Organizing pneumonia: What is it? 
A conceptual approach and pictorial review

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Abstract Organizing pneumonia (formerly named bronchiolitis obliterans with organizing pneumonia or BOOP) is a clinical, radiological and histological entity that is classified as an Interstitial Lung Disease. The understanding of this family of diseases has seen great progress over the past twenty years. CT presentation of organizing pneumonia is polymorphous but a few patterns have been recently recognized as being more specific to this diagnosis. The aim of this work is to summarize new understandings of the clinical and histological presentation of the disease and to review the most relevant CT features.

Introduction

Organizing pneumonia has been described as a pathological entity since the 1980s [1,2] and our now well-established understanding of the disease has continued to deepen through histological and radiological progress [3]. However, various conceptual changes have led to some degree of confusion, partly due to a change in the name of the disease from BOOP (bronchiolitis obliterans with organizing pneumonia) to OP (organizing pneumonia) [4]. The difficulty also lies with the fact that there is an idiopathic form of the disease known as cryptogenic organizing pneumonia (COP), as well as several secondary forms [5].
Definitions

OP is a process of pulmonary tissue repair that can be either:

• cryptogenic;
• secondary to a lung injury such as infection, drug toxicity, inhalation of a pathogen (cocaine), inhalation of toxic gas, gastroesophageal reflux, collagenosis, organ transplant, or radiotherapy [5–8];
• it can be histologically associated with pulmonary lesions of another nature such as vasculitis, lymphoma, lung cancer [9], hypersensitivity pneumonitis, eosinophilic pneumonia, acute interstitial pneumonia, non-specific interstitial pneumonia, or usual interstitial pneumonia [5] (Table 1).

These three different situations share the same terminology, but they need to be distinguished based on their clinical and radiological features and their prognoses.

Histological diagnosis, in the same way as in other interstitial lung diseases, is no longer considered to be the gold standard [3]; it is the review of all available data in a multidisciplinary meeting that will allow the final diagnosis to be made and an underlying or associated aetiology to be excluded.

Pathology of OP

OP is initiated by lung injury: the alveolar epithelium reacts to produce granulation tissue that is similar to that generated during the healing process of a skin wound [10,11]. Inflammatory debris are filling the alveoli and spreading to the alveolar ducts and terminal bronchioles, with characteristic endoluminal buds of granulation tissue known as Masson bodies. These abnormalities can be associated with an interstitial inflammatory infiltrate, which is why OP is classified as an interstitial lung disease [3–5].

Clinical features of OP

In the literature, the descriptions of the clinical picture of OP broadly report the signs of COP, as the symptoms of secondary forms of OP can be clinically influenced by the underlying pathology.

COP is a rare disease that affects both sexes indiscriminately between the ages of 50 and 60 with a relative prevalence of non-smoking patients [12]. Within a few days, the patient develops hyperthermia, malaise, cough, and dyspnoea, all of which can become severe, associated with signs of inflammation and an increase in blood neutrophil levels. Bronchoalveolar lavage is not specific but often shows an increase in lymphocytes. Symptoms regress quickly with steroid therapy but can return when treatment is stopped, or progress into a chronic and fibrosing form with a poorer prognosis.

Radiology of OP

Imaging patterns of OP are well recognized and new characteristic features have recently been described, meaning that an earlier diagnosis of OP is becoming easier to suggest [5].

In order to keep our descriptions succinct, the terms used are in keeping with the definitions of the "Glossary of Terms for Thoracic Imaging" established by the Fleischner Society in 2008 [13].

Classic form: fluctuating multifocal parenchymal consolidation

In over 70% of cases, OP produces focal sub-pleural and/or peribronchovascular consolidation areas, often bilateral and asymmetrical [5,14,15], usually described as predominating

<table>
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<th>Table 1 Aetiologies of secondary organising pneumonia.</th>
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<td><strong>OP secondary to a lung injury</strong></td>
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<td>Infection</td>
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<td>Drug toxicity</td>
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<td>Drug intoxication</td>
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<td>Inhalation of toxic gas</td>
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<td><strong>OP associated with another lung pathology</strong></td>
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<td>Vasculitis (Wegener’s granulomatosis)</td>
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<td>Tumours (lymphoma, lung cancer)</td>
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<td>Eosinophilic pneumonia</td>
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<td>Interstitial lung diseases UIP, NSIP, AIP</td>
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in the lower lobes although some studies do not support this [16] (Figs. 1, 2, 3). This may be associated with ground glass opacities or areas of traction bronchiectasis (reversible under steroid treatment) and there may be an air bronchogram sign. These features are usually migratory, with some abnormalities disappearing spontaneously and new areas of consolidation appearing simultaneously in different sites.

A number of differential diagnoses may be considered when multifocal parenchymal consolidation is present [17]: bronchioloalveolar carcinoma (Fig. 4), primary pulmonary lymphoma, eosinophilic pneumonia, multifocal pneumonia, alveolar haemorrhage, multiple pulmonary infarcts, alveolar sarcoidosis, or ANCA-associated vasculitis, which can all take on a similar appearance. The fluctuating appearance of images over a series of repeat CT scans (Figs. 5a and 5b) is a distinguishing factor because it reduces the list of differential diagnoses to four aetiologies: OP, eosinophilic pneumonia (similar CT features to OP but usually accompanied by raised blood and/or alveolar eosinophilia), alveolar haemorrhage, and vasculitis [5].

If other suggestive features of OP, as described below, are present, they will contribute to greater diagnostic specificity.

Figure 1. OP presenting as multiple areas of sub-pleural and peribronchovascular consolidation.

