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Case Report

SUCCESSFULLY TREATED ACUTE INTERSTITIAL PNEUMONIA

Marija Gomerčić Palčić[1,2], Ivan Turalija[1], Luka Vrbanić[1], Ivana Folnožić[1], Eugenija Basioli Kasap[3] and Monika Ulamec[1,2]

[1]Sestre milosrdnice University Hospital Center, Zagreb; Croatia;
[2]University of Zagreb, School of Medicine, Zagreb, Croatia;
[3]Zadar General Hospital, Zadar, Croatia

SUMMARY – Acute interstitial pneumonia (AIP) is a rare idiopathic interstitial pneumonia with histology finding of diffuse alveolar damage (DAD). It is characterized by progressive hypoxic respiratory failure, high mortality rate, and absence of guidelines for its treatment. Here we present a case of a 64-year-old woman with progressive dyspnea, acute respiratory failure, diffuse bilateral reticulonodular opacities on standard chest radiograph, diffuse ground-glass opacities on computed tomography, and biopsy proven DAD. Diagnosis of AIP was established after extensive work-up that excluded the known risk factors for acute respiratory distress syndrome. Oxygen therapy and high-dose parenteral corticosteroids led to gradual improvement and resulted in complete respiratory recovery. Since there are no existing guidelines for treating AIP, more case reports and case series if not randomized control trials are warranted in order to define the most effective therapeutic modality.

Key words: *Acute interstitial pneumonia; Corticosteroid therapy; Acute respiratory distress syndrome; High-flow nasal cannula*

Introduction

Acute interstitial pneumonia (AIP, Hamman-Rich syndrome) is a rare disease that can be described as idiopathic acute respiratory distress syndrome (ARDS) with histology finding of biopsy proven diffuse alveolar damage (DAD). It is characterized with furious health deterioration and high mortality that tends to occur in patients without pre-existing lung disease, usually affects middle aged adults, has no gender bias, and cigarette smoking does not appear to be a predisposing factor[1-4]. At the time of the COVID-19 pandemic, it is of interest that clinical presentation of AIP mimics viral respiratory tract infection with the most common symptoms of dyspnea, non-productive cough and high temperature[5], together with radiologic findings of diffuse, bilateral, air-space opacifications, and high-resolution computed tomographic scans showing bilateral, patchy, symmetric areas of ground-glass attenuation, air space consolidations, as well as traction bronchiectasis in the late phase[6]. We recognize a problem here, while the majority of AIP patients have severe hypoxemia at presentation and many require intensive care and mechanical ventilation with mortality higher than 60%[5,7], and currently there are no guidelines providing standardized AIP treatment recommendations.

Case Report

Here we present a case of a 64-year-old female who was admitted to our department due to progressive dyspnea and cough followed by fever a week prior

Correspondence to: *Marija Gomerčić Palčić, MD, PhD,* Sestre milosrdnice University Hospital Center, Vinogradska c. 29, HR-10000 Zagreb, Croatia
E-mail: marijagomercic@yahoo.com

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to admission. She was a heavy smoker (40 pack/years) and reported morning cough for several years, which worsened one month before presentation. Her history included psoriasis (diagnosed at 17, in remission for the last 20 years). Initial symptoms were mild, as she complained of exertional dyspnea but on the day of admission, she was dyspneic at rest. Physical examination revealed diffuse bilateral inspiratory crackles. Arterial blood gas analysis showed pH 7.47, partial pressure of carbon dioxide ($PaCO_2$) 4.5 kPa, partial pressure of oxygen (PaO_2) 7.5 kPa, and arterial blood oxygen saturation (SaO_2) 91%. Total leukocytes were elevated ($24x10^9$/L), C-reactive protein level was 275.6 mg/L, and procalcitonin level was 0.08 ng/mL. Standard chest radiograph showed diffuse, bilateral reticulonodular opacities (Fig. 1a).

