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Case Report

Organizing pneumonia associated with SARS-CoV-2 infection

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ABSTRACT

Organizing pneumonia is a nonspecific pulmonary response pattern associated with a variety of clinical contexts including viral infections. The classic radiological manifestations are peribronchovascular/peripheral ground glass opacities or consolidations and may be accompanied by nodules, masses, and interstitial opacities. We describe the case of a 62-year-old male patient with SARS-CoV-2 pneumonia and torpid clinical and radiological evolution in whom organizing pneumonia was documented through transbronchial biopsy and imaging findings, with a good response to corticosteroids. The importance of recognizing the development of organizing pneumonia lies in the better prognosis and outcome in those patients who receive treatment with corticosteroids, however, the clinical and radiological suspicion must be confirmed with biopsy because radiological findings associated with bacterial coinfection may overlap.

Introduction

Viruses are currently recognized as a major cause of community acquired pneumonia in immunocompetent and im-

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munocompromised adults[1,2] being the massive pneumococcal vaccination and the increased use of RT-PCR (real-time polymerase chain reaction) decisive factors in this epidemiological change. The impact of the pandemics related to viral pneumonias such as Influenza A (H1N1) in 2009 and SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) from 2020 to the present, has revealed the importance of viral pneumonia as a major public health problem.

Radiological manifestations may overlap in patients with viral, bacterial, mycotic or parasitic pneumonia and the association of certain radiological findings to specific germs may lead to diagnostic errors. On the other hand, diverse pulmonary response patterns to infection including diffuse alveolar damage [3,4,[5]], organizing pneumonia and acute fibrinous and organizing pneumonia are associated with multiple etiologies. Organizing pneumonia has been described as a pulmonary response in patients with SARS-CoV-2 pneumonia[6].

We present the case of a patient with SARS-CoV-2 pneumonia and torpid clinical and radiological evolution in whom organizing pneumonia was documented through transbronchial biopsy.

Case report

A 62-year-old male patient with a history of controlled arterial hypertension and type 2 diabetes mellitus arrives to the emergency room with 8 days of cough, dyspnea, fever and musculoskeletal pain with the following vital signs: blood pressure 149/102 mm Hg, heart rate: 92 bpm, respiratory rate: 27 rpm, oxygen saturation: 88% and temperature: 36°C without relevant findings at physical examination. The admission laboratory tests are shown in **Table 1**. The initial radiograph showed bibasal consolidations with right predilection. The patient was diagnosed with multilobar pneumonia and hyperglycemic crisis (diabetic ketoacidosis). Treatment with ampicillin/sulbactam and clarithromycin was indicated.

In the 72-hour follow-up, the patient presented respiratory deterioration requiring orotracheal intubation and admission to intensive care unit (ICU), where SARS-CoV-2 infection was confirmed and treatment with hydroxychloroquine and lopinavir/ritonavir was started. Later, he was diagnosed with acute respiratory distress syndrome and acute kidney injury requiring renal replacement therapy and multisystem support in the ICU.

Control radiographs showed persistence of parenchymal opacities (**Fig. 1**). A chest CT scan performed to rule out complications associated with viral pneumonia demonstrated multilobar ground glass opacities, peribronchovascular basal areas of consolidation and free bilateral pleural effusion (**Fig. 2**). Bronchoalveolar lavage did not show germs and the transbronchial biopsy revealed intra-alveolar fibroblastic foci with collagen in different stages of maturation confirming the diagnosis of organizing pneumonia (**Fig. 3**). Prednisolone 1 mg/kg/day was started with a favorable evolution and a significant imaging improvement was seen 15 days after steroid initiation (**Fig. 4**). Steroid withdrawal was carried out on day 30.

Table 1 – Admission laboratory tests.

