

# Clinico-etiological characteristics of organizing pneumonia: A retrospective study

Vikas Marwah<sup>1</sup>, Deepu K Peter<sup>1</sup>, Neeraj Sharma<sup>2</sup>, Saikat Bhattacharjee<sup>3</sup>, Arun Hegde<sup>4</sup>, Divya Shelly<sup>5</sup>, Virender Malik<sup>3</sup>, Gaurav Bhati<sup>1</sup>, Shalendra Singh<sup>6</sup>

<sup>1</sup>Department of Pulmonary, Critical Care and Sleep Medicine, Army Institute of Cardio Thoracic Sciences (AI CTS), Pune, Maharashtra, India, <sup>2</sup>Medical Division, Command Hospital (EC), Kolkata, West Bengal, India, <sup>3</sup>Department of Radiology, Army Institute of CardioThoracic Sciences (AI CTS), Pune, Maharashtra, India, <sup>4</sup>Department of Medicine, Command Hospital (SC), Pune, Maharashtra, India, <sup>5</sup>Department of Pathology, Armed Forces Medical College, Pune, Maharashtra, India, <sup>6</sup>Department of Anesthesia, AFMC, Pune, Maharashtra, India

## ABSTRACT

**Introduction:** Organizing pneumonia (OP) is an idiopathic interstitial pneumonia characterized radiologically by the patchy peripheral areas of ground-glass opacities and consolidation. It is commonly associated with a variety of conditions such as connective tissue diseases (CTD), drugs, infections, malignancy, radiation exposure, post-transplant, and other interstitial pneumonia. There are no specific clinical manifestations unless there is an underlying etiology. We present a series of such cases. **Aims and Objectives:** The aim of the study was to identify the clinical characteristics and etiological spectrum of patients manifesting radiologically with OP pattern. **Materials and Methods:** This was a retrospective analysis of clinico-radiological profile and etiological diagnosis of 23 patients, who had a radiological diagnosis of OP during the period of January 2017–September 2019. **Results:** Our patients presented with nonspecific symptoms of cough, fever, breathlessness, and occasionally with hemoptysis. The various etiologies identified were CTD ( $n = 4$ ), infection ( $n = 2$ ), drugs ( $n = 4$ ), radiation ( $n = 1$ ), chronic aspiration syndrome ( $n = 1$ ), malignancy ( $n = 2$ ), hypersensitivity pneumonitis ( $n = 1$ ), and chronic heart failure ( $n = 2$ ), and in majority ( $n = 7$ ), no underlying etiology was evident and were labeled as cryptogenic organizing pneumonia. **Conclusion:** OP is an underdiagnosed entity and is associated with numerous diseases varying from pulmonary tuberculosis to malignancy. Identification of the underlying disease process is of paramount importance as it enables the treating physician to implement necessary therapeutic interventions.

**KEY WORDS:** Bronchiolitis obliterans organizing pneumonia, cancer-associated organizing pneumonia, cryptogenic organizing pneumonia, drug-induced pneumonitis

**Address for correspondence:** Dr. Saikat Bhattacharjee, Department of Radiology, Army Institute of CardioThoracic Sciences (AI CTS), Golibar Maidan, Pune - 411 040, Maharashtra, India. E-mail: saikatbongo@gmail.com

**Submitted:** 25-Feb-2020 **Revised:** 19-Apr-2020 **Accepted:** 23-Apr-2020 **Published:** 02-Mar-2021

## INTRODUCTION

Organizing pneumonia (OP), formerly known as bronchiolitis obliterans with organizing pneumonia, is a type of interstitial pneumonia characterized radiologically

by the patchy peripheral consolidation. OP is a rare entity with previous studies showing an incidence varying from 1.1 to 7 cases/100,000.<sup>[1]</sup> It is associated with a variety of

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Marwah V, Peter DK, Sharma N, Bhattacharjee S, Hegde A, Shelly D, et al. Clinico-etiological characteristics of organizing pneumonia: A retrospective study. Lung India 2021;38:144-8.