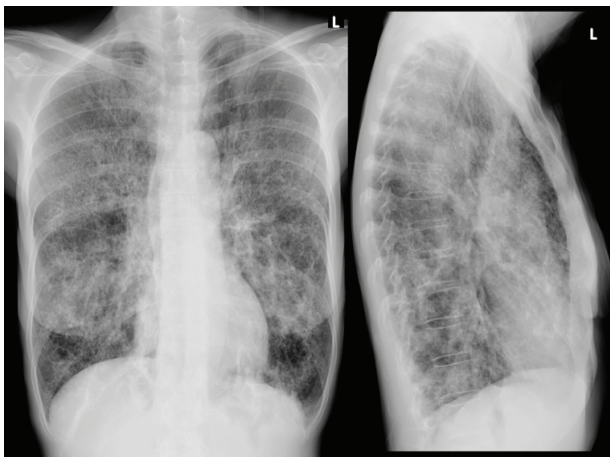

Fig. 1. Chest x-ray taken at presentation.

Computed tomography angiography was performed excluding pulmonary embolism but revealing diffuse ground-glass lung pattern with hyperinflation, especially in the upper lobes of the lungs (Fig. 1b).

After initial work-up including microbiological and serological testing, cultures of sputum and blood, dual antibiotic therapy (ceftriaxone and clarithromycin) was initiated together with oxygen therapy *via* nasal cannula. Day after admission, fiber bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial lung biopsy was performed. Three days after admission, her condition deteriorated with progression of respiratory

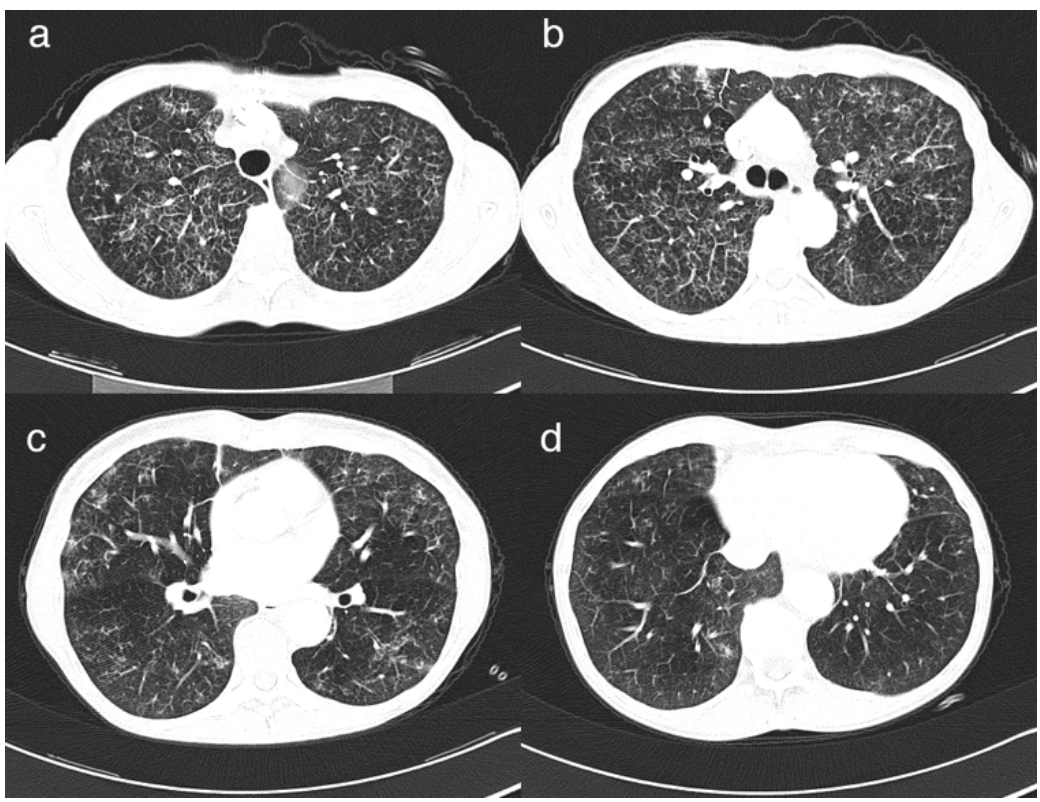

Fig. 2. High-resolution computer tomography at presentation: (a) and (b) slices of upper lung parts; (c) and (d) slices of middle and lower lung parts, respectively.