Blood count	
Leukocytes	10.600 /μL
Neutrophils	9.680 /μL (91,4 %)
Lymphocytes	5100 /μL (4,8 %)
Monocytes	190 /μL
Eosinophils	0 /μL
Basophils	90 /μL
Hemoglobin	14.8 g/dL
Hematocrit	43.8 %
Platelets	255.000/μL
Arterial blood gases	
pH	7.34
PaO2 (partial pressure of oxygen)	66.3 mm Hg
PaCO2 (partial pressure of carbon dioxide)	24.6 mm Hg
HCO3 (concentration of bicarbonate)	15.5 mmol/L
Base excess/deficit	-7.6 mmoL/L
Fraction of inspired oxygen	0,21
Blood chemistry	
Glucose	347 mg/dL
Blood urea nitrogen	15.00 mg/dL
Creatinine	1.0 mg/dL
Sodium	123.6 mmol/L
Potassium	4.0 mmol/L
Lactate dehydrogenase	308 UI/L
C reactive protein	8.70 mg/dL
Lactate	4.40 mmol/L
D - dimer	2364 ng/mL
Troponin I	<0.12 ug/L
Glycosylated hemoglobin	9.8%

Discussion

The pathophysiology of lung damage associated with viral pneumonia is related to direct cytopathic effect (cell lysis or inhibition of the synthesis of RNA, DNA or fundamental proteins) and nuclear changes leading to bronchial, bronchiolar and alveolar damage [7]. The outcome of patients with viral pneumonia is related to inflammatory responses including diffuse alveolar damage, organizing pneumonia, and acute fibrinous and organizing pneumonia.

Diffuse alveolar damage (DAD) presents variable histological findings according to the phase, with hyaline membranes and edema of alveolar wall in the acute phase and interstitial and alveolar fibrosis in the organized phase. Radiologically, DAD in the acute phase is characterized by bilateral, multilobar, ground glass opacities and/or consolidation. Interstitial alterations are associated with the progression of the condition, including reticulation, traction bronchiectasis, thickening of interlobular septa, and distortion of the lung architecture[8]. DAD is a relatively common but nonspecific response in patients with viral pneumonia and it has also been related to influenza, parainfluenza, human metapneumovirus, respiratory syncytial virus, herpes viruses, and adenovirus infection.

