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Cryptogenic Organizing Pneumonia: A Case Report

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Abstract **Case Report**

Cryptogenic organizing pneumonia (COP) is an uncommon interstitial lung disease characterized by heterogeneous clinical and radiological features, often leading to diagnostic challenges. We report the case of a 64-year-old patient presenting with exertional dyspnea and initial computed tomography findings suggestive of pulmonary infection. Follow-up imaging demonstrated a characteristic migratory pattern of pulmonary lesions, combining ground-glass opacities and bilateral consolidations with temporal fluctuation. The absence of identifiable infectious, neoplastic, or systemic causes, together with the migratory nature of the lesions, supported the diagnosis of organizing pneumonia of cryptogenic origin. Initiation of corticosteroid therapy resulted in rapid clinical improvement and complete radiological resolution. This case underscores the pivotal role of serial imaging in identifying lesion migration, a key feature suggestive of COP. It also highlights the importance of thoroughly excluding secondary causes before establishing the diagnosis. Early recognition and appropriate management are generally associated with a favorable prognosis.

Keywords: Cryptogenic organizing pneumonia, Interstitial lung disease, Migratory pulmonary infiltrates, Corticosteroids, Computed tomography, Differential diagnosis.

1. INTRODUCTION

Organizing pneumonia has been recognized as a distinct pathological entity since the 1980s [1,2]. Previously referred to as bronchiolitis obliterans organizing pneumonia (BOOP), it is a rare interstitial lung disease affecting men and women equally, typically occurring between the fifth and sixth decades of life, with no established association with smoking [4].

Advances in histopathology and medical imaging have significantly improved the understanding and characterization of this condition over recent decades [3].

However, organizing pneumonia often presents with nonspecific and heterogeneous clinical and radiological features, which frequently leads to a delayed diagnosis after symptom onset.

This diagnostic complexity is further compounded by the existence of an idiopathic form, termed cryptogenic organizing pneumonia (COP), as well as multiple secondary forms related to underlying infections, drug exposure, or systemic diseases [5].

2. OBSERVATION

Observation (07/07/2023)

A 64-year-old male patient with a history of arterial hypertension and treated depression presented with progressive exertional dyspnea classified as stage III according to the Sadoul scale.

Clinical examination

The patient was hemodynamically stable. Pulmonary auscultation revealed bilateral fine crackles.

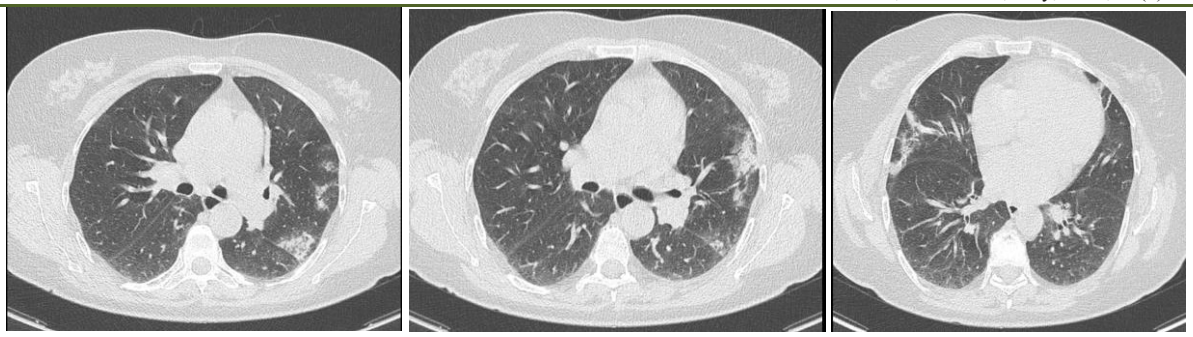


Figure 1: Thoracic imaging demonstrating a bilateral interstitial syndrome with basal predominance. Computed tomography (CT) of the chest reveals ground-glass opacities associated with bilateral areas of consolidation, more pronounced in the upper lobe (culmen) and lingular segments, suggestive of an infectious etiology.