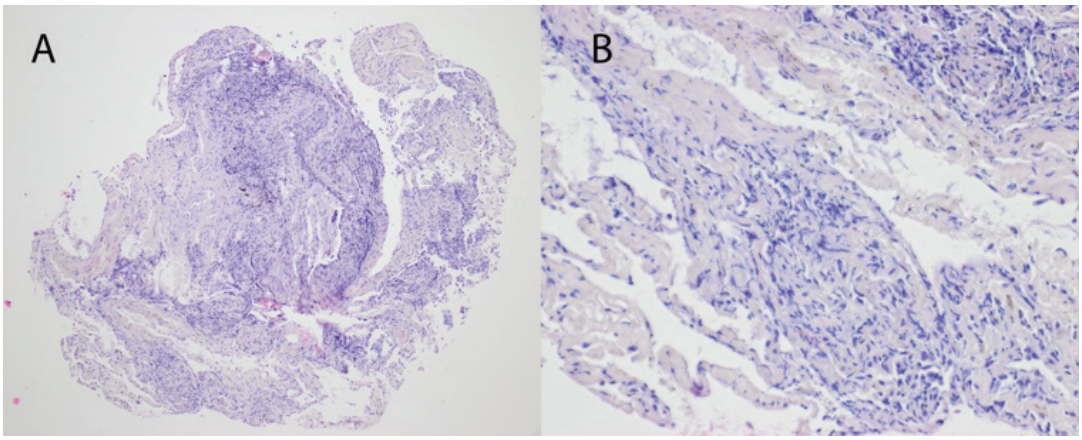

Fig. 3. Bronchoscopy sample: (A) HEx100; and (B)) HEx400: compressed alveoli with lymphocytic infiltrate in thickened septa and hyalinized fibrotic stroma.

failure, as well as radiographic appearance of her lungs. After initial microbiological findings together with clinical and radiological suspicion of AIP, we initiated parenteral methylprednisolone in a dose of 2 mg/kg (120 mg) and oxygenation *via* high-flow nasal cannula (HFNC). For more than a week, our patient's clinical status was stationary (tachypneic with SaO_2 90% despite HFNC). After 8 days of systemic corticosteroid therapy, she started to feel better and supplemental oxygen could gradually be tapered down. One month of admission, she was no longer oxygen-dependent and all laboratory results were within the normal range. All microbiological specimens were negative including BAL; therefore the infectious etiology was ruled out (bacteria, fungi, *Legionella pneumophila*, *Chlamydia pneumoniae*, mycobacteria, influenza, adenovirus, herpes simplex, syncytial respiratory virus and cytomegalovirus). BAL result was non-specific with predominant neutrophilia. Connective tissue disease was excluded by negative laboratory findings. Drug toxicity was ruled out. Echocardiography showed good systolic function of both ventricles (ejection fraction 53%, incomplete relaxation, TAPSE 18 mm, TAP 25 mm Hg). Biopsy confirmed DAD (Figs. 2 and 3) and, since other etiologies were excluded, a diagnosis of AIP was established.

The patient was discharged from the hospital with corticosteroid therapy (prednisolone at a dose of 30 mg *per* day), protein-pump inhibitor, vitamin D, and calcium. Standard chest radiograph on the day of discharge showed significant regression. At one-month follow-up, chest radiograph finding was without change. The patient quit smoking, gained body weight (around 3 kilograms) and was able to withstand usual physical activities with little or no dyspnea. A diagnosis of chronic obstructive pulmonary disease, which was probably preexisting to AIP, was confirmed with spirometry. Gradual tapering of corticosteroid therapy was done and long-acting bronchodilator was introduced. After a total of 6 months, corticosteroid therapy was suspended. Follow-up chest radiograph showed significant improvement (Fig. 4).

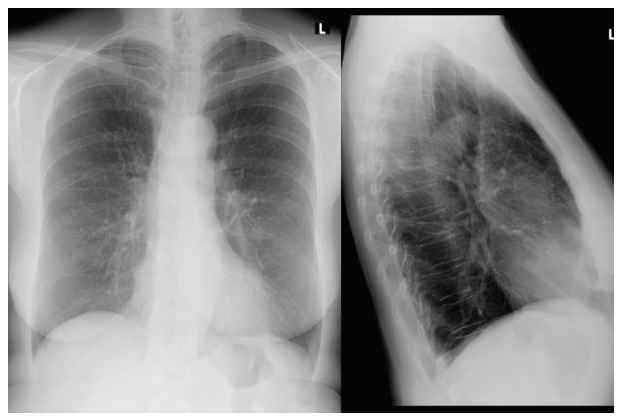

Fig. 4. Chest x-ray taken after full recovery.

