Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Case Report

Life after acute fibrinous and organizing pneumonia: a case report of a patient 30 months after diagnosis and review of the literature

Catherine Kuza, MD a,b,⁎, Theofilos Matheos, MD b, Deirdre Kathman, DO c, Stephen O. Heard, MD b

a Department of Anesthesiology and Critical Care Medicine, Brigham and Women's Hospital, 75 Francis Street, Boston, MA, 02115, USA
b Department of Anesthesiology, University of Massachusetts Medical School, 55 North Lake Avenue, Worcester, MA, 01655, USA
c Department of Medicine (Pulmonary/Critical Care Medicine), University of Massachusetts Medical School, 55 North Lake Avenue, Worcester, MA, 01655, USA

ARTICLE INFO

Keywords:
Acute fibrinous and organizing pneumonia
Interstitial lung diseases

ABSTRACT

Acute fibrinous and organizing pneumonia (AFOP) is a rare histologic interstitial pneumonia pattern recently described in the literature with fewer than 120 cases published. AFOP is often difficult to diagnose and may be mistaken for other pulmonary disorders such as interstitial pneumonias or pneumonitides. Patients often present with vague symptoms of cough, dyspnea, hemoptysis, fatigue, and occasionally respiratory failure. Radiological findings show diffuse patchy opacities and ground glass appearance of the lungs. On histologic examination, intra-alveolar fibrin balls are observed. We discuss a case of a man who presented with hemoptysis and dyspnea and whose open lung biopsy revealed AFOP. We will describe the presentation, diagnosis, and post-discharge course, and review the current literature. There are only 4 cases which have reported the patients’ course of disease after 1 year, the longest being 2 years. To our knowledge, this is the only case of AFOP in the literature that describes the course of a patient more than 2 years after the diagnosis of AFOP, and is the most comprehensive review of the current literature.

© 2015 Elsevier Inc. All rights reserved.

1. Introduction

Acute fibrinous and organizing pneumonia (AFOP) is a rare histologic interstitial pneumonia pattern that is histologically characterized by intra-alveolar fibrin “balls” and organizing pneumonia with a patchy distribution. It is associated with viral, bacterial, and fungal infections, connective tissue disorders, autoimmunity, drugs, environmental exposures, and occupational/environmental exposures such as asbestos, various dusts, exotic animals, aerosol products, and coal; it may also be idiopathic in nature. Patients present with cough, dyspnea, or acute respiratory distress syndrome. Radiological findings demonstrate diffuse patchy opacities. The diagnosis requires a lung biopsy which can be obtained surgically, via bronchoscopy, or under ultrasound- or computed tomographic (CT) scan-guidance. The definitive management of this disease is still unknown; however, there is a role for steroids and other immunosuppressive agents [1].

We present the case of a man diagnosed with AFOP and describe his 30-month post-discharge course, the longest follow-up in the literature to our knowledge. In addition, we will also present the most comprehensive review of the AFOP literature. Patient characteristics, suspected etiology, diagnostic modality, treatments, and outcomes will be reported.

2. Case report

A 60-year-old male smoker was transferred from an outside hospital presenting with progressively worsening dyspnea and blood-tinged sputum over the course of 2 months. He was otherwise healthy and reported a history of working with asbestos and fiberglass from 1975 to 1988, and recent occupational dust exposure. He complained of low grade fevers and sweats and denied weight loss, other significant exposures, recent travel, pets, and sick contacts. At an outside hospital, a chest x-ray showed bilateral diffuse opacities and small bilateral pleural effusions (Fig. 1A). A CT scan of the chest demonstrated diffuse bilateral ground glass densities (Fig. 1B). Bronchoscopy was performed and biopsies were negative for malignancy, granulomas, Pneumocystis jiroveci cysts, and trophozoites. Gram stain and culture, periodic acid–Schiff stain, and acid fast-bacilli culture were negative. Bronchoalveolar lavage (BAL) showed many red blood cells, few white blood cells, and no organisms. The BAL culture grew few Candida albicans. Routine laboratory work up was normal, except for an elevated white blood cell count. Laboratory work for rheumatoid factor, cold agglutinins, antinuclear antibodies, Scl-70 scleroderma antibody, and histone antibody were negative. In addition, HIV-1 and HIV-2, influenza A and B, urine Legionella antigen, and Mycoplasma pneumoniae IgG and IgM were negative. He received a 7-day course of antibiotics (ceftriaxone, azithromycin, and doxycycline) and methylprednisolone 125 mg IV every 6 hours for 6 days. Despite therapy, his symptoms did not improve and he was transferred to our hospital for further work up.

