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CASE REPORT

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# Acute Respiratory Distress Syndrome (ARDS) from Endemic Influenza A/H1N1: Prehospital Management

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## ABSTRACT

Acute respiratory distress syndrome (ARDS) is a form of acute life threatening respiratory failure. In daily practice there is difficulty in diagnostic and therapeutic management of Acute respiratory distress syndrome (ARDS). We observed delay in diagnostic and therapeutic procedures in patients with clinical signs for the presence of severe respiratory disorders. Finding timely evidence of the presence the clinical signs of threatening ARDS and underlying diseases like influenza A/H1N1 during prehospital period in early stage of disease it is possible introduce early adequate treatment: high flow oxygen, fluid replacement and pharmacological and antiviral therapy. This measure can reduce high mortality in patients who develop ARDS. It is important to improve diagnostic criteria for a precise definition of ARDS and transfer it in practice of emergency and family medicine, microbiology, intensive care units, hospital departments of infectious and respiratory diseases. In this article we underlined the key elements of the new definition of ARDS, diagnostic criteria and the importance of early diagnosis in prehospital period following clinical feature and course (a presence of severe dyspnea) by adding chest x-ray and laboratory investigations.

**Key words: ARDS, diagnostic criteria, Influenza A/H1N1/, prehospital management, antiviral therapy.**

## 1. INTRODUCTION

Acute respiratory distress syndrome (ARDS) is severe respiratory failure characterized by diffuse inflammation of alveolar and vascular (capillary) lung structures which produces progressive hypoxemia. Alveolar and capillary damage passes through different phases: inflammation, fluid exudation and cellular proliferation with development of different degree of pulmonary fibrosis. In the exudative phase activated immune system and vasoactive pro-inflammatory mediators (TNF alpha cytokines, interleukin proteolityc enzymes), direct damage alveolar-capillary membrane produce edema and inactivate surfactant. This patophysiologic change increase pulmonary vascular resistance and pulmonary hypertension advances (1, 2, 3). The need for strong and deep breathing leads to the weakness of respiratory muscles with consequences of severe respiratory failure and multiple organ dysfunction. Death is usually due to sepsis and MODS (multi organ dysfunction) and refractory respiratory failure. The average mortality rate is 52%. Improved diagnostic criteria and early specific management can decrease mortality rate much under 50% (4). ARDS was first described by Ashbaugh and Petty in 1967 in case series of 12 patients with hypoxemia but with different diseases (5). Definition and classification of ARDS with specific criteria performed the American-European consensus conference (AECC) which was published 1994. Definition of ARDS was: the acute onset of respiratory failure, bilateral infiltrates on chest X-ray, hypoxemia as defined by a PaO2/FiO2 ratio less than 200 mmHg and no evidence of left atrial hypertension. Because of low specificity of AECC criteria new definition and classification performed in Berlin conference 2011 and published 2013. In Berlin definition ARDS is an acute diffuse, inflammatory lung injury, leading to increase pulmonary vascular permeability, increased lung weight and loss of aerated lung tissue classified as mild, moderate and severe according to the value of PaO2/FiO2. In Berlin definition defined the timing of acute onset of respiratory failure: worsening respiratory symptoms within one week (4, 5, 6).

## 2. CASE REPORT

We have observed two patients with influenza infection A/H1N1) with early development of ARDS. 58-year-old man was treated in Health center Gracanica family medicine setting

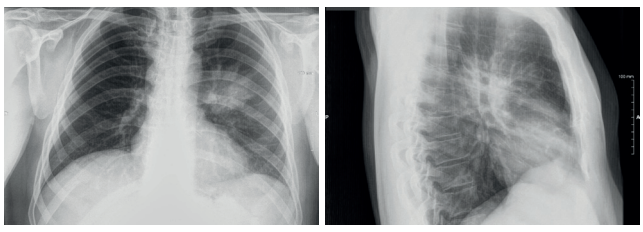

**Figure 1 and 2. chest X-ray third day of disease**

because of cough, dyspnea, wheezing, fever, chills, sore throat and other respiratory symptoms. General condition and respiratory symptoms have worsened in next three days in spite of symptomatic and antibiotics therapy. Laboratory evaluation shows Erythrocyte sedimentation rate, CR, AST, ALT, LDH have been elevated. Chest X-ray revealed bilateral opacities and infiltrates (Figure 1 and 2).

