleural lungs in 59% of them. In their study, the disease disappeared completely in 27% of cases, the disease
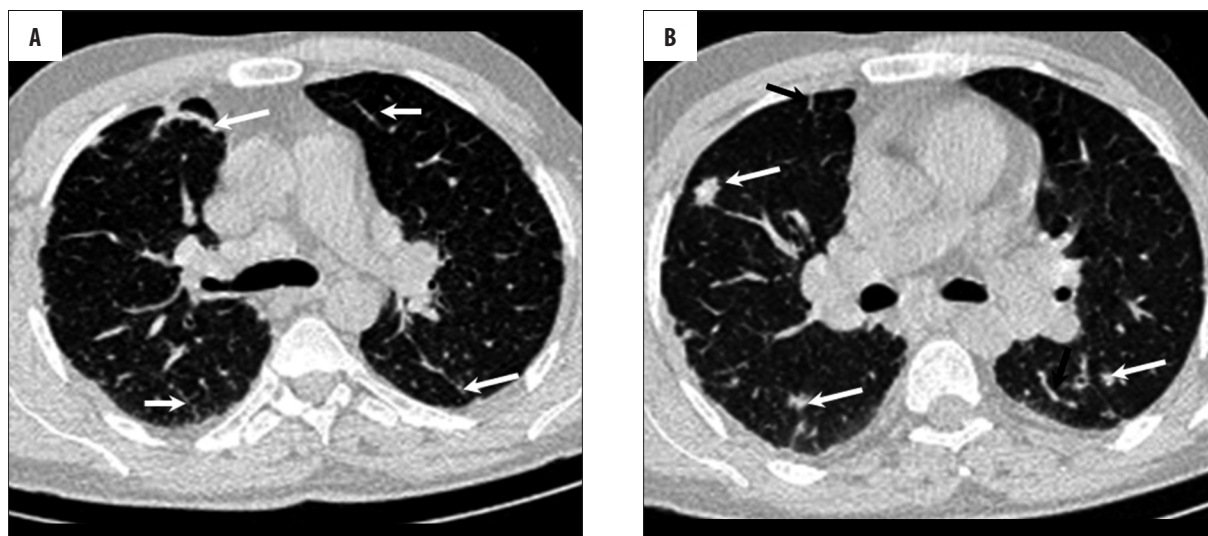
Figure 3. Chest HRCT of a 58-year-old man with COP. (**A**) Multiple bilateral parenchymal and subpleural bands (arrows). (**B**) Bilateral nodules of various size (white arrows) accompanied by subpleural bands (black arrows).

decreased in extent in 68% and also in 15 patients (68%), and no change in its extent was detected on follow-up CT in 5%. It seems that the observed differences in HRCT patterns in different studies may be probably related to the stage of the disease and also to the level of the operator's experience to describe HRCT findings. Furthermore, the sample size of the studies is different; our study was conducted on 31 patients, which is higher than in the majority of previous studies.

The reverse halo is a characteristic sign of COP. In our study, the prevalence of this sign (48.4%) was higher than in the previous studies (up to 25%) [14–16,19–23].

In total, HRCT seems to be a relatively accurate modality for diagnosing COP with hallmarks of GGO and consolidation in the lower lobes along with the reverse halo sign for discriminating from other causes of pneumonia.

Conclusions

The main presentations of COP on HRCT include bilateral GGOs and consolidation in the lower lobes along with the reverse halo sign.

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