Access this article online	
<b>Quick Response Code:</b> 	<b>Website:</b> <a href="http://www.lungindia.com">www.lungindia.com</a>
	<b>DOI:</b> 10.4103/lungindia.lungindia_105_20

conditions such as connective tissue diseases (CTDs), various drugs, infections, malignancy, radiation exposure, post-transplant, and other interstitial pneumonias. When no underlying pathology is identifiable, the individual is diagnosed as a case of cryptogenic OP (COP) which is found to constitute around 58%–60% of OP.<sup>[1,2]</sup>

Multiple studies on OP have been reported from the West, however experience in our country is sparse spanning mostly case reports and one large series and is still a highly underdiagnosed entity. Review of the Indian literature revealed numerous case reports of OP, however there has been only one case series comprising a total of 34 patients with OP.<sup>[3]</sup> Thirteen years have elapsed since the conduct of this study, and various diagnostic modalities have enabled the identification of secondary causes of OP. This study aims to outline the clinico-radiological profile and to elaborate the various etiological diagnoses in a patient presenting with OP.

## MATERIALS AND METHODS

A retrospective analysis of records of 23 patients presenting to a tertiary care hospital in Maharashtra from January 2017 to September 2019 with radiological features of OP was performed. All patients involved in the study underwent chest radiography and high-resolution computed tomography (HRCT) of the chest. One millimeter thin scans were done in all our patients using a 256-slice computed tomography (CT) scanner (Brilliance ICT, 256 Slice, Philips).

The presence of peripheral patchy consolidation of airspaces with a subpleural distribution and predominance of the peribronchovascular region, which may be unilateral or bilateral with associated nodular opacities and scattered ground-glass opacities (GGOs), with or without the “atoll sign” (area of consolidation with central GGO), was considered suggestive of a radiological diagnosis of OP. Their demographic characteristics, symptoms, laboratory data, serological analysis, sputum analysis, bronchoalveolar results, lung biopsy reports (if available), and follow-up data were collected from the hospital records.

C-reactive protein (CRP), rheumatoid factor, erythrocyte sedimentation rate (ESR), and antinuclear antibodies were done in all the patients. Transbronchial/CT-guided biopsy diagnosis was made only if an underlying etiology was inconclusive after adequate laboratory evaluation of the patient was done. Transbronchial lung biopsy was performed in all patients with COP. Inflammatory exudates in the alveolus, alveolar ducts, and terminal bronchioles with or without the characteristic Masson bodies, which are intraluminal buds of granulation tissue, were considered the pathological finding identifiable as OP.

In the absence of histopathological diagnosis, a multidisciplinary approach based on clinical and

radiological features was used to arrive at a diagnosis. Since it was a retrospective analysis, the ethical committee approval was not obtained.

## RESULTS

In our study, 23 patients with radiological features of OP were included. Table 1 shows the characteristics of the patients involved in the study group. The mean age at presentation was 57 years (standard deviation: 16.64 years, age range: 22–80 years). Ten patients (43%) were male and 13 patients (57%) were female, with a male-to-female ratio of 0.76.

Cough was present in 22 (95.6%) patients, out of which 11 had a history of expectoration. Among the patients with COP, all had cough (seven patients) with five complaining of minimal mucoid sputum production. Nineteen patients (82.6%) complained of dyspnea. Fever was seen in 7 (45.45%) individuals, and weight loss was present in 6 (26%) patients. Chest pain and hemoptysis were seen in 4 (17.4%) and 1 (4.35%) cases, respectively.

In 18 patients (78.26%), ESR was elevated along with a positive CRP. Rheumatoid factor was tested positive in three patients (13%). Nonhomogeneous opacities were visualized in all the chest radiographs. The zone-wise involvement on chest radiography has been depicted in Table 1. On HRCT, 22 patients (95.65%) had consolidation, 10 patients (43.47%) had GGOs, 5 patients (21.73%) had nodules, and mediastinal lymphadenopathy was also seen in 5 (21.7%) of the patients. “Atoll sign” was seen in only four (17.39%) of our patients as shown in Table 2. Bilateral radiologic findings were seen in 22 patients (95.48%). The various etiologies identified are elaborated in Table 2.