Impression

Findings are consistent with a pulmonary process of probable infectious origin.

Management

Appropriate antimicrobial therapy was initiated, with recommendation for clinical and radiological follow-up to assess evolution.

Observation (19/10/2023)

The patient was re-evaluated during follow-up computed tomography performed for persistent dry cough associated with exertional dyspnea, without any extra-thoracic symptoms.

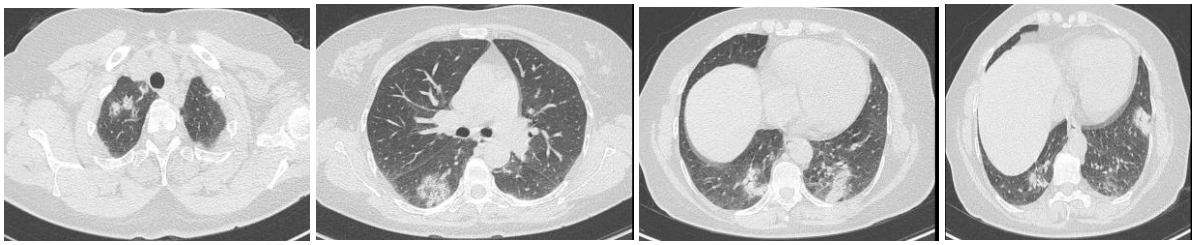


Figure 2: Chest CT scan showing marked evolution of pulmonary lesions, with complete resolution of the previously described nodular intra-parenchymal and subpleural ground-glass opacities, particularly at the right apex and within both lower lobes. A significant decrease in the number of residual lesions is also noted.
In contrast, a new arcuate consolidation is identified in the posterior basal segment of the right lower lobe, surrounded by a peripheral ground-glass opacity.

Observation (07/12/2023)

The patient was reassessed five months after the initial episode due to persistence of the same symptoms, mainly exertional dyspnea.

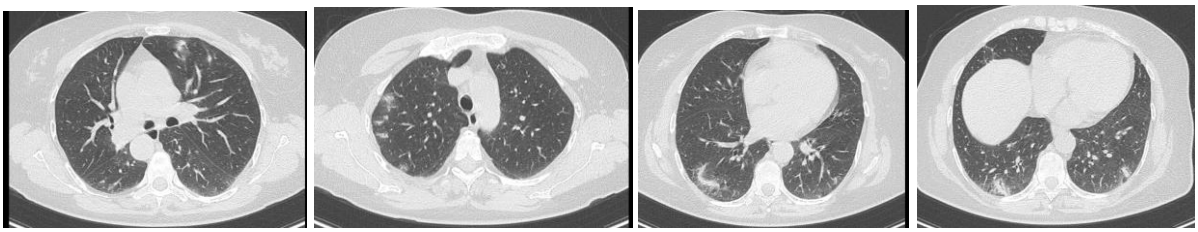


Figure 3: Chest CT scan showing partial regression of previously described bilateral, asymmetrical nodular and patchy ground-glass opacities.
In addition, new ground-glass opacities are identified in different pulmonary locations, indicating a migratory pattern of the lesions.

The radiological evolution is characterized by partial regression of the initial lesions associated with the appearance of new opacities in different pulmonary territories, suggesting a non-resolving and migratory process.

Management / Impression

The presence of migratory lesions with a peripheral consolidation pattern strengthens the suspicion of organizing pneumonia.

Observation (23/02/2024):

The patient was re-evaluated after initiation of appropriate corticosteroid therapy following a confirmed diagnosis of organizing pneumonia.

Conclusion

A favorable outcome was observed, with complete resolution of radiological abnormalities under corticosteroid treatment, consistent with the diagnosis of organizing pneumonia.

Management

Gradual tapering and continuation of corticosteroid therapy were recommended according to clinical response, along with regular clinical and radiological follow-up.

