

# A Case of Cryptogenic Organizing Pneumonia Managed without a Diagnostic Biopsy

Kamal Amer, MD, McKensie Walker, BSc, and Vincent Yeung, MD

## INTRODUCTION

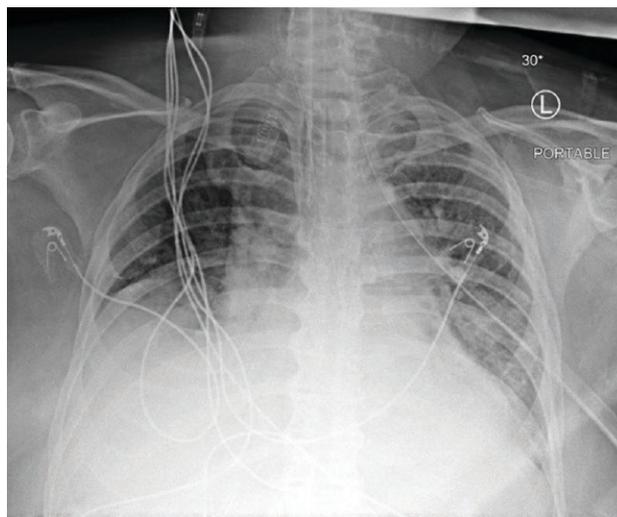
Organizing pneumonia (OP) is a type of diffuse interstitial lung disease characterized by a specific histopathologic pattern of response to lung injury. When the etiology of the injury is unknown and in the absence of inflammatory or connective tissue disease, this entity is termed cryptogenic organizing pneumonia (COP) or primary organizing pneumonia (POP). Disease states in which the etiology of underlying injury is known is termed secondary organizing pneumonia (SOP). Causes of SOP include drug toxicity, chronic heart or renal failure, rheumatic disease, collagen vascular disease, infection, immunodeficiency, autoimmune disease, and interstitial lung disease.<sup>1</sup>

OP is characterized by the accumulation of inflammatory cells, fibroblasts, and myofibroblasts in the lumens of bronchioles and alveoli creating plugs of debris. This leads to alveolar epithelial injury, which is followed by leakage of plasma cells and the recruitment of fibroblasts and fibrin within the alveolar lumen. This accumulation of granulation tissue within the alveolar sacs extends into the alveolar ducts as well as the bronchioles causing symptom onset. The clinical presentation of OP is variable and involves nonspecific symptoms such as mild fever, cough, malaise, anorexia, weight loss, and progressive dyspnea.<sup>2</sup> Some reports describe wheezing and clubbing, but these symptoms occur in only 5% of cases. While “crackles” is the most common abnormal finding of OP on auscultation, 25% of reported cases present with a completely normal pulmonary exam.<sup>3</sup>

The decision to treat patients for OP depends on the clinician’s ability to rule out other potentially reversible causes of dyspnea as well as the number of criteria met for this diagnosis of exclusion, based on histopathologic, radiographic, and clinical findings.<sup>4</sup> Diagnosis is made via biopsy; though surgical biopsy via thoracoscopy has remained the gold standard, trans-bronchial biopsy has recently gained prevalence.<sup>5</sup> We aim to present a suspected case of COP as an uncommon cause of interstitial lung disease.

## CASE PRESENTATION

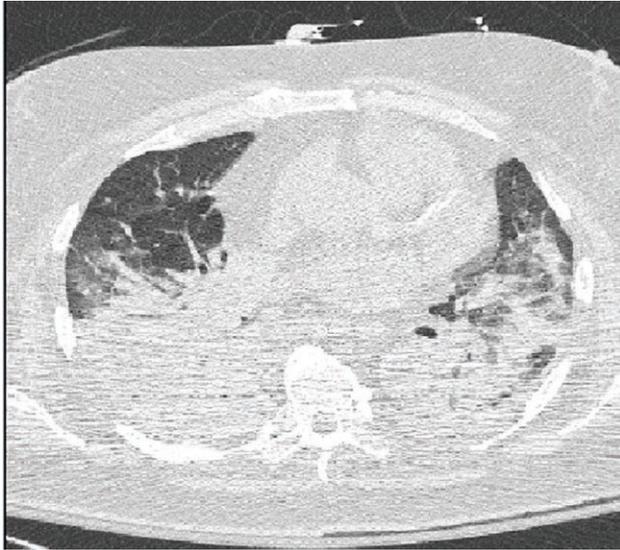
Our patient is a 75-year-old man with a past smoking history of 50 pack-years as well as a history of heart failure with preserved ejection fraction, hypertension, non-insulin dependent type 2 diabetes mellitus, obstructive sleep



**Figure 1.** Chest x-ray upon presentation with multifocal opacities.

apnea, peripheral vascular disease, and gout who presented to the emergency department (ED) with one week of shortness of breath and dyspnea on exertion. He did not endorse any associated fevers, productive cough, sick contacts, weight loss, paroxysmal nocturnal dyspnea, or chest pain. He had stable orthopnea and lower extremity edema. On arrival to the ED, he was hypoxemic to 72% on room air and required 4 liters of oxygen via nasal cannula to maintain oxygen saturations above 90%. His chest x-ray demonstrated multifocal opacities with a left lung predominance that was distinct from prior imaging studies (**Figure 1**). He was started on a course of broad spectrum antibiotics (vancomycin and zosyn) without clinical improvement. His oxygen requirements increased and he was transitioned to 6 liters of oxygen via nasal cannula with a periodic need for continuous positive airway pressure (CPAP).