All our patients of COP were treated with oral corticosteroids at a dose of 0.75 mg/kg for 4–6 weeks which was later tapered. The patients were followed up for a minimum of a 6-month duration, and the mean follow-up duration was 10.8 months. Only one patient was lost to follow-up in this group. All COP patients had near total to complete resolution of their symptoms and radiological lesions. Patients with OP secondary to CTD, chronic hypersensitivity pneumonitis (HP), radiation, and thalidomide-induced OP were also administered steroids, but there was residual fibrosis at the end of treatment. There was a near-total clinico-radiologic response to steroids in a

**Table 1: Zone-wise involvement on chest radiography in various cases of organizing pneumonia**

Chest Radiograph involvement (n=23)	
Zone	n (%)
Right upper zone	6 (26.08)
Right middle zone	14 (60.86)
Right lower zone	20 (86.95)
Left upper zone	3 (13.04)
Left middle zone	17 (73.91)
Left lower zone	20 (86.95)

**Table 2: Etiology, mode of diagnosis, and outcome of the patients**

Age/Sex	Etiology	Mode of diagnosis	Follow up	Outcome
56/F	Polymyositis	Radiological OP, Elevated CPK, LDH, Positive Muscle biopsy	02 years	Regression of GGO, significant residual fibrosis
36/F	Polymyositis	Radiological OP, Elevated ANA, aldolase, CPK, LDH, Positive Muscle biopsy	01 year	Near complete resolution of consolidation/GGO, minimal fibrosis
45/F	RA	Serological	02 year	Clinico-radiological improvement with oral immunosuppressants
37/F	RA	Serological	02 year	Clinico-radiological improvement with oral immunosuppressants
36/M	Chronic HP	Radiological OP, Bronchoalveolar lavage lymphocytosis 46%, Transbronchial lung Biopsy proven	06 months	Clinical improvement with oral steroids
22/M	Tuberculosis	Biopsy proven	01 year	Total resolution with antituberculous medication
69/M	H1N1	Throat swab H1N1, Radiological OP with atoll sign, CT guided lung biopsy	01 year	Significant resolution with conservative management. After 01 year found to have minimal fibro-bronchiectasis
68/F	Amiodarone	Clinico-radiological	06 months	Withdrawal of inciting drug showed clinical and radiological improvement
62/F	Amiodarone	Clinico-radiological, Atoll sign present	06 months	Withdrawal of inciting drug showed clinical and radiological improvement
79/M	Phenytoin	Clinico-radiological, Atoll sign present	01 year	Withdrawal of inciting drug showed total clinical and near total radiological improvement
53/M	Thalidomide	Clinico-radiological	06 months	Withdrawal of inciting drug showed clinical and radiological improvement. Was also administered oral steroids
67/F	Radiation	Consolidation left lower lobe (Only patient with unilateral involvement)	06 months	Near total resolution after 6 weeks of oral steroids
32/M	Adenocarcinoma lung	CT guided lung Biopsy (Figure 1)	04 months	Died 04 months after diagnosis
67/M	Adenocarcinoma lung	Radiological OP atoll sign present, CT guided Biopsy	06 months	Clinically better on chemotherapy, No radiological deterioration
51/F	Heart failure	Clinico-radiological	01 year	Death
75/M	Chronic aspiration syndrome	Biopsy proven	06 months	Significant clinical improvement with proton pump inhibitors and dietary modifications. Radiological lesions were persistent
70/M	COP	Biopsy proven	01 year	Complete clinico-radiological improvement
60/M	COP	Biopsy proven	01 year	Complete clinico-radiological improvement
65/F	COP	Biopsy proven	01 year	Complete clinico-radiological improvement
65/F	COP	Biopsy proven	06 months	Asymptomatic, Near total radiological resolution
56/F	COP	Biopsy proven	01 year	Complete clinico-radiological improvement
80/F	COP	Biopsy proven	-	Lost to follow up
60/F	COP	Biopsy proven	06 months	Complete clinico-radiological improvement

OP: Organizing pneumonia, GGOs: Ground-glass opacities, COP: Cryptogenic OP, CPK: Creatine phosphokinase, LDH: Lactate dehydrogenase, ANA: Antinuclear antibodies, CT: Computed tomography

young female with polymyositis as well as in patient with radiation-induced OP (RIOP). The patient with chronic heart failure who was scheduled for a heart transplant and the patient with metastatic lung adenocarcinoma died during follow-up. The results of the follow-up of other patients of secondary OP are described in Table 2.

## DISCUSSION

OP is known to have an onset in the fifth or the sixth decades of life, and no difference in age of onset has been observed between cases of COP and secondary OP. In a study conducted by Drakopanagiotakis *et al.*,<sup>[4]</sup> on 61 biopsy-proven OP, the mean age at presentation was  $60.46 \pm 13.57$  years as compared to our study in which the mean age was  $57 \pm 15.77$  years. Ten patients were male and 13 were female, which was unlike other studies which

have reported an equal male and female predominance.<sup>[1]</sup> This disparity might be because of the smaller number of patients included in our study as compared to other studies.