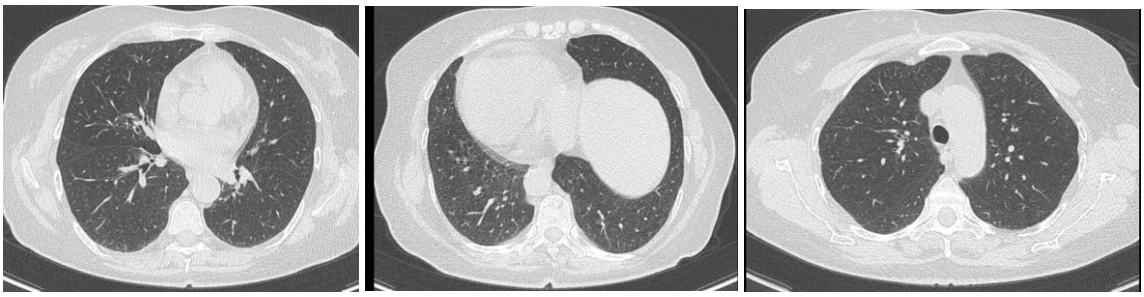
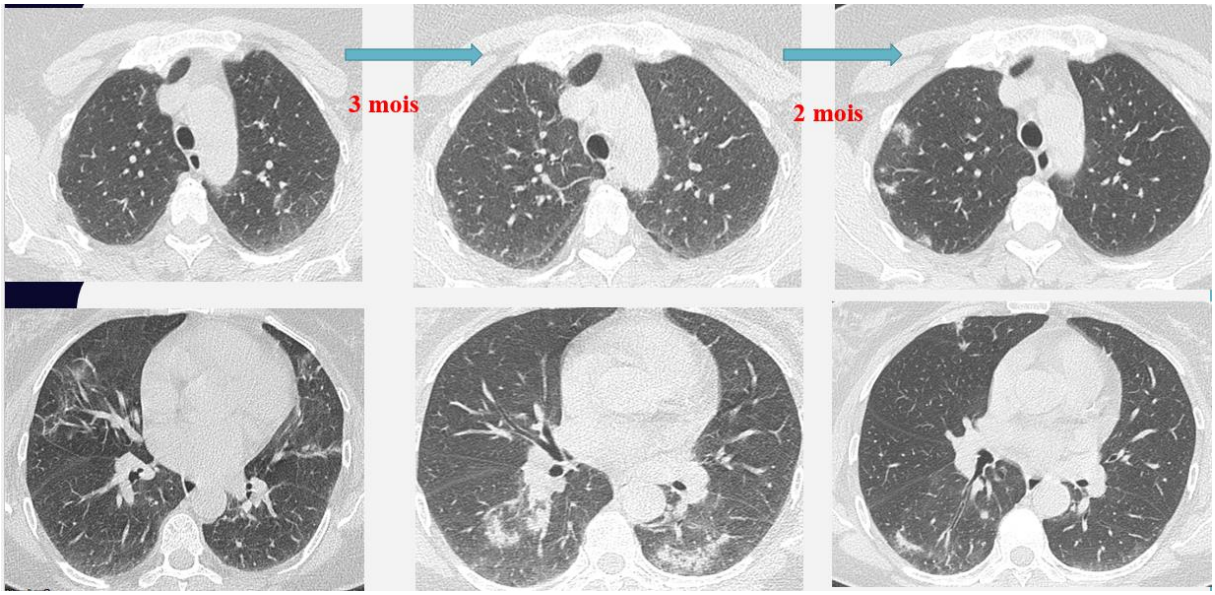


Figure 4: Chest CT scan demonstrating complete resolution of the previously described nodular and patchy ground-glass opacities

There is also complete disappearance of the prior intra-parenchymal and subpleural consolidations.

Key Images (Figure 5) : Representative imaging illustrating the migratory pattern of pulmonary lesions over time, followed by complete radiological resolution after treatment



DISCUSSION

Organizing pneumonia (OP) represents a pattern of lung injury characterized by an excessive and disorganized repair process of the pulmonary parenchyma. It may occur in two main clinical contexts:

- Cryptogenic organizing pneumonia (COP), when no identifiable cause is found
- Secondary organizing pneumonia, when an underlying etiology is identified

Secondary forms have been associated with multiple triggering conditions, including pulmonary infections, drug toxicity, inhalation of toxic substances (e.g., cocaine or industrial gases), gastroesophageal reflux disease, connective tissue disorders, organ transplantation, and prior thoracic radiotherapy [5–8].

