

Understanding and Managing Post-COVID-19 Organizing Pneumonia

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Mini Review

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ABSTRACT

The global impact of the rapid spread of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) since late 2019 has been substantial. COVID-19-related pneumonia has significantly contributed to the resulting fatalities. The most common findings of COVID-19 pneumonia in chest computed tomography scans include peripheral ground-glass opacities and consolidation, presenting in bilateral and multifocal distributions, which closely resemble to Organizing Pneumonia (OP). COVID-19-related OP is not uncommon and can mimic infectious pneumonia. The onset of OP following a COVID-19 varies, OP can occur from a few weeks to three months after COVID-19 infection. OP can be cryptogenic (COP) or secondary to various causes, with post COVID-19 OP classified as a secondary form of OP. Definitively diagnosis OP requires a lung biopsy, although acquiring sufficient tissue can pose challenges in real clinical practice. Rapid diagnostic tools can help exclude infectious pneumonia and assist promptly diagnosing OP, facilitating the initiation of steroid treatment. This is particularly critical for patients who are severely or critically ill. In cases of OP related to COVID-19, patients in the early phase should follow standard COVID-19 guidelines, receiving treatment with steroids, or a combination of anti-Interleukin-6 Inhibitors or Janus kinase inhibitors. On the other hand, late-onset cases are predominantly treated with corticosteroids, as observed in most case series and studies. For mild to moderate cases, treatment with a low dose of steroids and maintaining the steroid regimen for 8 ± 4 weeks can lead to favorable outcomes. The optimal steroid dosage and treatment duration for

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severe cases remain unclear. The dose and duration of systemic steroids for these severe patients should be tailored based on the severity of the disease and their responsiveness to treatment.

Keywords: COVID-19; Organizing pneumonia; Treatment; Corticosteroid

INTRODUCTION

The rapid spread of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) since late 2019 has significantly impacted global public health systems. Severe disease accounts for 14% of overall COVID-19 cases, and the overall fatality rate is estimated to range from 2.3%-5% for different regions or countries in the early stages of a disease outbreak [1]. With widespread disease transmission and vaccine usage, the disease's severity and mortality rate have gradually declined [2]. Among the causes of death from COVID-19, deaths caused by pneumonia account for a high proportion [3]. Clinical and radiological characteristics of COVID-19 pneumonia have been systematically analyzed. The most common findings on chest computed tomography scans are peripheral ground glass opacity, consolidation, or both, predominantly in bilateral and multifocal distributions, highly resembling a pattern of Organizing Pneumonia (OP) [4]. One previous study evaluated five patients who later died in their disease course, revealing a histologic pattern of acute fibrinous and OP, characterized by extensive intra-alveolar fibrin, rather than hyaline membranes [5]. These findings indicate that a portion of post-COVID-19 pneumonia cases are OP. The time to develop OP after COVID-19 infection varies; one study showed interstitial lung disease, predominantly OP, was observed in 35 of 837 survivors (4.8%) more than 4 weeks after COVID-19 infection [6]. In another study, OP occurred from a few weeks to three months after COVID-19 infection [7].

LITERATURE REVIEW

OP can be classified as cryptogenic and secondary. Cryptogenic Organizing Pneumonia (COP) is a form of idiopathic interstitial pneumonia with no identifiable cause, formerly known as bronchiolitis obliterans organizing pneumonia. It is clinically significant as it is often misdiagnosed. Secondary forms of OP are attributable to specific causes such as viral infection, drug toxicity, inhalation injury, radiation therapy, connective tissue disorder, aspiration, or cancer. Corticosteroid therapy is the first-line treatment for OP, often resulting in improvements in symptoms, radiographic findings, and oxygen requirements [8]. A definitive diagnosis of OP depends on a lung biopsy demonstrating typical histopathologic features in a patient with a compatible clinical and radiographic pattern. The characteristic histopathologic features of OP include intraluminal plugs of inflammation debris predominantly within small airways, alveolar ducts, and adjacent alveoli, with the absence of histopathologic features of another process (e.g., hypersensitivity pneumonitis, chronic eosinophilic pneumonitis, and usual interstitial pneumonia). To obtain sufficient tissue for diagnosis, video-assisted thoracoscopic surgery is generally preferred over transbronchial lung biopsy [9]. However, routine lung biopsy is not practical in real clinical practice for patients with suspected OP, especially in cases of pneumonia after COVID-19. The under-reporting of OP is partly because it can be challenging

