Review

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Acute fibrinous and organizing pneumonia

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ABSTRACT

Acute fibrinous and organizing pneumonia (AFOP), first described histologically by Beasley et al.1 in 2002. AFOP occurs in a wide age range (38-78 age) and in a non-sexist spectrum of patients. Although idiopathic cases have been reported, case series in which the underlying etiology is known. The histologically specific pattern is the presence of organized intra-alveolar fibrin and is the essential parameter for diagnosis. There is no significant difference in the radiological pattern except for the halo finding in the comparison of AFOP and COP. In patients presenting with an acute and more fulminant picture, the clinic presents with rapidly worsening respiratory failure. The main complaints were fever, cough and chest pain respectively. Since AFOP is a diagnosis of exclusion, most patients are diagnosed with pneumonia that does not respond to treatment or has delayed resolution during follow up. Although the clinical presentations of the fulminant and subacute forms of AFOP are different, a clear distinction cannot be made for treatment due to the high mortality of the fulminant form. The prognosis is poor in acute fulminant cases.

Keywords: Organized pneumonia, interstitial lung disease, acute acute fibrinous

INTRODUCTION

Acute fibrinous and organizing pneumonia (AFOP), first described histologically by Beasley et al.[1] in 2002, has a specific histological pattern of its own and in 2022 American Thoracic Society (ATS), European Respiratory Society (ERS), Japanese Respiratory Society (JPS) and AssociacionLatinoamericana de Torax (ALAT) consensus is an idiopathic interstitial lung disease excluded from idiopathic pulmonary fibrosis (IPF).[2]

ETIOLOGY

AFOP occurs in a wide age range (38-78 age) and in a non-sexist spectrum of patients.[3] Although idiopathic cases have been reported, case series in which the underlying etiology is known and AFOP has been attributed to it has been published.[4-8] Basically, the most common condition is the diagnosis of AFOP with a tissue sample followed by a background rheumatologic disease, immunosuppressive comorbidities or drug use (Table).

In studies on COP patients, it was reported that those with intra-alveolar fibrin consistent with AFOP had a worse prognosis, but no significant radiological involvement difference was reported except for the halo finding.[4]For this reason, although it was thought to be a subtype of COP in the first evaluation, it has been accepted as a different interstitial lung disease in current guidelines due to its histological differences, and there is no consensus in favor of increased mortality or significant clinical difference in the co-occurrence of COP-AFOP compared to other etiologies.

Table. Probable etiologies in acute fibrinous and organizing pneumonia[5]

Autoimmune diseases	Polymyositis, dermatomyositis, ANCA-related vasculitides, rheumatoid arthritis, systemic sclerosis
Lung diseases	Cryptogenic organizing pneumonia, hypersensitivity pneumonia, acute and chronic eosinophilic pneumonias
Drug utilization	Statin, bleomycin, busulfan, abacavir, decitabine
Immunosuppressive conditions	Lung transplantation, myelodysplastic syndrome, monoclonal gammopathies, autologous bone marrow transplantation,
Infectious conditions	Human Immunodeficiency Virus, previous influenza, Pneumocystis carinii, Mycoplasma subtypes, history of fungal infection
Post-treatment conditions	Radiation pneumonitis
Hematological malignancies	Hodgkin lymphoma, acute myeloid leukemia, multiple myeloma
Other	Environmental exposure (Charcoal, hairspray), Idiopathic

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HISTOLOGY

The histologically specific pattern is the presence of organized intra-alveolar fibrin and is the essential parameter for diagnosis.[1] After the presence of fibrin, there are findings in favor of other organizing pneumonia, but the absence of histological involvement specific to other interstitial lung diseases (such as the presence of hyaline membrane and eosinophils) is required for the diagnosis of AFOP. Diagnosis of AFOP with these three elements (intra-alveolar fibrin, organizing pneumonia and other specific involvement exclusion) can be seen patchy in 90% of preparations in multiple biopsies or large tissue samples. Granulomatous infiltration, bronchopneumonia or abscess formation is also not seen in AFOP, which is performed with the presence of fibrin and patchy involvement to exclude from diffuse alveolar damage, and with the absence of eosinophils to exclude from eosinophilic pneumonia.[9]

CLINIC

In patients presenting with an acute and more fulminant picture, the clinic presents with rapidly worsening respiratory failure. In a single-center study conducted by Gomes et al.[5], in which mostly patients who applied in the form of subacute AFOP were evaluated; the main complaints were fever (69.2%), cough (46.2%) and chest pain (30.8%), respectively. Chills, fatigue, and weight loss can also be seen as nonpulmonary symptoms. Examination findings are mostly non-specific and can be summarized as auscultation findings consistent with pneumonia and the presence of desaturation that varies according to the clinic.