Histologically, organizing pneumonia may also coexist with or be associated with other pulmonary pathologies, such as vasculitis, lymphoma, lung cancer [9], hypersensitivity pneumonitis, eosinophilic pneumonia, acute interstitial pneumonia, nonspecific interstitial pneumonia, or usual interstitial pneumonia [5].

Table 1: Etiologies of secondary organizing pneumonia

Etiologies des PO secondaires

- **à une agression pulmonaire**
  - Infection
  - Toxicité médicamenteuse (nitrofurantoine, carbamazépine, amiodarone, interferon)
  - Toxicomanie (cocaïne)
  - Inhalation gaz toxique (sulfure hydrogène, gaz industriel)
  - Collagénose (polymyosite, dermatomyosite)
  - Greffes organes (moelle osseuse)
  - Radiothérapie (parfois à distance de la zone d'irradiation)
- **à une autre pathologie pulmonaire**
  - Vascularites (Wegener)
  - Tumeurs (lymphome, cancer bronchopulmonaire)
  - Infarctus pulmonaire
  - Pneumopathie d'hypersensibilité
  - Pneumonie à éosinophiles
  - Pneumopathies infiltrantes diffuses PIC, PINS, PIA

Although the terms are often used interchangeably, these three entities must be clearly distinguished based on their clinical presentation, radiological features, and prognostic evolution.

In addition, histopathological analysis is no longer considered the sole gold standard for diagnosis, as is the case for other interstitial lung diseases [3]. Currently, an integrated multidisciplinary approach combining clinical, radiological, and biological data is required to establish the final diagnosis and to exclude underlying or associated conditions.

Pathophysiology of organizing pneumonia (OP)

Organizing pneumonia results from an injury to the pulmonary parenchyma. In response, the alveolar epithelium initiates a reparative process characterized by the formation of granulation tissue, similar to cutaneous wound healing [10,11].

Inflammatory cells accumulate within the alveolar spaces and extend into alveolar ducts and terminal bronchioles, leading to the formation of characteristic intraluminal buds of granulation tissue known as *Masson bodies*. These lesions may be associated with an interstitial inflammatory infiltrate, which justifies the classification of OP among interstitial lung diseases [3–5].

Clinical features of organizing pneumonia

Most clinical descriptions in the literature concern cryptogenic organizing pneumonia (COP), as secondary forms may have modified presentations depending on the underlying disease.

COP is an uncommon condition affecting both men and women, typically between the fifth and sixth decades of life, with a slightly higher incidence in non-smokers [12]. The onset is usually subacute, developing over several days to weeks, and characterized by fever, malaise, cough, and progressive dyspnea. These symptoms may be associated with biological inflammatory markers, including peripheral neutrophilia.

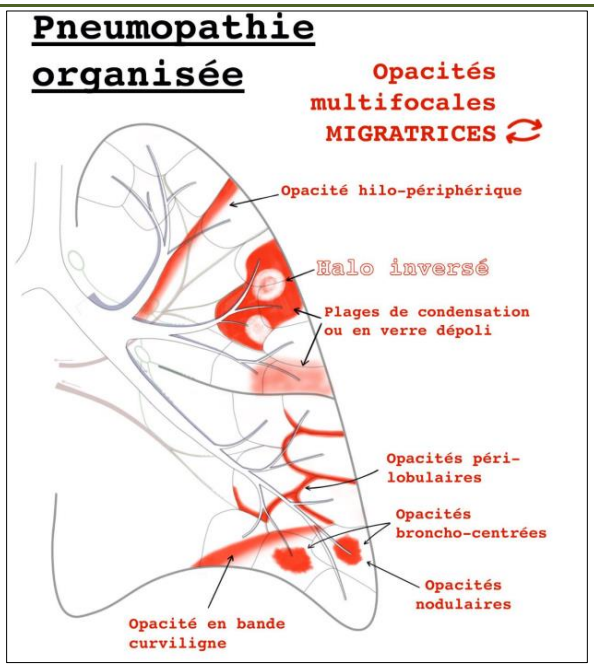
Bronchoalveolar lavage is generally nonspecific but frequently demonstrates lymphocytosis. The disease usually responds well to corticosteroid therapy, with rapid clinical improvement. However, relapses may occur after treatment withdrawal, and in some cases, progression to a chronic fibrosing form has been reported, associated with a less favorable prognosis.