to diagnose. To facilitate the diagnostic process, rapid diagnostic tools such as the multiplex polymerase chain reaction assay could be considered. The use of rapid diagnostic tools can help diagnose OP quickly and accurately, which is especially important for severe and critically ill patients who require prompt treatment.

Once infection is ruled out, physicians should initiate steroids to manage the condition. It is crucial to consider the possibility of OP and to exclude infection rapidly to ensure timely and appropriate treatment. The mainstay of treatment for COP is corticosteroid therapy. The British Thoracic Society guidelines recommend initiating prednisone at a dose of 0.75 to 1 mg/kg per day. However, a high proportion of patients with COP will still experience recurrence after steroid treatment, so it is suggested to taper the steroid slowly and maintain it for 6 to 12 months [10]. COP typically responds well to steroid therapy, but in some severe cases that respond poorly to steroids, other immunosuppressant agents may need to be combined for treatment [9]. For secondary OP that develops in the early phase of COVID-19 infection, patients are treated according to the COVID-19 guidelines with dexamethasone 6 mg for 10 days. Some severe cases may be combined with anti-Interleukin-6 Inhibitors (tocilizumab) or Janus kinase inhibitor (Baricitinib) [11]. However, there is no clear guide for the treatment of late-onset COVID-19 OP, particularly 3-4 weeks after infection. Some case reports have shown the presence of OP after stopping standard dexamethasone treatment, and resuming corticosteroid treatment successfully managed these patients [12-14]. Other reports have been published, and most cases of post-COVID-19 OP are treated with corticosteroids, with a high proportion of cases successfully recovering [15]. Corticosteroids are the mainstay of treatment, but the dosage for managing late-onset OP after COVID-19 infection has not been established. Steroids can cause many side effects, such as decreased immunity, susceptibility to infection, high blood sugar, increased psychosis events, increased atrial fibrillation and venous thrombosis events, and increased osteoporosis [16]. Therefore, using steroids that are too high and for too long can cause side effects, but not using them enough or for too short a duration can lead to uncontrollable disease or recurrence of OP. Some small-scale studies have been published, and one study compared high-dose (total prednisone dose of 910 mg) and low-dose steroid (420 mg) in the management of post-COVID-19 pneumonia. The results revealed similar clinical responses and recovery rates between the high and low-dose steroid groups [17]. Another case series suggests that the most effective and convincing therapy for COVID-19-induced Organizing Pneumonia (OP) is corticosteroid treatment at a dose equivalent to 0.5 mg/kg/day as an initial dose [18], with the dose reduced weekly according to the patient's clinical condition. The duration of steroid treatment is also variable; most case reports and small-scale studies showed a duration of 8 ± 4 weeks. Rarely, steroids are used for up to 6 to 12 months as COP. Approximately 90% of patients experience clinical and radiographic improvement with steroid use [7]. However, these studies excluded critical cases, and this steroid dosage may not be suitable for critical cases. These very serious cases require additional individual consideration. It is still not conclusive how many doses of steroids should be used and how long they should be used in this group of patients.

CONCLUSION

COVID-19-related organizing pneumonia is a possible non-infectious cause of lung inflammation that can occur from a few weeks to three months after COVID-19 infection. It is difficult to differentiate from infectious pneumonia, so physicians should be highly aware. For severe cases, rapid exclusion of infection is necessary, and systemic steroids should be rapidly prescribed. Systemic steroids are the mainstay of treatment. For mild to moderate cases,

initiating a low dose of steroids and maintaining the steroid regimen for several weeks is appropriate. For severe cases, the optimal steroid dosage and treatment duration remain unclear. The dose and duration of systemic steroids should be tailored based on the severity of the disease and the patient's responsiveness to treatment.

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