⁎ Corresponding author.
E-mail addresses: catherine.kuza@gmail.com, ckuza@partners.org (C. Kuza).
On initial physical examination he was afebrile, tachypneic, and hypoxic, requiring 80% oxygen to achieve a SpO2 of 92%. Lung auscultation revealed diffuse rhonchi and rales. Additional tests performed at our institution included blood and sputum cultures, ANCA, Jo-1 antibody, glomerular basement membrane antibody, cyclic citrullinated peptide IgG and IgA, and creatine phosphokinase, which were negative. On admission to our hospital, methylprednisolone 60 mg IV every 6 hours was given for 2 days, and the dose was later increased to 125 mg IV every 6 hours. Two days later a steroid taper was initiated, decreasing the methylprednisolone dose to 60 mg PO daily for 5 days, and then prednisone 60 mg PO daily was started. He required oxygen with a high flow nasal cannula. On the fourth day of hospitalization, he underwent an anterior thoracotomy, right wedge lung biopsies, and right chest tube placement. He was brought intubated from the operating room for ventilator weaning in the intensive care unit and he was extubated on postoperative day 1. Specimens of the lung biopsy were sent for pathology, microbiology, and virology. The pathology demonstrated AFOP with a background of chronic interstitial pneumonia (Fig. 2A and B). A trichrome stain revealed fibrosis. Tissue specimens were negative for acid fast bacilli, mycobacteria, fungi and cytomegalovirus. Gram stain and culture were also negative. However, an anaerobic and aerobic culture grew a coagulase negative Staphylococci. Sulfamethoxazole/trimethoprim was initiated on postoperative day 3. On repeat chest x-ray, the lungs appeared unchanged. The chest tube was eventually removed and he was discharged to pulmonary rehabilitation on prednisone 60 mg PO daily and continuous oxygen via nasal cannula at 3 L/min.

Upon discharge, the patient was followed by the pulmonology team. Eight months after his hospital discharge, he experienced arthralgias and Raynaud’s syndrome, and developed telangiectasias. On further evaluation, blood work was positive for antinuclear antibodies and Sjogren’s syndrome antibody and he was diagnosed with an unspecified connective tissue disease (CTD). He was started on azathioprine, but because of an adverse reaction, his therapy was changed to mycophenolate mofetil 500 mg PO 3 tablets in the morning and 2 tablets at night. Over 2 years, several steroid tapers were attempted unsuccessfully. His symptoms worsened at lower doses. Thirty months after discharge he remains dependent on mycophenolate mofetil, prednisone 10 mg PO daily, and oxygen, requiring 4 L/min via nasal cannula at rest and during sleep, and 8 to 10 L/min via an oxymizer pendant with activity. He is currently on disability. Although his exercise tolerance improved after completing pulmonary rehabilitation, his functional status has not returned to his pre-illness baseline. He has been evaluated and listed for lung transplantation.

3. Discussion

Acute fibrinous and organizing pneumonia (AFOP) is a rare histologic interstitial pneumonia pattern; as of 2015, there have been 111 cases reported in the literature (Table 1). Of these cases, 43 were male, 35 were female; gender was not specified in 33 cases. It most commonly occurred in patients in their fifth and sixth decade of life; however, there were 5 reports in children. In most cases, the etiology was unknown. Possible causes of AFOP include connective tissue disease, infections, environmental or occupational exposure, drug reactions, autoimmune disease, after organ transplantation, and cancers.
Table 1
Summary of patient characteristics, diagnosis, treatment, and outcome in AFOP from literature