Radiological features of organizing pneumonia

Radiological manifestations of organizing pneumonia are now well established, and recognition of more recently described imaging patterns may allow earlier diagnosis [5]. For clarity and consistency, terminology follows the *Fleischner Society Glossary of Terms for Thoracic Imaging* (2008) [13].

In more than 70% of cases, organizing pneumonia presents as patchy areas of consolidation with a peripheral and subpleural distribution and/or along the peribronchovascular bundles. These abnormalities are often bilateral and asymmetric, with a reported predilection for the lower lobes, although this distribution remains debated in the literature [5,14–16].

These consolidations may be associated with ground-glass opacities and traction bronchiectasis, the latter being potentially reversible under corticosteroid therapy. Air bronchograms can also be observed.



Typical form: multifocal and migratory parenchymal consolidations

A key imaging feature is the dynamic and fluctuating nature of the lesions, with partial spontaneous regression of some opacities and simultaneous appearance of new lesions in different areas of the lung parenchyma.

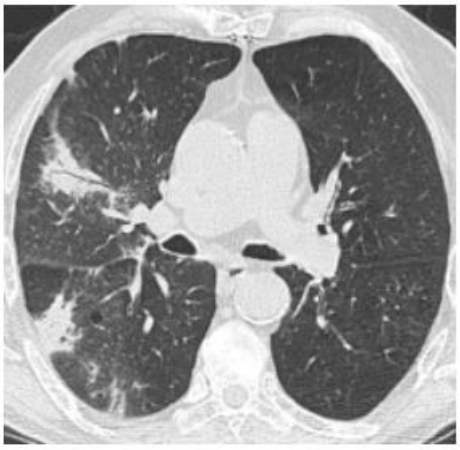


Figure 5: Organizing pneumonia (OP) presenting as multiple subpleural and peribronchovascular areas of consolidation

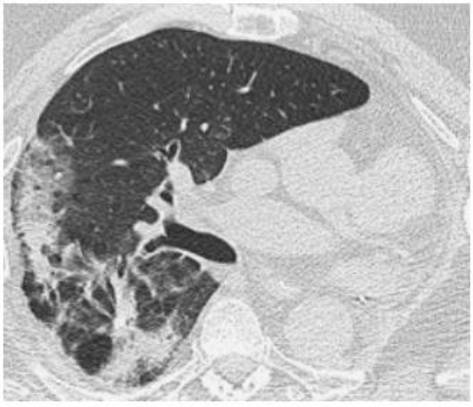


Figure 6: Subpleural areas of consolidation corresponding to two foci of organizing pneumonia (OP)

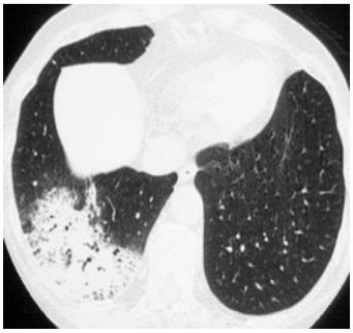


Figure 7: Large posterior basal subpleural consolidation in the right lung, mimicking infectious pneumonia, secondary to organizing pneumonia (OP), with lesion regression following corticosteroid therapy

Diagnostic considerations and differential diagnosis

Several diagnostic hypotheses should be considered when confronted with multifocal parenchymal consolidations. The main differentials include bronchioloalveolar carcinoma, primary pulmonary lymphoma, eosinophilic pneumonia, multifocal infectious pneumonias, alveolar hemorrhage, multiple pulmonary infarcts, alveolar-type sarcoidosis, and ANCA-associated vasculitides, all of which may present with overlapping imaging features [17].

