Organizing pneumonia: Typical and atypical CT manifestations of a great mimicker in chest radiology

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Objectives

To present an overview of the spectrum of typical and atypical CT findings in organizing pneumonia (OP) and to discuss the most important differential diagnoses.
Organizing pneumonia (OP) is one of the main reparative reactions to various forms of acute lung injury. It is noninfectious and nonneoplastic but is considered a distinct histologic pattern based on the incomplete resolution of the inflammation mainly occurring in the alveoli and to a lesser extent in the distal bronchioles\textsuperscript{1}.

**Histopathology**

The term bronchiolitis obliterans organizing pneumonia was previously used for this condition but was considered inaccurate by the ATS/ERS, since the majority of the pathology is localized mainly in the airspaces and distal airways\textsuperscript{2}. Histopathologically, *organizing pneumonia* (OP) is characterized by buds of granulation tissue, consisting of connective tissue and myofibroblasts, within the distal bronchioles, alveolar ducts and alveoli, without constriction or obstruction of the bronchioles. *Bronchiolitis obliterans*, is a different entity, characterized by small airways obstruction due to fibrosis.
Fig. 1: Open lung biopsy specimen. Hematoxylin and eosin stain. A polyp (yellow arrow) of granulation tissue extends into the lumen of a bronchiolus (arrow heads) consisting of fibroblasts and inflammatory cells.

References: Erasmus MC - Rotterdam/NL

Conditions causing OP
Multiple clinical conditions may cause an OP of which the most common ones are drugs, infection, lung- and bone marrow transplantation, and connective tissue disease. In 30-44% of cases an underlying disease or condition can be identified. The term Cryptogenic Organizing Pneumonia is used when no underlying cause can be identified.

According to Kane et al. the presence of pleural effusion is the only significant differentiating imaging feature between Cryptogenic OP (never pleural effusion) en OP (in about 60% pleural effusion).

Clinical Symptoms, diagnosis and therapy
Patients with OP typically present with variable degrees of dyspnoea and productive cough. Often they report a short period of illness including myalgia, fever, chills and weight loss. Frequently, the abnormalities seen on CXRs in patients with OP are initially interpreted as pulmonary infections. Subsequent prescribed antibiotics lead, in case of OP, to little or no response. OP is mostly a diagnosis of exclusion based on imaging and clinical findings. Especially cases with atypical imaging findings, however, require more invasive diagnostics and histology remains the gold standard.

The therapy of OP consists of prolonged administration of high doses corticosteroids, which is gradually reduced over months. Relapses often occur often when therapy is ceased too early or even during therapy. Overall, OP has a favourable prognosis. In 70-80% complete clinical and radiological remission is achieved. 10-15% of the OP cases are self-limiting. A minority of the cases are progressive resulting in irreversible fibrosis. In patients with underlying connective tissue disease, OP outcome tends to be less favourable.

Imaging features
Organizing pneumonia (OP) can present with very different morphologic features and mimics various other lung pathologies. That makes it a `challenging` differential diagnosis.

The `classic`, most frequent CT features of OP are consolidations with air bronchogram that are sharply demarcated by lobular septa and mostly in peripheral and/or peribronchovascular distribution. Consolidations may be associated with ground glass to a variable degree. Ground glass opacities may also present as crazy paving.
Macro- or micronodular opacities are also observed in OP. The first may be located peripherally or bronchovascular, the latter centrilobular or with a tree-in-bud pattern.

Certain imaging features, though non-specific, are very suggestive for an OP especially if occurring in combination. Such signs refer to the `Halo sign`, the perilobular pattern and the `Atoll sign`.

- Patchy non-segmental consolidations 80 - 90%
- In subpleural distribution 60%
- Lower >> upper lobes, multiple >> solitary
- Bronchiectasis, bronchial wall thickening 60 - 80%
- Ill defined, centrilobular nodules 30 - 50%
- Ground glass, crazy paving

**Table 1: Imaging features suggestive for OP.**

The purpose of this exhibit is to provide an overview of the spectrum of CT imaging findings, including classic patterns and more atypical patterns that could be solved only through open lung biopsy. Imaging features of differential diagnosis are presented in the sidebar.