Cough was the predominant symptom seen in 95.6% of our patients and was associated with expectoration in few of them. Expectoration was more commonly observed in the group of patients with COP (71.4%). This is much more than what was previously noted in the only other large Indian study conducted in the year 2008 in which 76% had cough.<sup>[3]</sup> Apart from productive cough, clinical presentation in patients of COP and secondary OP did not have any significant variation, and most of them had nonspecific symptoms. Breathlessness was another common symptom seen in more than 80% of the cases in our study which was also the case in other major series. Fever was, however, seen

in less than one-third of the patients, which was less than what was seen in other studies.<sup>[4]</sup> Hemoptysis and chest pain were comparatively rare symptoms.

ESR and CRP were found to be elevated in 18 (84%) patients, and similar findings have been observed in other studies as well.<sup>[5]</sup>

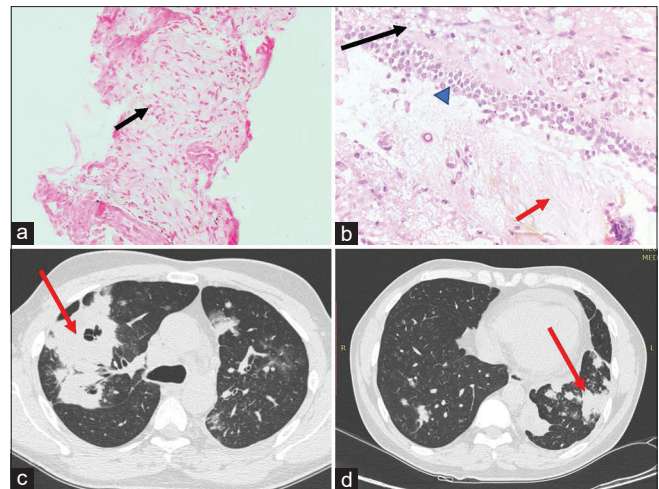
In a study of 129 patients by Johkoh *et al.*,<sup>[6]</sup> the diagnosis of COP was made in 79% patients from the characteristic appearance on thin-section CT. In our study, the predominant radiological finding on both chest radiograph and CT was bilateral patchy peripheral consolidation, and the same has been observed in other studies.<sup>[2]</sup> Chest radiographs showed a prominent middle and lower zone involvement. Multilobar lesions were seen in more than two-third of the patients, with 95.48% showing bilateral lung involvement. Pleural effusion was a rare finding and was seen in a patient with OP secondary to tuberculosis. This was contradictory to what was observed in a study by Vasu *et al.*, in which 60% of patients with secondary OP had pleural effusion.<sup>[7]</sup> Reverse halo sign, which was previously described as a highly specific finding in OP, is generally seen in only one-fifth of the cases of OP,<sup>[8]</sup> but it was seen in 4 (17.39%) of our patients.

CTD were identified in four cases which comprised of two patients with polymyositis and 2 with rheumatoid arthritis (RA). Previous studies have also documented a higher incidence of OP secondary to RA and polymyositis/dermatomyositis among various other CTD.<sup>[9]</sup>

HP was seen in a patient working in a flour mill for the past 8 years. He had dyspnea and radiological features of OP. HP can also manifest as OP; however, it classically presents with GGO, centrilobular nodules, and other signs of fibrosis which predominantly spare the lower lobes.<sup>[10,11]</sup> One patient who underwent radiotherapy for breast cancer presented with RIOP after nearly 6 months. Adenocarcinoma of the lung presented as OP in one of our patients [Figure 1], which was diagnosed on CT-guided trucut biopsy.

Amiodarone, phenytoin, and thalidomide were the culprit drugs identified to cause OP in our patients. Apart from these drugs, others such as nitrofurantoin, busulfan, bleomycin, methotrexate, gold, sulfasalazine, cocaine, and carbamazepine have also been implicated as a causative agent of OP.<sup>[12]</sup> One of our patients who was started on thalidomide for refractory multiple myeloma and developed worsening respiratory symptoms with radiological evaluation revealed features of OP. Thalidomide was stopped, and the patient showed symptomatic improvement along with the regression of opacities on repeat chest CT. Our literature review revealed only one case report from Turkey in which the patient developed OP following the initiation of thalidomide.<sup>[13]</sup>

Patients were diagnosed as COP after exhausting all available diagnostic modalities and with the demonstration