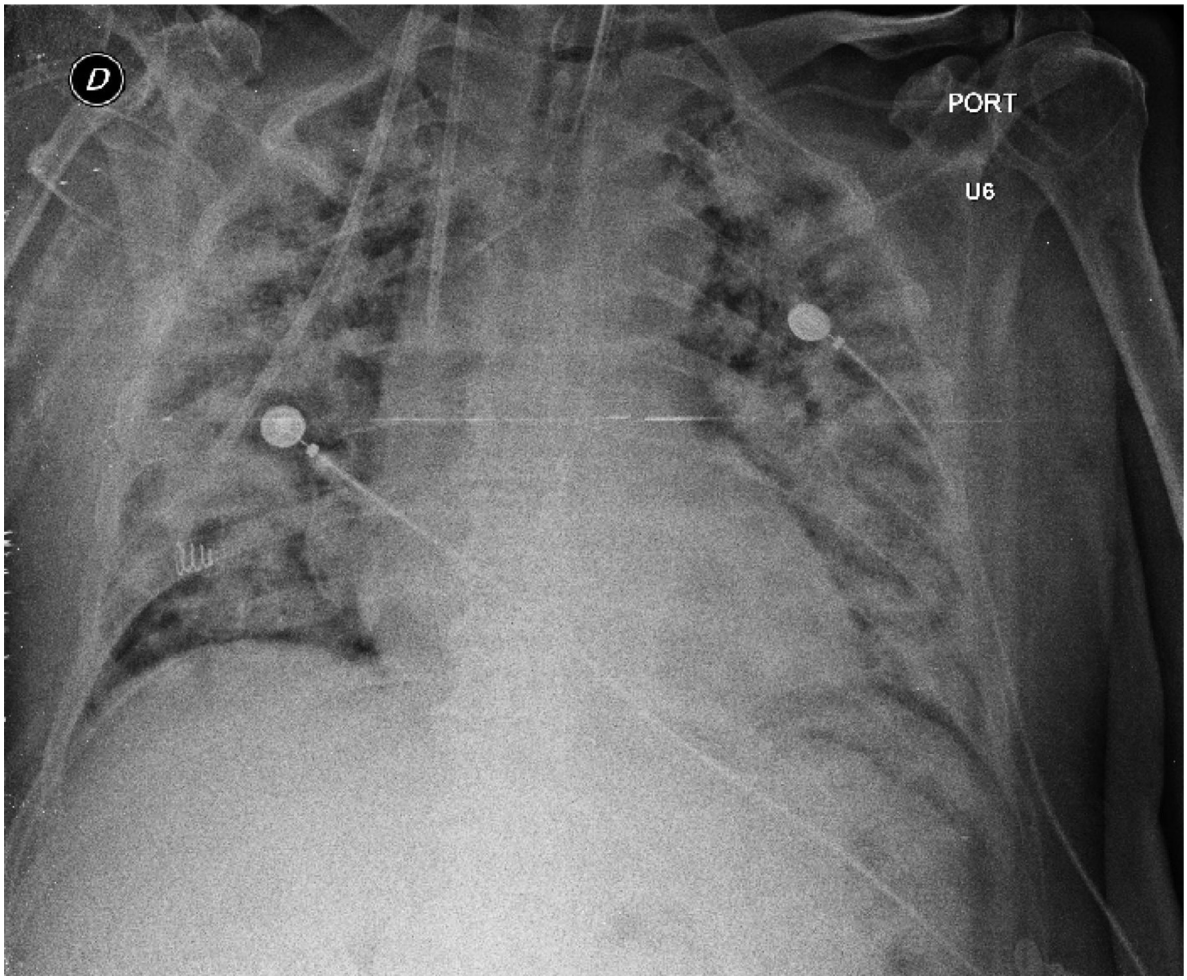

Fig. 1 – Portable chest X-Ray (AP projection): Multilobar consolidations. Also note enteral probe and endotracheal tube.

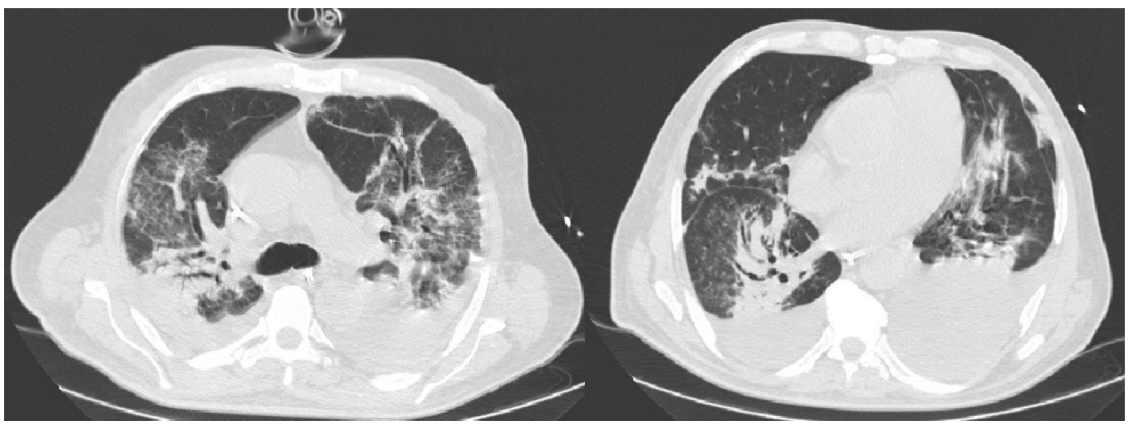

Fig. 2 – Initial chest CT: Multilobar ground glass opacities, peribronchovascular basal areas of consolidation and free bilateral pleural effusion.