Clinical signs of severe respiratory failure and chest- X ray finding directed to ARDS and patient was admitted in hospital as a emergency case. In next 5 days clinical coarse progressed in severe pneumonia, septic shock and multiple organ failure. In intensive care unit patient died (Figure 3).

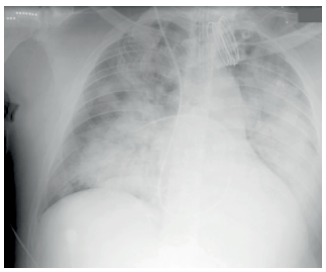

**Figure 3. Chest X-ray sixth day of disease. Bilateral diffuse inflitrates**

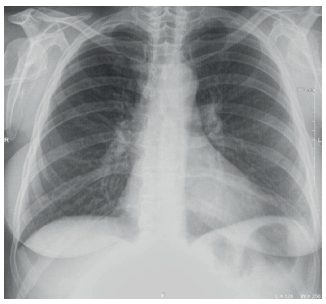

**Figure 4. Chest X-ray in the beginning (the third day) of disease Influenza A/H1N1**

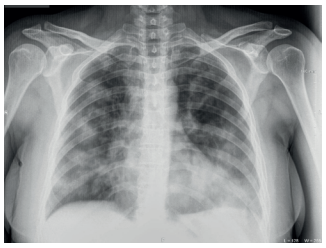

**Figure 5. Chest X-ray thirth day of disease-ARDS. Bilateral lung infiltrates Influenza A/H1N1**

The second patient was 52 year-old women who was treated in the same institution: Health care center Gracanica. Before present troubles she was in healthy condition. Disease started with the same clinical signs: fiver, cough, fatigue and dyspnea. Laboratory investigation revealed elevated CRP, SE rate, liver functional tests. Chest x-ray examination revealed very small diffuse opacities (Figure 4). During next two days respiratory symptoms suddenly worsened with signs of progressive hypoxia. Repeated chest X-ray showed diffuse bilateral infiltration (Figure 5). Patient was admitted in hospital intensive care unit. A diagnostic test for influenza A/H1N1 performed immediately. Molecular methods test (RT PCR) was positive. Specific treatment for ARDS started but patient had serious complication with multiple organ failure and died.

## 3. DISCUSSION

Different conditions can lead to ARDS. Direct cause can be primary respiratory diseases and indirect many conditions like sepsis, shock, trauma and burns. Regardless of etiology progressive hypoxemia results in critical acute clinical condition with dyspnea, tachypnea, fatigue, dry cough, retrosternal discomfort and mental disorders. This acute medical condition usually occurs during first two days of the precipitating diseases and with high mortality or long term consequence in survivors (7). Influenza A /H1N1 infection can develop severe type of ARDS with very high mortality (8, 9, 10). Despite of progress in the management of ARDS mortality still remains high. Influenza A/H1N1 infection can be responsible for development of extremely severe type of ARDS which clinical course is different, prolonged, more complicated and with increased mortality. Extracorporeal membrane oxigenation (ECMO can be used in such cases with extremely severe type of ARDS. Recent literature shows varynig mortality rates for the use of ECMO for ARDS (1, 11). Our two patients who died had the acute onset in first week and similar clinical course with rapid progression in multiple organ failure. This severe ARDS can be based on high virulence of virus H1N1 inducing aberrant immune response and extensive lung damage. Pathological findings revealed that the virus replicated in alveolar cells making diffuse alveolar damage. Antiviral therapy is strong recommended for the patients with high risk for development ARDS but must be started during first 48 hours (8, 9). The timing of recognition first signs of ARDS, early introduction antiviral therapy and lung-protective ventilation may be key points in disease management. We observed in our cases delayed recognition diagnostic criteria for ARDS and antiviral therapy which is general observation for clinicians in practice (12). Wider dissemination of new definition of ARDS is recommended (4, 6, 10, 12).

## 4. CONCLUSION

We described two patients with ARDS with lethal outcomes based on influenza A/H1N1 infection. Influenza with ARDS is significant public health problem. Criteria for new definition of ARDS (Berlin definition) with recommendation for early treatment still is not implemented in practice. Wider dissemination of new definition of ARDS and recommendations for early treatment in prehospital medical settings is key point for better medical care of this syndrome. A better knowledge of epidemiology, pathophysiology, etiology, clinical course and new possibility of therapy can help to improve the outcomes of ARDS.

**CONFLICT OF INTEREST: NONE DECLARED.**

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