| Publication | Patient characteristics | Proposed cause | Diagnostic method | Treatment | Outcome | Duration of Follow-up | Still on treatment at follow-up? |
|-------------|-------------------------|----------------|-------------------|-----------|---------|-----------------------|----------------------------------|
| Lopez-Cuenca et al [2] | 27 yo F | Marden-Walker syndrome/sepsis/ARDS | Autopsy | Corticosteroids, antibiotics, mechanical ventilation | Death | 15 days | NA |
| Bharti et al [3] | 56 yo M | Idiopathic | SB | Corticosteroids, mycophenolate mofetil, mechanical ventilation | Improved | 12 months | Yes |
| Beasley et al [1] | 77 yo M | Haemophilus influenzae | SB or autopsy* | Antibiotics | Death | NS | NA |
| | 33 yo M | Occupational exposure (construction worker)/ Acinetobacter baumannii | SB | Antibiotics | Improved | NS | NS |
| | 55 yo M | Ankylosing spondylitis/occupational exposure (zoologist exposed to exotic animals)/ amiodarone | SB | Antibiotics | Improved | NS | NS |
| | 76 yo F | Environmental (excessive hair spray) | SB | Corticosteroids, antibiotics | Improved | NS | NS |
| | 74 yo M | Environmental exposure (coalminer) | SB or autopsy* | Furosemide, dopamine, mechanical ventilation | Death | NS | NA |
| | 78 yo F | Polymyositis | SB or autopsy* | Corticosteroids | Death (unrelated cause) | NS | NA |
| | 58 yo F | Idiopathic | SB | Antibiotics | Improved | NS | NS |
| | 47 yo M | Idiopathic | SB | Antibiotics | Improved | NS | NS |
| | 39 yo M | Ki-1 lymphoma | SB or autopsy* | Corticosteroids, mechanical ventilation | Death | NS | NA |
| | 59 yo F | Idiopathic | SB or autopsy* | Antibiotics, corticosteroids, mechanical ventilation | Death | NS | NA |
| | 70 yo M | Idiopathic | SB | Antibiotics | Improved | NS | NA |
| | 72 yo F | Idiopathic | SB | Antibiotics, corticosteroids | Improved | NS | NA |
| | 36 yo M | Idiopathic | SB or autopsy* | Mechanical ventilation | Death | NS | NA |
| | 76 yo M | Idiopathic | SB or autopsy* | Antibiotics, corticosteroids | Death | NS | NA |
| | 65 yo F | Idiopathic | SB or autopsy* | Antibiotics | Death | NS | NA |
| | 68 yo F | Idiopathic | SB or autopsy* | NA | Death | NS | NA |
| | 66 yo M | Idiopathic | SB or autopsy* | Antibiotics, corticosteroids, mechanical ventilation | Death | NS | NA |
| Guimaraes et al [4] | 55yo F | Primary biliary cirrhosis | SB | Corticosteroids | Improved | 14 months | Yes |
| Rapaka et al [5] | 38 yo M | HIV | FTBB | Corticosteroids | Improved | NS | NS |
| Kobayashi et al [6] | 55 yo M | Chronic glomerulonephritis | SB | Corticosteroids | Improved | 3 months | NS |
| Tzouvelekis et al [7] | 65 yo F | Idiopathic | SB | Corticosteroids, antibiotics | Improved | 3 months | Yes |
| Zhang et al [8] | 73 yo M | Idiopathic | Ultrasound-guided percutaneous lung biopsy | Corticosteroids | Improved | 1.5 months | Yes |
| Valim et al [9] | 39 yo F | Systemic sclerosis | SB | Cyclophosphamide, corticosteroids, mechanical ventilation | Death | 3 days | NA |
| Damas et al [10] | 66 yo M | Idiopathic | SB | Antibiotics, corticosteroids, cyclophosphamide | Improved | NS | NS |
| Yokogawa et al [11] | 52 yo F | Abacavir | SB | Antibiotics, corticosteroids, discontinue Abacavir | Improved | NS | NS |
| Balduin et al [12] | 47 yo M | Collagen vascular disease | SB | Corticosteroids, azathioprine, noninvasive mechanical ventilation | Improved | NS | NS |
| Lee et al [13] | 60 yo M | Hematopoietic stem cell transplantation/Acute myelogenous leukemia | FTBB | Corticosteroids | Death | 61 days | NA |
| Canessa et al [14] | 60 yo F | Whipple's disease | SB | Antibiotics | Improved | NS | NS |
| Vasu et al [15] | 64 yo M | Decitabine/Acute myelogenous leukemia/myelodysplastic syndrome | SB | Corticosteroids, discontinuation of decitabine | Improved | NS | NS |
| Hariri et al [16] | 47 yo M | Systemic lupus erythematosus | SB | Corticosteroids, cyclophosphamide | Improved | NS | Yes |
| Heo et al [17] | 40 yo M | HIV/Pneumocystis jiroveci | SB | Antibiotics, corticosteroids | Improved | 8 months | No |
| Santos et al [18] | 44 yo M | Idiopathic | SB | Surgical resection | Improved | NS | NA |
| Otto et al [19] | 66 yo F | Influenza virus/history of double lung transplant | Autopsy | Antiviral, antibiotics, mechanical ventilation, ECMO | Death | 11 months | NA |