Acute fibrinous and organizing pneumonia (AFOP) was first described in 2002 by Beasley et al [9] and is considered a pattern that does not meet the requirements to be fully included in either diffuse alveolar damage or organizing pneumonia [10]. AFOP can be idiopathic or associated with a wide variety of etiologies such as: drug reactions, hematological malignancies, collagen diseases and viral infections, for example the case report associated with influenza AH1N1 pneumonia in a patient with lung transplant described by Otto et al in 2013[11]. Histologically is characterized by alveolar fibrin de-

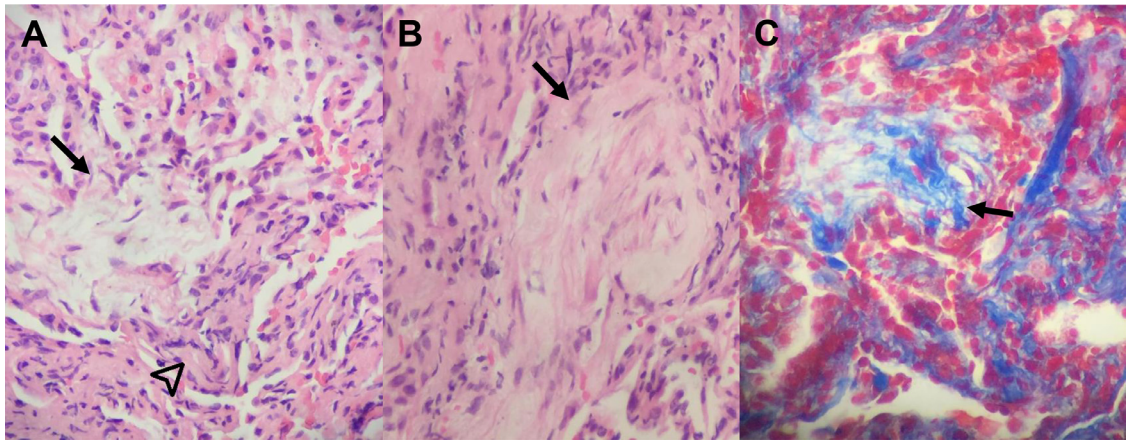

Fig. 3 – Transbronchial pulmonary biopsy. (A) Hematoxylin-eosin stain, original magnification × 40. Alveolar space occupied by masses of immature connective tissue, fibroblasts, and inflammatory cells (arrows). Adjacent parenchyma with mild chronic inflammatory infiltrate and interstitial thickening (arrowhead). (B) Hematoxylin-eosin stain, original magnification × 40. Intra-alveolar obliteration (arrow) with organized fibroblastic tissue as plugs (Masson body). (C) Masson Trichrome stain, original magnification × 40) Trichrome stain highlights in blue elongated fibroblastic plugs (arrow).

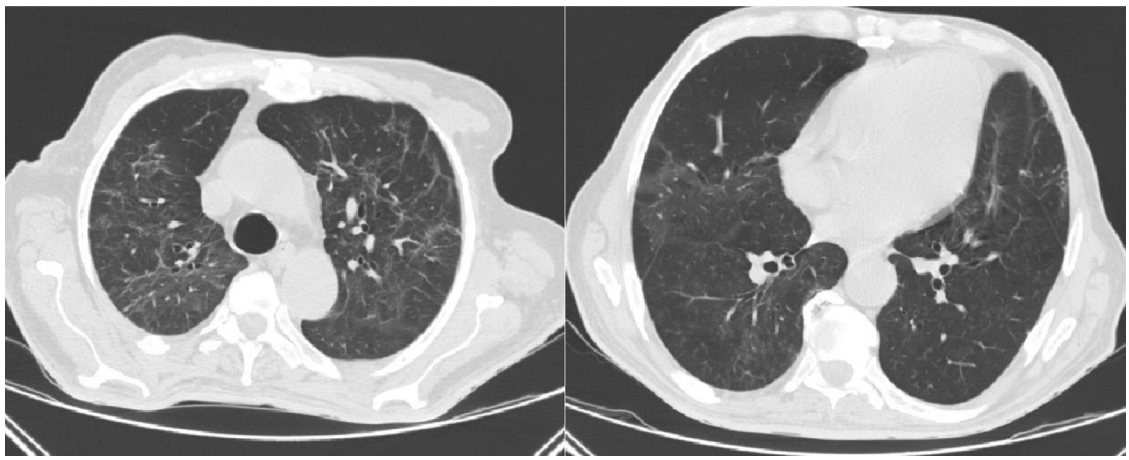

Fig. 4 – Control chest CT 15 days after steroid initiation. Note the disappearance of consolidation areas with persistence of some ground glass areas.

position in the form of "conglomerates/tangles" with hyperplasia of type II pneumocytes and patchy foci of organizing pneumonia without associated hyaline membranes. Radiological findings are variable and include ground glass opacities, bibasal consolidations, and manifestations described in patients with organizing pneumonia pattern [8].