However, the migratory pattern observed on serial CT examinations represents a key discriminating feature. This dynamic evolution significantly narrows the differential diagnosis to a limited group of entities, mainly organizing pneumonia (OP), eosinophilic pneumonia (which may show a similar CT appearance but is often associated with peripheral blood and/or bronchoalveolar eosinophilia), alveolar hemorrhage, and certain vasculitic processes [5].

The presence of additional imaging features suggestive of OP, as detailed below, further increases diagnostic confidence.

Nodular form: single or multiple nodules or masses

Organizing pneumonia may also present as solid nodules, mixed-density lesions (Fig. 5), or more rarely ground-glass nodules (Fig. 6), typically larger than 1 cm in diameter [18]. Their distribution is variable and non-specific: they may be scattered throughout the lung parenchyma (Fig. 7) or follow a peribronchovascular pattern.

In this setting, OP is often not the first diagnostic consideration, particularly when malignancy or infection is suspected. These nodules may display irregular or spiculated margins, making differentiation from neoplastic lesions challenging, especially since OP can demonstrate increased uptake on PET-CT.

In immunocompromised patients, a “halo sign” may be observed, consisting of a solid nodule surrounded by a ground-glass opacity. In this context, invasive pulmonary aspergillosis should be considered as a leading differential diagnosis.

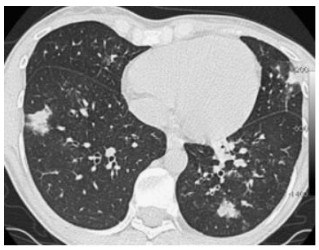


Figure 8: Multinodular form of organizing pneumonia (OP), showing scattered nodules larger than 1 cm in diameter, with migratory behavior and spontaneous resolution

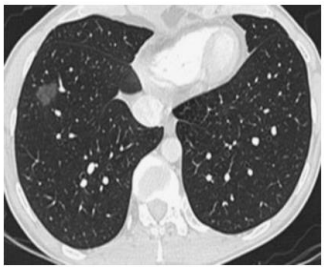


Figure 9: Persistent nodular ground-glass opacity suggestive of adenocarcinoma; organizing pneumonia (OP) confirmed by lung biopsy

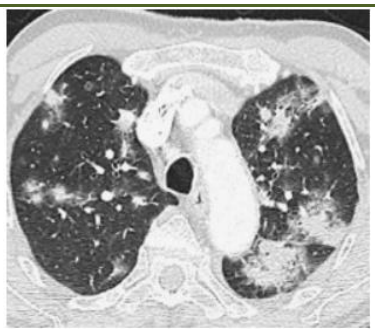


Figure 10: Multiple nodules and areas of parenchymal consolidation surrounded by ground-glass opacities (halo sign), suggestive of angioinvasive aspergillosis in an immunocompromised patient; organizing pneumonia (OP) diagnosed on lung biopsy

Nodular Presentation and Suggestive Radiological Signs

When organizing pneumonia (OP) presents exclusively as nodular lesions, the initial diagnosis may be challenging. However, the identification of a dynamic pattern characterized by fluctuating and migratory lesions, sometimes associated with spontaneous regression, strongly supports this diagnosis.

Atoll Sign (Reversed Halo Sign)

The reversed halo sign, also known as the atoll sign, is defined by a central ground-glass opacity surrounded by a ring or crescent-shaped area of parenchymal consolidation [13]. The margins of this ring may be smooth or, conversely, irregular or spiculated.

Although initially considered relatively specific for organizing pneumonia, this sign has subsequently been described in a variety of other conditions, including ANCA-associated granulomatous vasculitides (such as granulomatosis with polyangiitis), sarcoidosis, certain infections (paracoccidioidomycosis, pneumocystosis, tuberculosis), lipoid pneumonia, and in some post-therapeutic settings, particularly following radiofrequency ablation [19]. In such contexts, its presence may reflect a secondary or associated histopathological pattern of organizing pneumonia.