(continued on next page)
| Publication        | Patient characteristics | Proposed cause                      | Diagnostic method | Treatment                                      | Outcome                  | Duration of Follow-up | Still on treatment at follow-up? |
|-------------------|-------------------------|-------------------------------------|-------------------|-----------------------------------------------|--------------------------|-----------------------|----------------------------------|
| Ribera et al [20] | 69 yo F                 | *Chlamydia pneumoniae*              | FTBB              | Antibiotics, steroids, mechanical ventilation | Death                    | 20 days               | NA                               |
| Cincotta et al [21]| 38 day old F           | ARDS/RSV                           | SB                | Mechanical ventilation                         | Death                    | NS                    | NA                               |
| Sverzellati et al [22]| 62 yo F             | Pulmonary mycosis fungoides         | SB                | Corticosteroids                               | Improved                 | NS                    | NS                               |
| Cho et al [23]    | 79 yo M                 | Idiopathic                         | SB                | Corticosteroids                               | Improved                 | NS                    | NS                               |
| Saurer et al [24] | 66 yo F                 | Idiopathic                         | FTBB              | Antibiotics, corticosteroids, IV immunoglobulin, cyclosporine, cyclophosphamide, oscillating mechanical ventilation | Improved                 | 2 years               | Yes                              |
| White et al [25]  | 1 patient               | 14 yo F                            | FTBB              | NS                                            | NS                       | NS                    | NS                               |
| Prahalad et al [26]|                     |                                     |                   |                                               |                          |                       | NA                               |
| Hwang et al [27]  | 6 patients with mean age of 68 yo | Severe acute respiratory syndrome (SARS) | Autopsy           | NS                                            | Death                    | NS                    | NA                               |
| Qiu et al [28]    | 5 patients, 2 male and 3 female, age 43-61 yo | NS                           | CT-guided percutaneous lung biopsy | Corticosteroids                              | Improved                 | NS                    | NS                               |
| Al-Khouzaie et al [29]| 45 yo M              | NS                                 | Lung biopsy       | Corticosteroids                               | Improved                 | NS                    | NS                               |
| Labarinas et al [30]| 10 yo M               | NS                                 | Lung biopsy       | Antithymocyte globulin, cyclosporine, hematopoietic stem cell transplant | Improved                 | NS                    | NS                               |
| Moreira et al [31]| 44 yo M                | NS                                 | Surgical resection| Corticosteroids, antibiotics, surgical resection | Improved                 | NS                    | No                               |
| Bawa et al [32]   | 31 yo F                | Idiopathic                         | Lung biopsy       | Corticosteroids                               | Improved                 | 9 months              | Yes                              |
| Jarbou et al [33] | 70 yo M                | Idiopathic                         | FTBB              | Corticosteroids                               | Improved                 | 6 months              | Yes                              |
| Alici et al [34]  | 48 yo F                | Idiopathic                         | FTBB              | Corticosteroids                               | Improved                 | 1 week                | Yes                              |
| Feng et al [35]   | 64 yo M                | *Mycobacterium tuberculosis*        | Percutaneous needle lung biopsy | Corticosteroids, anti-tuberculosis antibiotics | Improved                 | 9 months              | NS                               |
|                   | 84 yo M                | Lung adenocarcinoma                | Percutaneous needle lung biopsy, surgical lung biopsy | Corticosteroids, anti-tuberculosis antibiotics | Improved                 | 10 months             | NA                               |
| Garcia et al [36] | 46 yo M                | Idiopathic                         | SB                | Corticosteroids                               | Improved                 | NS                    | NS                               |
| Hara et al [37]   | 70 yo M                | Idiopathic                         | SB                | Corticosteroids                               | Resolved                 | 3 months              | NS                               |
| Kassir et al [38] | 53 yo M                | Idiopathic                         | Peripheral lung biopsy | Corticosteroids                               | Resolved                 | 3 months              | NS                               |
| Lococo et al [39] | 65 yo F                | Idiopathic                         | SB                | Corticosteroids                               | Resolved                 | 2 weeks               | Yes                              |
| Picciucci et al [40]| 79 yo M               | Amiodarone                         | FTBB              | Corticosteroids                               | Resolved                 | 3 months              | NS                               |
| Mittal et al [41] | 14 yo F                | Idiopathic                         | CT-guided percutaneous transbronchoscopic lung biopsy | Corticosteroids          | Resolved                 | 1 month               | No                               |
| Renaud-Pocard et al [42]| 22 yo M              | Cystic fibrosis; lung transplant    | FTBB              | Corticosteroids, antibiotics, re-transplantation of lungs | Improved                 | 2 years               | No                               |
| Alikhar et al [43]| 68 yo F                | Idiopathic                         | SB                | Corticosteroids                               | Improved                 | 2 months              | Yes                              |
| Feinstein et al [44]| 10 patients, 4 M, 6 F, average age 59.6 yo | NS                           | FTBB              | Corticosteroids                               | Improved                 | 6 patients improved; Death in 2 patients (unrelated to AFOP) | NS | NS |
| Rajan et al [45]  | 42 yo M                | Acute myelogenous leukemia/Aspergillosis | SB                | Antifungal                                    | Resolved                 | 5 months              | No                               |
required further diagnostic work up. The diagnosis of AFOP was made by surgical lung biopsy in 52 patients, transbronchial lung biopsy in 9 patients, percutaneous needle biopsy in 2 patients, image-guided (CT- or ultrasound-guided) percutaneous lung biopsy in 8 patients, peripheral lung biopsy in 1 patient, unspecified lung biopsy techniques in 3 patients, and autopsy in 10 patients [1–50]. Our patient’s BAL and bronchoscopic biopsy were inconclusive; the diagnosis was made with surgical lung biopsy. To make a definitive diagnosis of AFOP, histopathologic evaluation is required [1].