Tables 2 to 6 list the most important CT findings for the differential diagnoses of OP.

1 **Peripheral subsegmental consolidations**

The best known and most common presentation of OP consist of bilateral, patchy or peripheral, subsegmental consolidations with or without air bronchograms. There might be a variable degree of ground glass opacities associated. This pattern generally shows, if untreated, progression and consolidations may change in location over time. In a few cases the abnormalities resolve spontaneously.
Fig. 2: Classic OP: dense, sharply demarcated consolidations with air bronchogram and a subpleural (left) and peribronchovascular (right) distribution.

References: Erasmus MC - Rotterdam/NL
Fig. 3: Case 1: 55 year old female presenting with cough and fever. a) Chest X-ray shows consolidation interpreted as infectious infiltrate. b) Follow-up after administration of antibiotics. A new consolidation has formed in the left lung. c) CT scan with sharply demarcated consolidation and air bronchograms suggestive for OP. Note the consolidation on the left has disappeared. Transthoracic needle biopsy was performed. d) After a few weeks of steroid treatment, the lesions have almost disappeared.

References: Erasmus MC - Rotterdam/NL

2 Peribronchovascular consolidations
Consolidations are oriented along the bronchovascular bundle. They frequently contain air filled bronchi, which do not show signs of volume loss in opposition to patelike atelectasis. According to Lee et al.(5) bronchovascular consolidations were the dominant feature in about one third of a case series they analysed. This pattern is frequently described in patients with OP and collagenvascular disease, e.g., polymyositis and dermatomyositis, lupus erythematosus or rheumatoid arthritis.

**Fig. 4:** Classic OP: Predominant ground glass opacities that are relatively sharply demarcated and peribronchovascular in distribution.

*References:* Erasmus MC - Rotterdam/NL
**Fig. 5:** Classic OP: Patchy, peribronchovascular consolidations with ground glass opacities.

**References:** Erasmus MC - Rotterdam/NL

<table>
<thead>
<tr>
<th>Pulmonary lymphoma</th>
<th>Sarcoidosis</th>
<th>Aspergillus infection</th>
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<tbody>
<tr>
<td>• Hilar and mediastinal LNN</td>
<td>• 3-5mm nodules</td>
<td>• Neutropenic fever (patient history)</td>
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<tr>
<td>• Lymphatic spread with thickened bronchovascular interstitium</td>
<td>• Perilymphatic distribution</td>
<td>• Nodules with `halo` of ground glass attenuation</td>
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<tr>
<td></td>
<td>• Upper lobes predominance</td>
<td>• Pleural-based wedge shaped consolidations</td>
</tr>
<tr>
<td></td>
<td>• LNN +/- calcifications</td>
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<td></td>
<td>• Later stages: fibrosis with lung distortion</td>
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<table>
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<tr>
<th>Eosinophilic pneumonia</th>
<th>Pulmonary infarction</th>
<th>Aspiration</th>
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(Acute Eosinophilic pneumonia, Loeffler Church/Strauss)

- Asthma (patient history)
- Serum eosinophilia
- Transitory +/- migratory airspace opacities
- Multifocal peripheral consolidations

| Pleural based, wedge shaped opacities (apex points towards center) | Bilateral patches of consolidation |
| Dependent regions, posterior segments |
| P. aeruginosa |

Wegener's granulomatosis

- Extrapulmonary signs
- Nodules, masses, consolidations, GGO
- Irregular margins
- Cavitation

Bronchopneumonia

- Patchy, inhomogeneous consolidation
- Usually several lobes
- Less well-defined by interlobular septae

Lymphangitis carcinomatosis

- Known malignancy (patient history)
- Thickening of interlobular septa and centrilobular structures
- Hilar and mediastinal LNN
- Pleural effusion

Kaposi sarcoma

- In 15-20% of pat. with AIDS
- Irregular and ill-defined nodules
- Thickening of peribronchovascular structures