A computed tomography (CT) scan of his chest demonstrated diffuse patchy bilateral airspace opacities with lower lobes predominance as well as scattered ground-glass opacities concerning for multifocal pneumonia (**Figure 2**). He had a speech and swallow assessment to evaluate for aspiration, which was negative. Sputum cultures and blood cultures were negative. Urine streptococcal and legionella antigens, influenza and RSV viral swabs, as well as a MRSA swab were sent but failed to identify a pathogen for the



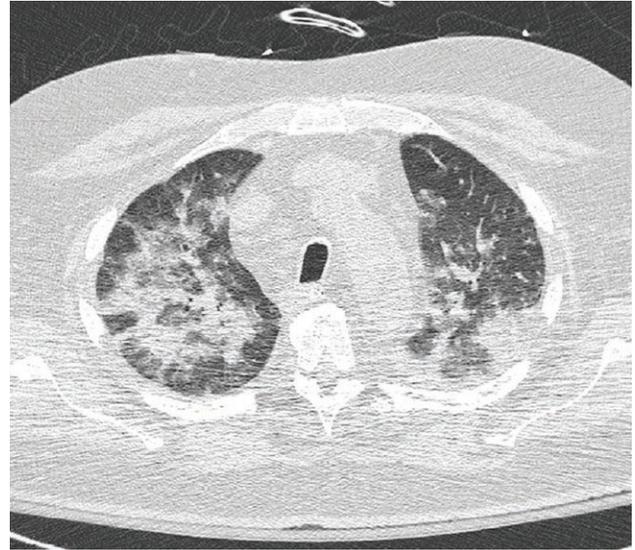
**Figure 2.** Computed tomography scan of the chest showing patchy bilateral airspace opacities, most predominant in the lower lobes, with associated scattered ground-glass opacities bilaterally.

patient's suspected pneumonia. He also underwent evaluation for autoimmune and connective tissue diseases that could have contributed to his presentation, with negative ANA, ANCA, anti-Scl 70, anti-dsDNA, and anti-Jo1 testing. He never presented with an elevated eosinophil count.

Prednisone was added to his empiric broad spectrum antibiotics given concern for possible organizing pneumonia based on his imaging findings with clinical improvement. By the third day of his admission, the oxygen saturations were consistently 98% on 2L nasal cannula. His antibiotics were de-escalated to moxifloxacin to complete a five-day course and he was started on a prolonged prednisone taper to empirically treat cryptogenic organizing pneumonia, as the patient declined surgical and trans-bronchial biopsy to confirm this suspicion. At the time of discharge, he was stable on room air at rest but required 1-2L of supplemental oxygen with ambulation and CPAP at night.

## FOLLOW UP

The patient was followed closely at the outpatient pulmonary office. He was readmitted every couple of months after his initial presentation with shortness of breath and increased work of breathing that notably flared toward the end of his prednisone tapers and rapidly improved with intravenous steroids administered in the hospital. These admissions were attributed to COP flares though his diagnosis was never confirmed; an infectious workup as detailed during his initial admission were repeated at each subsequent admission and was similarly



negative every time. The last time he was seen in the outpatient pulmonary office, he reported fevers at home with a newly-productive cough. His outpatient labs demonstrated a leukocytosis of 16.1 billion/L, although whether this was related to ongoing steroid use or underlying infection was uncertain. He was readmitted and started on stress-dose steroids as well as broad-spectrum antibiotics and anti-fungal therapy, as a repeat CT scan revealed a worsening of the diffuse airspace opacities seen on prior imaging studies concerning for superimposed infectious pneumonia. His sputum cultures at this interval grew yeast. He developed hypoxic respiratory failure, requiring intubation and tracheostomy, and septic shock complicated by disseminated intravascular coagulation and pulseless ventricular tachycardia resulting in his eventual death. The patient's family declined autopsy.

## DISCUSSION

Treatment of COP has not been well evaluated in clinical trials and therefore is based upon clinical experience. Prednisone is the first-line treatment for COP due to its anti-inflammatory effects and 65-85% of patients respond to this therapy.<sup>6</sup> Relapses are common in up to 58% of cases and are associated with corticosteroid tapers.<sup>7,8</sup> For refractory or recurrent cases, Vaz et al. found macrolides to be effective at achieving remission after one year of treatment.<sup>9</sup> Cytotoxic and immunomodulating agents such as rituximab have also shown efficacy in treating refractory COP in preliminary case reports.<sup>10</sup> In patients where steroids are difficult to taper, azathioprine has been suggested as a steroid-sparing agent although evidence for this therapy is limited.<sup>11</sup> Cyclophosphamide has also been used in patients who fail to improve with glucocorticoids but data regarding its use is similarly sparse.<sup>12</sup>

About 33% of patients who are treated for less than one year with corticosteroids experience recurrence.<sup>13</sup> Studies have shown that relapse is associated with multiple factors such as gastroesophageal reflux disease, a decrease in functional vital capacity, a decrease in serum protein, and severity of illness at diagnosis.<sup>2,14,15</sup> Lazor et al. studied relapses in 48 cases and found that a delay in initial diagnosis was also associated with an increase in relapse.<sup>8</sup> Watanabe et al. found that the level of hypoxemia at time of diagnosis was the most important factor in predicting relapse.<sup>7</sup>

In this report, we described a patient with suspected COP based on clinical presentation and response to empiric prednisone with recurrence of presenting symptoms toward the end of prolonged steroid tapers. His negative infectious workup during each of his four hospital admissions and his negative evaluation for autoimmune and connective tissue diseases helped guide our clinical suspicion for COP even in the absence of a confirmatory biopsy. Our patient originally presented with recurrent episodes of presumed community-acquired pneumonia. The most common presentations of COP are nonspecific flu-like symptoms such as cough, fever, dyspnea, and malaise; most patients are thus started on antibiotic treatment but remain unresponsive to this therapy. As this case reflects, the diagnosis of COP is usually delayed and therefore a high index of suspicion is required to correctly and promptly address this disease.

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