Figure 2. Sub-pleural areas of consolidation, due to two foci of OP.

Figure 3. Large area of sub-pleural consolidation in the right posterior lung base mimicking an infectious lung disease, secondary to OP. Regression of the lesions on steroid therapy.

Figure 4. Bilateral sub-pleural areas of mixed density combining consolidation and ground glass opacities. No regression of the lesions over a series of repeat studies, leading to the biopsy-confirmed diagnosis of multifocal adenocarcinoma.

Figure 5. Female patient with history of right breast cancer who had undergone radiotherapy and chemotherapy six months previously. a: sub-pleural area of consolidation and ground glass opacity; b: follow-up study three months later. The ground glass opacities have migrated producing a reverse halo sign, in keeping with a delayed onset of OP secondary to the radiotherapy.
Nodular form: solitary or multiple nodules or masses

OP can present in the form of solid, mixed density (Fig. 6), or more rarely ground glass nodules (Fig. 7) that are one centimetre or more in size [18]. The distribution of these nodules is not specific, being scattered (Fig. 8) or peribronchovascular, so the diagnosis of OP will rarely be suggested at first, especially when there is underlying cancer or infection. The nodules may have spiculated borders making distinction from a neoplasm difficult, especially since OP often show increased uptake on PET scan. In an immunocompromised patient, there is sometimes a halo sign (solid nodule surrounded by a ring of ground glass opacity) and in this context, angio-invasive pulmonary aspergillosis is the first diagnosis to consider.

Excavated nodules are rare but may mimic tuberculosis or septic embolism (Fig. 9). In rare cases, OP has a micronodular appearance with milliary opacities or branching “tree in bud” micronodules.

When OP presents in a purely nodular form, the diagnosis is thus rarely made at first, but if lesions are found to fluctuate and migrate, sometimes resolving spontaneously, they become highly suggestive of the diagnosis.

Atoll or reverse halo sign

The reverse halo sign is an area of ground glass opacity surrounded by a crescent or ring of parenchymal consolidation [13] that may present smooth or spiculated borders (Figs. 10 and 11).

It was for a long time considered to be pathognomonic of OP, but this sign has now been described in other conditions such as granulomatous vasculitis associated with ANCA (Wegener’s granulomatosis), sarcoidosis, paracoccidioidomycosis, pneumocystosis, tuberculosis, and lipid pneumonia, as well as a complication of radio frequency
Organizing pneumonia: What is it? A conceptual approach and pictorial review

Perilobular abnormalities

Characterised only recently, perilobular abnormalities present as curved or arcade-like bands of parenchymal consolidation with blurred borders, distributed along the structures that surround the secondary pulmonary lobule [13] and often reaching the surface of the pleura (Fig. 14).

These abnormalities are characteristic and suggest the diagnosis of OP. In a series described by Ujita et al. [16] they were present in 57% of cases although they were often not very pronounced.

Bands of consolidation

Organizing pneumonia can also produce thick radial bands of consolidation (>8 mm) extending towards the pleura, containing an air bronchogram that differentiates them from linear atelectasis [5] (Fig. 15) as well as sub-pleural curvilinear bands of consolidation parallel to the pleura (Fig. 16). These often-misunderstood signs are very evocative of OP.

Crazy-paving sign

The presence of ground glass opacity adjacent to focal areas of consolidation is common and when it is seen in combination with septal thickening, it produces a crazy-paving appearance.

Figure 11. Reverse halo sign, also known as the atoll sign.

Figure 12. Ring of consolidation with micronodular walls associated with areas of branching micronodules secondary to tuberculosis.

Figure 13. Coronal reconstruction of a micronodular ring of consolidation, secondary to tuberculosis.

Figure 14. Multiple areas of perilobular consolidation in an arcade-like pattern, characteristic of OP due to amiodarone lung-toxicity.

Figure 15. Radial band of consolidation containing an air bronchogram suggestive of OP to differentiate from linear atelectasis that usually do not contain air bronchogram.
Progressive fibrotic pattern

In approximately a quarter of cases, OP produces areas of sub-pleural reticulation and persistent architectural distortion that have a similar appearance to findings in non-specific interstitial pneumonia [5]. These fibroing forms appear to convey a poorer prognosis.

Organizing pneumonia: conceptual approach and uncertainties

The appearances of OP on computed tomography are polymorphic, and the most common features are areas of focal consolidation and ground glass opacities. The most specific signs are perilobular abnormalities, reverse halo sign, radiol bands of consolidation containing an air bronchogram (5) as well as evolution and migration of the lesions over time, even in the absence of treatment. If nodules or areas of non-specific consolidation are seen, other aetiologies such as cancer, infection, or vascular causes must of course be investigated before a diagnosis of OP can be made. However, when these features are found together with more specific signs, or when the lesions fluctuate, the diagnosis of OP can easily be suggested.

To assess whether OP is cryptogenic, the aetiologies that can commonly be associated with this condition need to be excluded, and this will require additional investigations including blood tests, BAL to look for infection, and a detailed patient history that covers environmental exposure, toxins and treatments.

If OP is secondary to radiotherapy, consolidation may be found either in the irradiated area (Fig. 17) or outside it, including in the contralateral lung. It may appear while radiotherapy is ongoing or several months after the end of the treatment.

OP is a relatively common pattern in drug-induced lung disease, especially with products based on nitrofurantoin, carbamazepine, interferon, and amiodarone. In amiodarone toxicity, abnormalities can include OP with more diffuse interstitial lesions producing a clinical picture of UIP; the areas of consolidation in this case sometimes appear to be of increased density, and are often combined with increased density of the liver, spleen and/or thyroid parenchyma.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