It is important to differentiate this sign from other ring-shaped opacities with nodular inner margins, typically observed in granulomatous diseases such as tuberculosis and sarcoidosis [20].

Perilobular Opacities

More recently described, perilobular opacities correspond to areas of parenchymal consolidation with ill-defined margins, showing an arcade-like or curvilinear band pattern. These opacities are distributed along the interlobular septa delineating the secondary pulmonary lobule [13] and frequently extend to the pleural surface (Fig. 11).

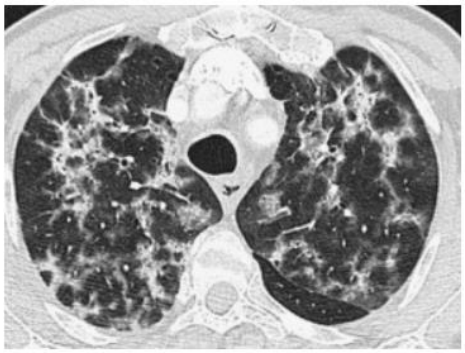


Figure 11: Multiple perilobular areas of consolidation in an arcade-like pattern, characteristic of organizing pneumonia (OP) secondary to amiodarone-induced pulmonary toxicity

Additional Suggestive Imaging Features

Although sometimes subtle, these findings are considered suggestive of organizing pneumonia (OP). In the series reported by Ujita *et al.,*[16], such abnormalities were identified in approximately 57% of cases.

Consolidation Bands

Organizing pneumonia may also manifest as thick consolidation bands with a radial orientation (> 8 mm), extending toward the pleural surface and often containing air bronchograms. This feature helps differentiate them from linear atelectasis [5] (Fig. 11).

Subpleural curvilinear opacities, running parallel to the pleural surface, may also be observed (Fig. 12). Although these patterns can be overlooked, they are highly suggestive of organizing pneumonia.

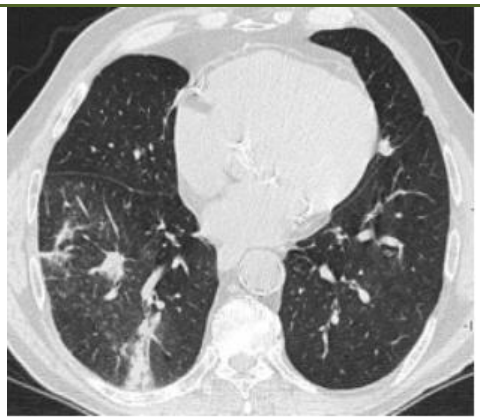


Figure 12: Radial band-like consolidation with air bronchograms, suggestive of organizing pneumonia (OP) and to be distinguished from linear atelectasis, which typically does not contain air bronchograms.

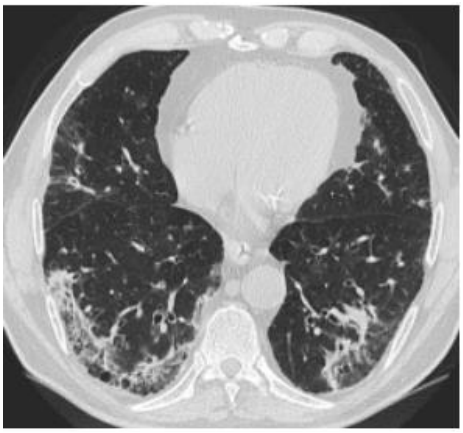


Figure 13: Curvilinear subpleural band of consolidation associated with traction bronchiectasis and architectural distortion, consistent with a fibrosing form of organizing pneumonia (OP).

Crazy-paving sign

Ground-glass opacities adjacent to areas of consolidation are commonly observed. When associated with interlobular septal thickening, they may result in a characteristic "crazy-paving" pattern.

Progressive Fibrosing Pattern

In approximately 25% of cases, organizing pneumonia (OP) may evolve toward fibrotic changes, characterized by subpleural reticulations and persistent architectural distortion, resembling non-specific interstitial pneumonia [5]. These fibrosing forms are generally associated with a poorer clinical outcome.