The major histopathologic features of AFOP are intra-alveolar fibrin “balls”, organizing pneumonia, and a patchy distribution within the lung parenchyma. It involves up to 90% of the alveolar spaces within a tissue sample. Minor features that may be associated with AFOP include inflammatory changes of the alveolar walls surrounding the areas of fibrin, myxoid connective tissue in the alveolar septum, type 2 pneumocyte hyperplasia, and minimal changes in the lung tissue areas without fibrin. It does not demonstrate hyaline membranes and lacks eosinophils, which distinguishes it from diffuse alveolar damage and eosinophilic pneumonia, respectively. Although fibrin deposition has been associated with diffuse alveolar damage, it is not the prominent feature and does not display the intra-alveolar fibrin ball pattern. In addition, diffuse alveolar damage is associated with diffuse changes, while AFOP presents in a patchy distribution. AFOP does not consist of granulomatous inflammation, broncho-pneumonia, or abscess formation [1].

An ideal treatment of AFOP has not been reported; it has been treated with antibiotics, corticosteroids, and immunosuppressants (mycophenolate mofetil, azathioprine, and cyclophosphamide) with varying responses [1,3,10,16,26]. Corticosteroids are the most common and successful treatment modality described in the literature [43]. Akhtar et al [43] recommended methylprednisolone 60 mg every 6 to 8 hours for the first 5 days, followed by a gradual taper and a maintenance dose of 40 mg daily for 3 months. Other therapeutic regimens described included methylprednisolone 0.5 to 1 mg/kg per day IV followed by prednisone 0.5 to 1 mg/kg per day which is gradually tapered [3,4,6,43]. The exact duration of therapy is unknown, and is based on the patient’s clinical course and underlying etiology. Some patients return to baseline within months of treatment [17,41,45]. Other patients experienced worsening of symptoms during steroid tapers or noncompliance with treatment; improvement was noted when higher doses were resumed [7,32,43]. Treatment may be as long as 2 years [1,3,4,10,24]. From our literature review, the follow-up course of only 19 patients was reported and ranged from 2 weeks to 2 years [3,4,6,8,17,24,32–35,37,39–41,43,45,47]. Only 4 reports gave information on the patients’ condition after 1 year [3,4,24,42]. Ten