**Figure 1:** Biopsy and computed tomogram of a patient diagnosed to have lung adenocarcinoma. (a) Computed tomography-guided biopsy of the lung shows a single layer of tall neoplastic cells with moderate amount of cytoplasm and hyperchromatic nuclei, lining the alveolar spaces with minimal disruption of the alveolar architecture (black arrow). (b) Endobronchial biopsy shows tissue lined by pseudostratified ciliated columnar epithelium with areas of fibrosis and proliferation of Type 2 pneumocytes (black arrow head), presence of inflammation comprising of foamy macrophages interspersed with neutrophils visualized (black arrow), and large areas of fibrinoid necrosis seen (red arrow). (c and d) Computed tomogram showing multifocal areas of consolidation in a peripheral subpleural distribution

of OP on biopsy. Steroids are the mainstay of treatment of COP, and these patients have been shown to have good clinical and radiological response. Studies have revealed that these patients require a prolonged duration of treatment with tapering doses of steroids as relapses are common,<sup>[14]</sup> however relapse was not noticed in any of our COP patients. Treatment of secondary OP depends on the management of the underlying condition like in the case of CTD-associated OP and would also depend on removing the inciting agent as in cases of drug or RIOP.

## CONCLUSION

The number of cases of OP being reported from tertiary care centers is increasing in view of improved awareness among physicians. OP is a manifestation of multiple underlying etiologies, and identification of the cause enables the treating physician to implement necessary therapeutic interventions.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

- Gudmundsson G, Sveinsson O, Isaksson HJ, Jonsson S, Frodadottir H, Aspelund T. Epidemiology of organising pneumonia in Iceland. *Thorax* 2006;61:805-8.



2. Baque-Juston M, Pellegrin A, Leroy S, Marquette CH, Padovani B. Organizing pneumonia: What is it? A conceptual approach and pictorial review. *Diagn Interv Imaging* 2014;95:771-7.
3. Sen T, Udawadia ZF. Cryptogenic organizing pneumonia: Clinical profile in a series of 34 admitted patients in a hospital in India. *J Assoc Physicians India* 2008;56:229-32.
4. Drakopanagiotakis F, Paschalaki K, Abu-Hijleh M, Aswad B, Karagianidis N, Kastanakis E, *et al.* Cryptogenic and secondary organizing pneumonia: Clinical presentation, radiographic findings, treatment response, and prognosis. *Chest* 2011;139:893-900.
5. Cordier JF. Organising pneumonia. *Thorax* 2000;55:318-28.
6. Johkoh T, Müller NL, Cartier Y, Kavanagh PV, Hartman TE, Akira M, *et al.* Idiopathic interstitial pneumonias: Diagnostic accuracy of thin-section CT in 129 patients. *Radiology* 1999;211:555-60.
7. Vasu TS, Cavallazzi R, Hirani A, Sharma D, Weibel SB, Kane GC. Clinical and radiologic distinctions between secondary bronchiolitis obliterans organizing pneumonia and cryptogenic organizing pneumonia. *Respir Care* 2009;54:1028-32.
8. Kim SJ, Lee KS, Ryu YH, Yoon YC, Choe KO, Kim TS, *et al.* Reversed halo sign on high-resolution CT of cryptogenic organizing pneumonia: Diagnostic implications. *Am J Roentgenol* 2003;180:1251-4.
9. Yoo JW, Song JW, Jang SJ, Lee CK, Kim MY, Lee HK, *et al.* Comparison between cryptogenic organizing pneumonia and connective tissue disease-related organizing pneumonia. *Rheumatology (Oxford)* 2011;50:932-8.
10. Selman M, Pardo A, King TE Jr. Hypersensitivity pneumonitis: Insights in diagnosis and pathobiology. *Am J Respir Crit Care Med* 2012;186:314-24.
11. Silva CI, Churg A, Müller NL. Hypersensitivity pneumonitis: spectrum of high-resolution CT and pathologic findings. *Am J Roentgenol.* 2007;188:334-44.
12. Epler GR. Drug-induced bronchiolitis obliterans organizing pneumonia. *Clin Chest Med* 2004;25:89-94.
13. Gündogan A, Aydogan M, Ozkisa T, Özgür G, Öngörü Ö, Uçar E, *et al.* A case of thalidomide induced organizing pneumonia. *Chest* 2013;144:440A.
14. Cordier JF. Cryptogenic organising pneumonia. *Eur Respir J* 2006;28:422-46.