Postprimary tuberculosis

- Patchy consolidations
- 2-10 mm nodules
- In upper lobe
- Cavitation
- Tree-in-bud pattern

Lymphomatoid granulomatosis

- Multiple bilateral nodules, up to 10 cm in diameter
- Irregular margins
- Rapid progression

Pulmonary edema

- Smooth thickening of bronchovascular bundle
- Smooth interlobular septal thickening

ARDS

- Densely opacified lung
- Gravity dependent - gradient
- Crazy paving
• Lower zone
• Patchy GGO
• Pleural effusions

**Table 2: Differential diagnosis of OP - Peripheral subsegmental and peribronchovascular consolidations**

3 Focal (solitary) OP

Focal OP presents with a solitary consolidation most frequently in the upper lobes. Ryu et al.\(^6\) reported a solitary lesion in 13% of a series of histologically proven OP cases. Focal OP has no specific features. Cavitation and even spiculated margins of the lesions may be seen making a distinction from bronchogenic carcinoma based on imaging findings impossible and diagnosis is mostly determined by biopsy.
Fig. 6: Focal OP: Solitary mass in the right lower lobe

References: Erasmus MC - Rotterdam/NL
**Fig. 7:** Focal OP: Focal lesion of OP with ground glass attenuation.

**References:** Erasmus MC - Rotterdam/NL
Fig. 8: Case 2: 62 year old male with supraglottic carcinoma. a) New mass on the left on the follow-up chest X-ray. b) Solid mass on CT scan. c) FDG PET/CT avid lesion. d) CT guided biopsy 2 weeks later shows spontaneous decrease in size. e) Pathology reveals OP. After a few week of steroid treatment, the lesion has vanished.

References: Erasmus MC - Rotterdam/NL

<table>
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<tr>
<th>Broncho-alveolar carcinoma</th>
<th>Pulmonary infection</th>
<th>Round pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Caveat: both OP and BAC may</td>
<td>• Mostly multiple and unsharply demarcated</td>
<td>• Mostly in children</td>
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</tbody>
</table>
be FDG avide on PET-scans
• Peripheral consolidation
• `Angiogram sign`
• Non-resolving GGO

• Resolves with antibiotic therapy

Primary tuberculosis | Round atelectasis

• Airspace consolidation
• No lobe predominance
• Hilar an mediastinal LNN

• Convergence of bronchovascular markings
• Pleural thickening adjacent to mass

Table 3: Differential Diagnosis of OP - focal lesion

4 Nodular Opacities

Both, macronodular and micronodular patterns are described in OP. Nodules vary in size between several mm and cm. They may be surrounded by a rim of ground glass or show the reversed halo sign. Multiple nodular lesions surrounded by a complete or incomplete rim of consolidations is also described as Atoll sign. Both features are not specific but quite suggestive for an OP in an appropriate clinical situation.
Fig. 9: Nodular OP: Peripheral consolidations with air bronchogram and multiple noduli.

References: Erasmus MC - Rotterdam/NL

Rarely nodules can be small and well defined in a centrilobular distribution. If the granulocytes are confined to the small bronchioli before floating over into the alveolar spaces, the imaging finding consists of a diffuse tree-in-bud pattern that is indistinguishable from a panbronchiolitis or a diffuse infectious bronchiolitis. Inappropriate response to antibiotics and heavy dyspnoea despite broncholytic and antibiotic therapy might be suggestive, though open lung biopt might be necessary to determine the diagnosis.
Fig. 10: OP: Diffuse ‘acinar’ nodules with a random (or centrilobular) distribution.

