



A Case Report of Acute Respiratory Distress Syndrome (ARDS) Complicating Influenza A/H1N1 Infection.

KEYWORDS

acute respiratory distress syndrome (ARDS), A/H1N1 influenza.

Dr. Pritam Jagansing Pardeshi

S.M.O (Tutor), Department of microbiology, LTMGH & MC, Sion, Mumbai.

Dr. Anuradha De

Professor, Department of microbiology, LTMGH & MC, Sion Mumbai.

Dr. Sujata Baveja

Department of microbiology, LTMGH & MC, Sion Mumbai

Dr. Pranay Gandhi

Dept. of community medicine, Assistant professor, Nagpur

ABSTRACT

ARDS is characterized with bilateral parenchymal lung infiltrates on chest radiograph and PaO₂ /FiO₂ ratio < 200 resulting from causes other than acute left ventricular dysfunction. Inflammatory lung lesions may be induced by different disorders, with sepsis being the leading cause of ARDS. Influenza A/H1N1 infection seems to be responsible for the development of extremely severe type of ARDS with poor response to routine treatment. Despite great progress in the management of ARDS with novel agents and sophisticated techniques, including antimicrobial drugs, extracorporeal membrane oxygenation, prostaglandins, nitric oxide, prostacyclin, exogenous surfactant administration and activated protein C, supportive treatment based mostly on advanced mechanical ventilation in the intensive care units seems to be the most important for the prognosis.

INTRODUCTION

The first reported Human infection with the novel influenza A/H1N1 virus was in April 2009. Since humans do not have immunity from the infection the incidence rates may be higher than those for seasonal influenza [1]. Novel influenza usually affects subjects below the age of 65, especially pregnant women, obese persons and patients with comorbidities, including asthma, chronic bronchitis, neoplasms and transplants. Young, previously healthy individuals can also be affected. Clinical presentation includes fever, cough, sore throat, hoarseness, malaise, muscular pain, diarrhea and vomiting, arthralgia, ostealgia, chills and headaches with ophthalmalgia, photophobia and touchable eyeballs [2]. Complications like bronchitis, pneumonia, myocarditis, pericarditis, encephalitis and shock affect people with immune system compromise. The course of influenza may be severe, especially in children and the elderly. The presented study describes a fatal case history of ARDS complicated by A/H1N1v infection.

CASE REPORT:

A 62-year-old patient with a history of hypertension and degenerative-discopathic lesions at L4-L5 previously treated in other departments was admitted to the Department of Internal Medicine because of dyspnea, dry cough and chest pain on deep breathing. In 2010 and 2011 the patient underwent operations because of lumbar discopathy and was perioperatively treated with analgesic drugs, including pethidine, paracetamol and ketoprofen. After the surgery the patient was hospitalized in the Department of Rehabilitation, where erythematous-edematous skin lesions with a haemorrhagic component and blisters, mostly on the internal surface of the upper limbs, developed. This was probably a side-effect of non-steroid anti-inflammatory drugs. The patient was transferred to the Department of Dermatology for further treatment based on intravenous dexamethasone and amoxicillin with clavulanic acid, which resulted in partial regression of skin lesions. After several days, symptoms of the lower respiratory tract infection oc-

curred and the patient was transferred to the Department of Internal Medicine.

On admission, the patient reported periodic dyspnea, cough productive of mucous sputum, sweating and weakness. Physical examination revealed fever of 38.5 °C, arterial hypertension of 160/95 mmHg, tachycardia reaching 104/ min, and a poorly tense pulse. Sibilant dry rales and dullness were found over the lung bases. ECG on admission showed regular sinus rhythm. The chest X-ray revealed increased bronchial markings in the right supradiaphragmatic region. Laboratory tests performed on admission demonstrated an increased white cell count (15,000/uL) with high percentage of neutrophils (81.2%) and elevated C-reactive protein level (CRP 88.9 mg/l, upper normal value-5mg/l). Based on the physical, laboratory results and chest X-ray, diagnosis of the lower respiratory tract infection without lung involvement was established. Repeated electrocardiographic examinations and troponin T measurements excluded recent myocardial infarction as the cause of dyspnea. D-dimer evaluation denied pulmonary embolism. Empiric antibiotic treatment with ceftriaxone and azithromycin as well as oxygen supply were administered. After two days, the patient's condition deteriorated rapidly, complaining of severe dyspnea, and he was unable to speak in full sentences. On physical examination, cyanosis of the accessory muscles for ventilation was found. Auscultation revealed bilateral crackles suggestive of acute pulmonary oedema. No organic heart disease confirming a cardiac origin of pulmonary oedema was found on echocardiography. No significant arrhythmia or hypertension was found. The patient became confused and sleepy. Blood gases with pO₂ of 39 mmHg and pCO₂ of 29 mmHg suggested respiratory distress with urgent need for mechanical ventilation. Repeated X-ray revealed scattered parenchymal infiltrates affecting half of both lungs. Bilateral pleural effusion was found. Laboratory findings demonstrated CRP of 260 mg/l and worsening kidney function (creatinine 1.3 mg/dl). Blood and urine cultures were negative. Procalcitonin level was normal – 0.19 ng/ml (reference range < 2). The primary diagno-