RADIOLOGY

In a study stating that there is no significant difference in the radiological pattern except for the halo finding in the comparison of AFOP and COP, Onishi et al.[4] argue that both the halo finding and the pathologic result are more significant in imaging and sampling performed at the early stage of the disease. Although there is a publication stating that a single nodule containing an air bronchogram in patients diagnosed at an early stage quickly turns into a common density, also in ground-glass, with multilobe involvement, there are studies that focus primarily on bilateral involvement of the lung basal progressively.[9] In most cases, the expected radiological appearance is consolidation in tomography sections in almost all patients and ground-glass accompanying consolidation, although it varies from study to study.[4,5,10]

DIAGNOSIS

Since AFOP is a diagnosis of exclusion, most patients are diagnosed with pneumonia that does not respond to treatment or has delayed resolution during followup. The role of laboratory results in diagnosis seems to be limited due to increased infective parameters in almost all patients.[5,9] In most cases, patients have increased C-reactive protein (CRP) levels either at the time of diagnosis or at follow-up, and CRP elevation is more pronounced in patients with AFOP than in other interstitial lung diseases.[5] Although different results were reported in studies evaluating the level of interleukin-6 (IL-6), they agreed that an increase was observed.[5,11] Pulmonary parenchyma biopsy is required for a definitive diagnosis, since the differential diagnosis cannot be made from the clinical presentation complaints of the patients and there may be a wide variety of diseases and exposure history in the background.

TREATMENT

Although the clinical presentations of the fulminant and subacute forms of AFOP are different, a clear distinction cannot be made for treatment due to the high mortality of the fulminant form. As seen in the literature, case reports are also seen in two general categories, like AFOP. In the first case, it is often not possible to prepare for the differential diagnosis in patients presenting with a very rapidly progressive clinic that cannot be differentiated from acute respiratory distress syndrome (ARDS). High-dose intravenous pulse methylprednisolone (1000 mg/day for 3 days) is used as a treatment in patient groups considered in favor of interstitial lung disease.[12] In the survivors of this group and in patients with slower clinical progression, mostly diagnosed with AFOP as a diagnosis of exclusion in the differential diagnosis, treatment protocols are mostly initiation of 1 mg/kg/day methylprednisolone as a maintenance steroidand 5-10 mg/day with weekly or biweekly titration. It consists of reducing the dose to methylprednisolone. As seen in the pulmonary vasculitis treatment protocols given for steroid sparing treatment and prevention of end organ damage, cases of AFOP using azathioprine, methotrexate, cyclophosphamide, tacrolimus and cyclosporine have been reported, but due to the number of treatment superiority and comparison, these additional treatment modalities have not been specified yet.[4,12]

It is known that the use of empirical antibiotics in acute fulminant cases is included in the treatment because ARDS and sepsis cannot be ruled out. There are no comparative studies on the role of adjunctive antibiotic therapy in these cases, with a group not given antibiotics. In the review of Kuza et al.[9], studies on both anti-biotherapy and steroid use were evaluated and although there is no definite treatment regimen, the steroid dose mentioned is appropriate in most patients, antibiotic therapy is started empirically by making a diagnosis of exclusion in subacute

patients, and non-steroid immunomodulatory agents are given, but mostly these patient groups are treated. It was stated that he currently has a rheumatological disease and, on the basis of this disease, the need for additional immunosuppressive therapy to steroids was decided.