Organizing Pneumonia: Conceptual Approach and Diagnostic Limitations

The computed tomography (CT) appearance of OP is highly polymorphic. The most common findings include focal consolidations and ground-glass opacities. More specific features include perilobular opacities, the reversed halo sign, and radial consolidation bands containing air bronchograms [5], as well as the characteristic migratory and fluctuating pattern of lesions over time, even in the absence of treatment.

When imaging findings are limited to non-specific nodules or consolidations, alternative diagnoses—particularly neoplastic, infectious, or vascular causes—must be carefully considered before suggesting OP. Conversely, the presence of typical imaging features or a dynamic evolution of lesions strongly supports this diagnosis.

Confirming the cryptogenic nature of OP requires exclusion of any underlying secondary cause. This process relies on complementary investigations, including laboratory testing, bronchoalveolar lavage for infectious assessment, and a detailed clinical history to identify potential environmental, toxic, or drug-related exposures.

In radiation-induced forms, consolidations may develop within the irradiated field (Fig. 13), but can also occur outside this area, including in the contralateral lung. These findings may appear during treatment or several months after its completion.

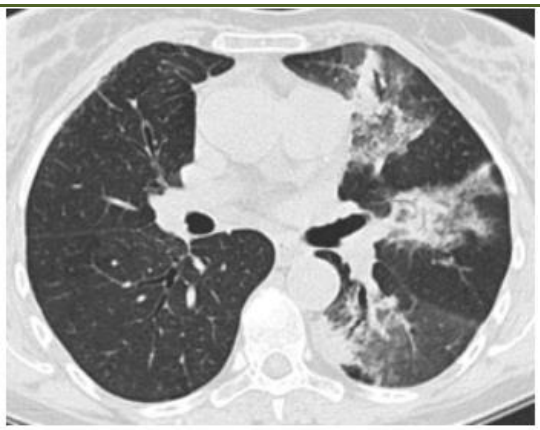


Figure 14: Multifocal areas of consolidation in the left lung within the current radiation therapy field for left breast cancer

Drug-induced organizing pneumonia and histopathological correlations

Organizing pneumonia (OP) is a relatively frequent manifestation of drug-induced lung disease, particularly associated with agents such as nitrofurantoin, carbamazepine, interferons, and amiodarone. In cases of amiodarone toxicity, imaging abnormalities may combine features of OP with diffuse interstitial involvement, sometimes mimicking usual interstitial pneumonia (UIP). Consolidations may appear hyperdense and may be accompanied by increased attenuation of the liver, spleen, and/or thyroid due to drug deposition.

In addition, histological analysis of multiple lung samples from the same patient may demonstrate an OP pattern associated with other interstitial lung diseases, including chronic hypersensitivity pneumonitis, UIP, nonspecific interstitial pneumonia (NSIP), or acute interstitial pneumonia (AIP). In the context of acute respiratory distress syndrome (ARDS), diffuse alveolar damage may also coexist with organizing pneumonia foci [21]. Some authors suggest that diffuse alveolar damage, OP, and NSIP may represent different stages along a continuous spectrum of lung injury and repair [5].

The diagnosis of organizing pneumonia relies on a multidisciplinary approach combining clinical and radiological data, and is supported by histopathological analysis when lung biopsy is performed. In atypical presentations, it is essential to emphasize that histological OP may be idiopathic, secondary to an identified insult, or represent a peripheral reaction to another underlying pulmonary disease. In selected cases, more extensive biopsies are required to avoid missing associated conditions, particularly malignancies or vasculitis.

CONCLUSION

Cryptogenic organizing pneumonia (COP) is a well-defined clinical, radiological, and histopathological entity occurring in an idiopathic context, typically rare, highly responsive to corticosteroid therapy, and associated with a favorable prognosis. However, its diagnosis becomes more complex—and likely underrecognized—when it is secondary or associated with other underlying diseases. Therefore, any atypical presentation should systematically prompt a thorough search for an underlying cause before confirming the diagnosis of COP.

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