References: Erasmus MC - Rotterdam/NL

<table>
<thead>
<tr>
<th>Miliary Tuberculosis</th>
<th>Silicosis/ Pneumoconiosis</th>
<th>Sarcoidosis</th>
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<tbody>
<tr>
<td>• Sharp 2-3mm nodules</td>
<td>• 2-5mm nodules</td>
<td>See table 2</td>
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<tr>
<td>• Random distribution</td>
<td>• Centrilobular,</td>
<td></td>
</tr>
<tr>
<td>• Cavitated lesions</td>
<td>upper lobes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Perihilar fibrosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>without air bronchogram</td>
<td></td>
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<tr>
<td></td>
<td>• LNN calcifications</td>
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<td></td>
<td>(egg-shell)</td>
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Viral infection

• Ill-defined acinar nodules, may be confluent diffuse distribution

Subacute EAA          RB-ILD          Histiocytosis
• Ill-defined centrilobular nodules, may confluent to diffuse ground glass air trapping

• Upper lobe predominance
• Chronic bronchitis associated with smoking

• Centrilobular nodules, that may cavitate and become cystic

**Pulmonary metastases**

- Known primary tumor
- Multiple
- Mostly in periphery
- Well defined or irregular margins

**Broncho-alveolar carcinoma**

- Peripheral consolidation
- `Angiogram sign`
- Non-resolving GGO

**Fungal infection**

E.g., aspergillus.

See table 2

**Postprimary tuberculosis**

See table 2

**Wegener’s granulomatosis**

See table 2

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**Table 4: Differential diagnosis of OP - nodular pattern**

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**5 Linear or perilobular pattern.**

OP may present with band like or linear opacities (7). They are usually more than 2 cm long and more than 8 mm in width. Air bronchograms are often present. Their borders may be smooth or irregular. These band-like consolidations may form complete or incomplete circles, surrounding an area of ground glass referring then to the `reversed halo sign`.

Multiple of these lesions resemble multiple islands (Atoll sign).
**Fig. 11**: OP: Typical band-like opacity (arrow) with air bronchograms.

**References**: Erasmus MC - Rotterdam/NL

The `Atoll sign` or `Reversed halo sign` is not specific for OP: it has also been reported in sarcoïdosis en other granulomateous infections like tuberculosis, schistosomiasis or cryptococcus infections(8).
Fig. 12: OP: Reversed halo sign in the right lower lobe.

References: Erasmus MC - Rotterdam/NL
Fig. 13: OP: Consolidations in the right lung and bilateral Atoll sign.

References: Erasmus MC - Rotterdam/NL

If the linear densities follow the periphery of the secondary lobule, it is described as perilobular pattern (9). It has to be noted that the opacifications are not confined to the interlobar septa as in lymphangitis carcinomatosa but only follow the interlobular septa and `flow over` into the adjacent alveolar spaces at the periphery of the secondary lobule.
Fig. 14: Bilateral OP with patchy consolidations following the perilobular pattern.  
References: C. Schaefer-Prokop, Amersfoort/NL

<table>
<thead>
<tr>
<th>Postprimary tuberculosis</th>
<th>Lymphomatoid granulomatosis</th>
<th>Lymphangitis carcinomatosis</th>
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<tr>
<td>See table 2</td>
<td>See table 2</td>
<td>See table 2</td>
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Fungal infections  
See table 2  
Sarcoidosis  
See table 2  
Pulmonary infarction  
See table 2

Atelectasis  
No air bronchogram  
Fibrotic band  
No air bronchogram  
Interstitial edema  
See table 2

Table 5: Differential Diagnosis of OP - Linear or perilobular pattern

6 Progressive fibrosis
Some cases of OP have an unfavourable outcome and can even lead to death. Mortality is related to progressive fibrotic OP. HRCT shows a reticular pattern with architectural distortion in a peribronchovascular distribution or at the lung bases. Traction bronchiectasis and honeycombing may also be seen (10). Frequently combinations with consolidation and nodules are encountered. This entity seems to be associated with connective tissue diseases, especially polymyositis and dermatomyositis.

Fig. 15: Fibrotic OP: Reticular pattern with architectural distortion in a peribronchovascular distribution. Traction bronchiectasis and some honeycombing. 