Although the duration of total steroid use is not clearly known, there are studies that successfully indicate 3-month early titration regimens and long-term low-dose steroid use for up to 24 months.[13,14] Since the average steroid response is 90% or more in the publications, the current treatment should be steroid-based if there is no underlying rheumatological pathology, and if there is a life-threatening condition (such as ARDS), this steroid should be administered as an intravenous pulse of 1 g/day for at least three days. If it is not, it is given as 1 mg/kg/day or as a dose where treatment response is seen according to clinical experience. In maintenance, close follow-up with progressive dose reduction after clinical response is seen can be done on a weekly or biweekly dose titration schedule. In this follow-up or initial diagnosis, if additional immunosuppressive therapy is needed, it should be planned to reduce the total steroid dose with combined therapy, especially in elderly patients.

PROGNOSIS

Survival expectancy is high in fulminant cases that survive the acute condition and in patients with subacute follow-up, and in most case series, patients who meet this definition survived to study termination. The absence of mortality in subacute patients seen in the first description is consistent with case series with similar clinics. Studies also support the relatively good survival in patients presenting with subacute clinics.[5,10]

CONCLUSION

Acute fibrinous and organizing pneumonia (AFOP) is an uncommon histologic interstitial pneumonia form that is distinguished by intra-alveolar fibrin deposition and organized pneumonia. Although the clinical manifestations of the fulminant and subacute forms of AFOP are different, a clear differentiation cannot be made for treatment due to the significant mortality of the fulminant form.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Beasley MB, Franks TJ, Galvin JR, Gochuico B, Travis WD. Acute fibrinous and organizing pneumonia a histologic pattern of lung injury and possible variant of diffuse alveolar damage. *Arch Pathol Laborat Med.* 2002;126(9):1064-1070.
2. Raghu G, Remy-Jardin M, Richeldi L, et al. Idiopathic pulmonary fibrosis (an update) and progressive pulmonary fibrosis in adults: an official ATS/ERS/JRS/ALAT clinical practice guideline. *Am J Respir Crit Care Med*. 2022;205(9):e18-e47.
3. Wang Y, Li Y, Wang Q, et al. Acute fibrinous and organizing pneumonia; a case report. *Medicine*. 2019;98(8):e14537.
4. Onishi Y, Kawamura T, Higashino T, Mimura R, Tsukamoto H, Sasaki S. Clinical features of acute fibrinous and organizing pneumonia: an early histologic pattern of various acute inflammatory lung diseases. *PLoS One*. 2021;16(4):e0249300.
5. Gomes R, Padrão E, Dabó H, et al. Acute fibrinous and organizing pneumonia: a report of 13 cases in a tertiary university hospital. *Medicine*. 2016;95(27):e4073.
6. Simmons GL, Chung HM, McCarty JM, et al. Treatment of acute fibrinous organizing pneumonia following hematopoietic cell transplantation with etanercept. *Bone Marrow Transplant*. 2017;52(1):141-143.
7. Kumar S, Mishra M, Goyal K, Bhatt R, Joshi P, Bansal S. Acute fibrinous organizing pneumonia: a rare lung pathology. *Monaldi Arch Chest Dis*. 2019;89(2):1016.
8. Ford D, Charoenpong P, Boparai S. Acute fibrinous organizing pneumonia: a new association. *Chest*. 2021;160(4):A1654.
9. Kuza C, Matheos T, Kathman D, Heard SO. Life after acute fibrinous and organizing pneumonia: a case report of a patient 30 months after diagnosis and review of the literature. *J Crit Care*. 2016;31(1):255-261.
10. Damas C, Morais A, Moura CS, Marques JA. Acute fibrinous and organizing pneumonia. *Pulmonol.* 2006;12(5):615-620.
11. Lu J, Yin Q, Zha Y, et al. Acute fibrinous and organizing pneumonia: two case reports and literature review. *BMC Pulm Med*. 2019;19(1):141.
12. Onishi Y, Kawamura T, Nakahara Y, et al. Factors associated with the relapse of cryptogenic and secondary organizing pneumonia. *Respir Investig* 2017;55(1):10-15.
13. Sauter JL, Butnor KJ. Expanding the spectrum of pulmonary histopathological manifestations of antisynthetase syndrome: anti-EJ-associated acute fibrinous and organizing pneumonia. *Histopathol.* 2014;65(4):581-582.
14. Ning YJ, Ding PS, Ke ZY, Zhang YB, Liu RY. Successful steroid treatment for acute fibrinous and organizing pneumonia: a case report. *World J Clin Cases*. 2018;6(15):1053-1058.