Discussion

Our patient presented at an older age (64-year-old) than most of the previously reported AIP patients. The sudden onset and rapid progression of the disease helped us differentiate AIP from other idiopathic interstitial pneumonias in which disease

progression takes from months to several years[4,8]. Standard chest radiograph and chest multi-slice computed tomography (MSCT) showed common findings for patients with AIP (Fig. 1a and 1b). The same MSCT findings can also be seen in heart failure, ARDS, pneumonia, COVID-19 (did not exist at the time our patient was treated), drug induced pneumonitis or chronic interstitial diseases. Infectious, cardiac, drug-induced and other causes were excluded until DAD was confirmed by histologic finding (Fig. 2). Our patient was initially treated with empiric broad-spectrum antibiotics, which was not beneficial, as in other cases of AIP reported. However, after initializing systemic corticosteroids, the patient's condition started to improve. Corticosteroid therapy is considered to be beneficial in most cases, but data are limited to small case series with widely varying results[5,7 9]. Severe hypoxia in our patient was successfully treated with HFNC oxygen therapy which not only improved short-term disease outcome, but averted the use of mechanical ventilation. After 6 months of corticosteroid therapy, our patient fully recovered and the disease did not leave any functional respiratory impairment. The in-hospital mortality in AIP remains high, and the majority of patients who survive die within 6 months after discharge[5,7]. A substantial number of those who survive may even develop recurrence of AIP and further develop chronic interstitial lung disease[4,10]. Earlier intervention and aggressive diagnostic approach may improve clinical outcome in patients with AIP[9]. Current data suggest that there is no laboratory or pathologic finding that could predict the outcome in patients with AIP. As published guidelines regarding the management of AIP do not exist, an experienced multidisciplinary team involvement (consisting of pulmonologists, pathologists and radiologists) is needed to quickly diagnose and successfully treat the disease. This case had a positive clinical outcome with no need for mechanical ventilation, partly owing to the use of HFNC oxygen delivery. Awareness of AIP and wide differential diagnosis could possibly make current workflows better in diagnosing and treating acute respiratory diseases. We also emphasize the importance of aggressive diagnostic approach, and especially diagnostic value of transbronchial lung biopsy.

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Sažetak

USPJEŠNO LIJEČENJE AKUTNE INTERSTICIJSKE PNEUMONIJE

M. Gomerčić Palčić, I. Turalija, L. Vrbanić, I. Folnožić, E. Basioli Kasap i *M. Ulamec*

Akutna intersticijska pneumonija (AIP) je rijetka idiopatska intersticijska pneumonija s patohistološkim značajkama difuznog alveolarnog oštećenja (DAO). Obilježava ju progresivno hipoksično zatajenje disanja, visoka stopa smrtnosti i nedostatak smjernica za liječenje. Ovdje ćemo prikazati bolesnicu u dobi od 64 godine s progresivnom zaduhom, akutnim zatajenjem disanja, difuznim obostranim retikulo-nodularnim zasjenjenjima na radiogramu prsnih organa, difuznim zasjenjenjima tipa mliječnog stakla na kompjutoriziranoj tomografiji i biopsijom dokazanim DAO. Dijagnoza AIP-a je postavljena nakon ekstenzivne obrade kojom su isključeni poznati rizični čimbenici za sindrom akutnog respiracijskog distresa. Liječenje kisikom i visokim dozama parenteralnog kortikosteroida dovelo je do postupnog poboljšanja i, u konačnici, potpunog oporavka funkcije disanja. Budući da ne postoje smjernice za liječenje AIP-a, potrebno je još prikaza slučajeva i serija slučajeva pa i randomiziranih ispitivanja kako bi se definirao najučinkovitiji modalitet liječenja.

Ključne riječi: *Akutna intersticijska pneumonija; Kortikosteroidna terapija; Sindrom akutnog respiraracijskog distresa; Nosna kanila visokog protoka*