(continued)
patients were still receiving treatment at the time of follow-up, 3 patients completed treatment and were asymptomatic, and in 6 patients it was not specified whether or not they were still receiving therapy at the time of follow-up. Fifteen patients received only corticosteroids. One patient required corticosteroids and anti-tuberculosis antibiotics [35], and 1 patient improved after 5 months with only oral antifungal therapy [46]. Two patient required immunosuppressive agents such as cyclophosphamide, azathioprine, and mycophenolate mofetil in addition to corticosteroids [3,24]. Of the 4 cases that reported on the patient’s condition over 2 years, 3 patients remained on therapy at 1 year, 14 months, and 2 years of follow-up [3,4,24]; treatment was not specified at 2-year follow-up in 1 patient [42]. None of the cases in the literature specified whether the patients were oxygen-dependent on discharge or at follow-up. Our patient was discharged on a steroid taper; however, he experienced relapses with decreased doses, requiring resumption of higher doses. After his diagnosis of a connective tissue disease, mycophenolate mofetil was added to his therapeutic regimen. At 30 month follow-up, he continues to require immunosuppressant therapy, remains oxygen-dependent, and has failed for lung transplantation.

Patients diagnosed with autoimmune or collagen vascular diseases may benefit from immunosuppressant therapy in addition to steroids. Cyclophosphamide and steroids were used to treat AFOP in patients with systemic sclerosis and systemic lupus erythematosus [9,16]. In addition to steroids, azathioprine was used to treat a patient with collagen vascular disease and AFOP [12]. Sauter et al used azathioprine, mycophenolate mofetil, and steroids in the treatment for a patient with AFOP and anti-synthetase syndrome [24]. Prahalad et al described a case of AFOP diagnosed in the setting of juvenile dermatomyositis in which the patient continued to decline despite therapy with azithromycin and increased doses of methylprednisolone. She received intravenous immunoglobulin (2 g/kg), cyclosporine 5 mg/kg IV, and cyclophosphamide 500 mg/kg IV. She eventually required mechanical and oscillating mechanical ventilation but died after a massive pneumothorax [26]. Mycophenolate mofetil and cyclophosphamide have also been reported in idiopathic cases of AFOP, resulting in improved outcomes [3,10]. Mycophenolate mofetil has been used to treat scleroderma-related interstitial lung disease and cyclophosphamide-refractory lupus nephritis. It is safe and effective in maintaining lung function in interstitial lung diseases associated with CTD [3]. It may be a useful adjunct to steroids in patients with associated autoimmune diseases and CTD.

Other therapeutic interventions include drug discontinuation, surgical resection, and organ transplantation. In cases caused by a medication (amiodarone, decitabine, abacavir, and bleomycin), treatment with corticosteroids and discontinuation of the drug resulted in improvement of symptoms [11,15,40,48,49]. There were 2 reports of surgical lung resection in the management of AFOP, without medical management, with subsequent improvement of symptoms [18,31]. Surgical resection may be an additional treatment option in the management of AFOP if the disease is relatively localized.

AFOP has been described following organ transplantation; however, organ transplantation may be indicated to treat AFOP refractory to medical treatment. AFOP developed in 1 patient after an allogenic hematopoietic stem cell transplantation for the treatment of AML and in 23 patients after double-lung transplantation. All of the patients failed treatment with antibiotics, steroids, and immunosuppressants and expired [13,19,46]. Four patients developed AFOP after lung transplantation and were treated with immunosuppressive agents and corticosteroids but the long-term outcome was not specified [47]. Alici et al reported a patient with AFOP associated with grade 2 primary graft dysfunction of a lung transplant whose condition improved after corticosteroid treatment; however, the follow-up duration was only 1 week [34]. Labarinas et al described a case of AFOP in the setting of aplastic anemia and fulminant liver failure, suspected to be autoimmune in nature. There was no response to treatment with antithymocyte globulin or cyclosporine. Disease resolution occurred after hematopoietic stem cell transplant [30]. Renaud-Picard et al described a patient with cystic fibrosis who received a lung transplant. After 42 months, he experienced respiratory failure unresponsive to antibiotics and steroids. He underwent a bilateral lung retransplantation, and surgical pathology of the explanted lungs revealed AFOP. At 2-year follow-up, the patient was reportedly doing well [42]. At 30 months of follow-up, our patient remains dependent on immunosuppressive agents, and was listed for lung transplantation after he experienced clinical worsening and increased oxygen requirements.