References: Erasmus MC - Rotterdam/NL

<table>
<thead>
<tr>
<th>NSIP</th>
<th>UIP</th>
<th>DIP</th>
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<tbody>
<tr>
<td>GGO</td>
<td>Reticular pattern</td>
<td>Reticulonodular pattern</td>
</tr>
<tr>
<td>Fine reticular pattern with</td>
<td>Honeycombing</td>
<td></td>
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traction bronchiectasis  
• Peribronchovascular distribution with subpleural sparing  
• Traction bronchiectasis  
• Destruction of lung parenchyma  
• Ground glass opacities in geographic distribution  
• Minimal signs of fibrosis

### Chronic EAA
- Air-trapping
- Irreversible fibrosis
- Honeycombing
- Occasional cystic airspace

### Endstage sarcoidosis
- Perihilar fibrosis
- Upper lobe volume loss
- Destruction of lung architecture

#### Table 6: Differential Diagnosis of OP - fibrosis

#### References:


**Fig. 16:** Pulmonary lymphoma; Pro OP: Sharply demarcated consolidations in a peribronchovascular distribution; some with peripheral location; presence of air bronchogram, can also be seen in lymphoma. Contra OP: Multiple nodular opacities, more centrally located.

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**Fig. 17:** Eosinophilic pneumonia; Pro OP: peripherally located consolidations surrounded by ground glass. Contra OP: unsharp demarcation, no air bronchogram.

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Fig. 18: Lymphomatoid granulomatosis; Pro OP: some subpleural consolidations with air bronchograms. Contra OP: more centrally located consolidations and nodules. Rapid progression. Irregular margins.

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Fig. 19: Pulmonary infarcts; Pro OP: subpleural consolidation with sharp demarcation. Contra OP: presence of pulmonary emboli.

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Fig. 20: Sarcoidosis; Pro OP: sharply demarcated consolidations with mildly dilated bronchi, in a peribronchovascular orientation, sparing of secondary lobules. Contra OP: hilar lymphadenopathy (not shown).

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**Fig. 21:** Morbus Wegener; Pro OP: consolidations with air bronchogram, peribronchovascular orientation. Contra OP: partly unsharp demarcation, no regard for secondary lobuli.

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Fig. 22: Broncho-alveolar carcinoma; Pro OP: consolidations with air bronchogram, sharp demarcation, some sparing of secondary lobuli. Contra OP: none. Biopsy needed!

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Fig. 23: Resistant Pseudomonas aeruginosa infection; Pro OP: large consolidation with air bronchogram. Contra OP: on imaging none; positive cultures.

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Fig. 24: Subacute EAA; Pro OP: poorly defined micronodules in a centrilobular distribution. Contra OP: air trapping (not shown).

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Fig. 25: Sarcoidosis; Pro of OP: micronodules, mixed dense and ground glass. Contra OP: perilymphatic distribution, relatively dense nodules.

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Fig. 26: Streptococcus pneumoniae infection; Pro OP: reversed halo sign, peribronchovascular orientation. Contra OP: focal, nodular ground glass opacities.

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**Fig. 27:** NSIP; Pro OP: perilobular pattern of consolidations with ground glass opacity (coarse reticulation). Contra OP: association with intralobular reticular densities and signs of parenchymal destruction (traction bronchiectasis).

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Fig. 28: NSIP; Pro OP: ground glass opacities, sharp demarcation, relative sparing of secondary lobuli. Contra OP: signs of fibrosis, e.g., irregular dilated airways (traction bronchiectasis), pleural tagging, distortion of the lung architecture.

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Fig. 29: DIP; Pro OP: fibrosis and ground glass with peribronchovascular orientation, sparing of secondary lobuli. Contra OP: none.

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Conclusions

Organizing pneumonia (OP) is one of the most challenging morphological mimickers in chest radiology. The classic CT features of OP constitute of consolidations with air bronchograms that are sharply demarcated by lobular septa and are peripheral and/or peribronchovascular in distribution. Often, consolidations are associated with ground glass to a variable degree. Less frequently, but quite typical findings refer to the reversed Halo sign, the perilobular pattern and the Atoll sign. Nodular opacities, diffuse tree-in-bud or exclusively ground glass can also be found in OP. OP is mostly a diagnosis of exclusion based on imaging and clinical findings, though findings may be so atypical or non-specific that only histology reveals the diagnosis.