Organizing pneumonia is defined as a nonspecific pulmonary response pattern associated with a variety of clinical contexts including drug reactions, connective tissue diseases and viral infection [12,13]. The term cryptogenic organizing pneumonia is reserved for the primary entity in which no cause or association is recognized [14]. The first histopathological description of organizing pneumonia dates back to the beginning of 20th century [15] characterized by inflammatory debris in the distal airway with myofibroblasts, fibroblasts and inflammatory cells immersed in a matrix of connective tissue and interstitial inflammatory process of the adjacent lung [16].

The classic radiological manifestations of organizing pneumonia are peribronchovascular/peripheral ground glass opacities or consolidations which can be migratory and may be accompanied by nodules, masses, and interstitial opacities. It is described the reverse halo sign a central ground glass area surrounded by a consolidation halo. Some authors propose considering organizing pneumonia in the spectrum of manifestations of acute lung injury and its repair together with DAD and nonspecific interstitial pneumonia. The importance of recognizing the development of organizing pneumonia lies in the better prognosis and outcome in those patients who receive treatment with corticosteroids [17].

The relationship between viral pneumonia and the organizing pneumonia pattern has been described in several publications. In 2001 the report case of a patient who developed organizing pneumonia associated with influenza A was published[18]. The case reports of Cornejo et al [19],Torrego et al

[20] and Gómez et al [21] show the association with Influenza AH1N1. In 2016 the first case report of organizing pneumonia associated with coinfection of Influenza B and *Streptococcus pneumoniae* was described[22]. Finally in 2017 was described the relation with influenza B pneumonia[23].

The association between SARS-CoV-2 pneumonia and organizing pneumonia pattern was suggested for the first time in the case report by Yan Wu et al [24] of a patient from the city of Wuhan (China) with COVID-19 and the finding of ground glass opacities and reverse halo sign, however the diagnosis was not confirmed by pathology. Okamori et al [25] and Sellares et al [26] suggested the diagnosis of organizing pneumonia in patients with COVID-19 based on imaging findings and response to corticosteroid treatment but histological confirmation of the entity was not performed.

Up to the moment of this review, two case reports and one case series have published histological confirmation of organizing pneumonia in patients with COVID-19; those described by Bae et al [27] in a 46-year-old female patient, by Pogatchnik et al [28] in a 61-year-old female patient and the case series by Vadász et al [6] which calculated an incidence of 12, 5% of organizing pneumonia associated with SARS-CoV-2.

It is probable that the torpid course of some patients with COVID-19 is related to the presence of organizing pneumonia as could be verified in our patient; however, the clinical and radiological suspicion must be confirmed with biopsy. In hospitalized patients and particularly those on mechanical ventilation a torpid clinical course can be related to bacterial coinfection. Radiological findings associated with coinfection or organizing pneumonia may overlap. Due to the above considerations, it does not seem reasonable with the available evidence to confirm the presence of organizing pneumonia in patients with SARS-CoV-2 pneumonia based solely on radiological alterations.

The importance of our report is related to the histopathological confirmation of organizing pneumonia pattern in a patient with a torpid clinical course with a good response to the management previously accepted in the literature for the entity.

Conclusions

Given the few biopsies available and the limited series of autopsies the incidence of organizing pneumonia in patients with COVID-19 cannot be quantified accurately but based on the reports and existing case series an important role of organizing pneumonia pattern is proposed in some patients with a poor evolution, considering that the manifestations of this viral infection and organizing pneumonia may be indistinguishable in imaging studies.

Patient consent

The patient declared his fully consent for the publication of the case.

Declaration of Competing Interest

The authors declare that there is no conflict of interest in the present case report.

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