Although case reports are considered to be at the bottom of the hierarchy of what is regarded as reliable evidence for basing clinical decisions, there is important knowledge that can be obtained from them [51]. The value of publishing case series and reviews is to educate providers on conditions which are rare, but may be more prevalent than expected. It informs clinicians of the diagnostic tools necessary to make the diagnosis, and provides them with treatment options that cannot be tested by randomized controlled trials because of the small number of subjects who have the rare disease [52]. It provides information on the clinical course of the disease and what therapeutic interventions have failed and succeeded. The goal of this case report and review is to provide clinicians with the presentation, diagnosis, and management of AFOP, a condition which may be more prevalent than we suspect. We presented the clinical presentation, radiological findings, diagnostic approach, associated conditions and how they affect management, and reported treatment options which have failed and succeeded. The literature does not clearly define the duration of the disease course or treatment; especially when it is associated with autoimmune, collagen vascular, or connective tissue disease. In addition, we describe that the disease course may be lengthy and may not resolve with medical management alone, and surgical intervention may be necessary. Through our literature review, we discovered localized disease may be curative by surgical resection, and lung transplantation may be considered in disease refractory to medical treatment with good long-term outcome.

4. Conclusion

The treatment and long-term outcome of acute fibrous and organizing pneumonia are not well defined. In the case presented, the patient was admitted with progressively worsening dyspnea and cough over 2 months and a ground glass appearance of lungs on CT scan. The diagnosis of AFOP was made by open lung biopsy and histology. His condition was complicated by a diagnosis of CTD. Thirty months after diagnosis he remains dependent on steroids, immunosuppressive agents, oxygen, and has been listed for lung transplantation. Our extensive literature review describes the associated medications and conditions with the disease, diagnostic modalities, various treatment strategies, and outcomes of AFOP. Definitive management of this illness is not yet clearly defined. Treatment includes steroids, immunosuppressive agents, and potentially surgical lung resection and organ transplantation. There are few studies which report the long-term outcomes of these patients. To date, we present the longest follow-up of a patient diagnosed with AFOP. It is important to raise awareness of this disease, so symptoms and radiological findings may be identified and lead to appropriate diagnostic tests and management. Further reports of therapeutic management and long-term outcomes are required.

Acknowledgment

We greatly appreciate the assistance of Ms Christine Ford, Dr Kristine Cornejo, MD, and Dr Thomas Stockl, MD, from the Department of Pathology for providing us with histologic images and interpretation. We also thank Dr Peggy Wu, MD, and Dr Raymond Pertusi, MD, from the Department of Rheumatology for their role in the patient’s care. We wish to thank Dr Mark Dershowitz, MD, from the Department of Anesthesiology for his help in preparing this manuscript.
References

[1] Beasley MB, Franks TJ, Galvin JR, Cochoius B, Travis WD. Acute fibrous and organizing pneumonia: a histological pattern of lung injury and possible variant of diffuse alveolar damage. Arch Pathol Lab Med 2002;126(5):1064–70 [PubMed PMID:12204055].

[2] Lopez-Cuenca S, Morales-Garcia S, Martin-Hita A, Frutos-Vivar F, Fernandez-Segoviano P, Esteban A. Severe acute respiratory failure secondary to acute fibrous and organizing pneumonia requiring mechanical ventilation: a case report and literature review. Respir Care 2012;57(8):1337–41 [PubMed PMID:22384347].

[3] Bhuiyan S, Makeen MA, Tricoci JP, Periere KC. Severe acute fibrous and organizing pneumonia (AOPF) causing ventilatory failure: successful treatment with mycostopnetol and corticosteroids. Respir Med 2009;103(11):1764–7 [PubMed PMID:19666121].

[4] Guimaraes C, Sanches I, Ferreira C. Acute organizing pneumonia and organising pneumonia: a case report and review of the literature. J Med Case Rep 2009;3:74 [PubMed PMID:19946530].

[5] Santos C, Fradinho F, Catarino A. Acute organizing pneumonia mimicking mesothelioma. Am J Respir Crit Care Med 2015;191(1):104 [PubMed PMID:26178128].

[6] Bawa AS, Delaney MD, Potter BM. Acute fibrous and organizing pneumonia: A case report of newly identified entity with follow-up data. Chest 2004;126(4_MeetingAbstracts):3952S–3.