sis was ARDS due to viral pneumonia. On admission to the Intensive Care Department the patient was responsive and alert (GCS 15), dyspneic with respiration rate 24/min; blood pressure 90/60 mmHg, regular pulse about 100/min, body temperature reached 38.5°C. The arterial blood gases were as follows: PaO₂ – 42 mmHg, PaCO₂ – 32 mmHg. Since the non-invasive ventilation with 50% oxygen supply had not been effective the patient was intubated. SIMV, the volume control mode, and 50% oxygen concentration were provided. A sedative infusion consisting of fentanyl and midazolam was initiated. Antibiotic therapy was continued with cefuroxime and ciprofloxacin; difluconazole was added. Dopamine and norepinephrine were administered because of hypotension and impaired peripheral perfusion. Chest X-ray repeated 8 hours later showed progression of bilateral scattered lung infiltrates (Fig. 1 and 2). Because of poor results of blood gases the inspiratory oxygen concentration was changed to 100% (FiO₂ 1.0). Insufficient response to mechanical ventilation and the need for pure oxygen supply confirmed the suspicion of ARDS. On the 2nd day, acute renal failure developed with creatinine level at 3.1 mg/dL, and hemofiltration was started. The laboratory tests were positive for the presence of A/H1N1 virus. Oseltamivir was added at the initial dose of 75 mg twice a day. On the 4th day, the dose was doubled. Since there an increase in the procalcitonin level was observed, antibiotics were continued despite negative cultures. On the 3rd day, the patient's condition improved; chest X-rays showed regression of lung infiltrates and oxygen concentration was switched to 50%. On the 5th day, the patient again deteriorated. Due to the lack of improvement and low PaO₂ despite the optimal treatment, the pressure-controlled ventilation (PCV) mode was started with reversed inspiratory/expiratory ratio (2 to 1) and FiO₂ 1.0. Neuromuscular relaxation with cis-atracurium infusion was required to improve oxygenation. On the 12th day, cardiac arrest occurred. The primary mechanism was pulseless ventricular tachycardia degenerating into asystole. After 20 minutes of resuscitation the patient died.

DISCUSSION

The mortality rate of ARDS ranges from 40% – 80%. Inflammatory lung lesions may be induced by different disorders, including infectious pneumonia, aspiration of gastric contents, drugs, severe trauma, fat embolism, surface burn, massive blood transfusion and sepsis being the leading cause [4, 5]. In the presented case, ARDS occurred in the course of influenza A/H1N1v infection, which has been found to be responsible for the development of this extremely severe type of ARDS with poor response to the treatment (e.g PaO₂ 60% and PEEP > 15 cmH₂ O). Approved predictors of the severe course of influenza A/H1N1 in humans, including radiographic changes, increase in C-reactive protein level, peripheral oxygen saturation below 94% on breathing air, hypotension and previous immunosuppression were present in the presented case [3]. Chest radiography is the first-line imaging technique for diagnosing lung disorders resulting in acute

respiratory distress. Henzler et al described alveolar consolidations, ground-glass opacities, reticular opacities and pleural effusion as the most common findings in 10 patients with A/H1N1 infection [6]. Busi Rizzi et al report that the major radiological abnormalities were interstitial changes (60.0%), with (22.0%) or without patchy ground-glass appearance, and located in the lower lung zones (7.5%). Such changes are observed in the most non-complicated cases of swine-virus infection [7]. We have also observed multifocal, bilateral consolidations, ground-glass opacities and reticular opacities which spread all over the lungs within several hours, indicating the fulminant course of the disease and fatal outcome. Skin lesions during influenza virus infection are rare and usually have a macular or maculopapular aspect. There is one case report of the pandemic 2009 A/H1N1 virus infection associated with purpuric skin lesions on the limbs [8]. In the patient in the presented case, the skin lesions were not specific for influenza infection, being presumably the side-effect of non-steroid anti-inflammatory drugs. Treatment of reversible causes, together with mechanical ventilation, are crucial for the management and prevention of MODS (multiple organ dysfunction syndrome). Since infection with influenza A/H1N1 virus was confirmed in the presented case, antiviral drug oseltamivir was applied. Other drugs – zanamivir, a combination of oseltamivir and amantadine or rimantadine – were tried in humans with swine flu [3]. Although non-invasive positive pressure ventilation may be applied in selected patients, most require invasive mechanical ventilation. In the patient in the presented case, typical volume-controlled positive pressure ventilation with sedation and muscle relaxation was applied. Since there was no improvement, pressure-controlled inverse ratio ventilation was started. There are some reports that PCV does not improve oxygenation and has impact on the peak pressure rather than on the plateau pressure [9]. All these methods need evaluation in clinical trials. Extracorporeal membrane oxygenation (ECMO) is considered the rescue therapy in patients with swine flu infection. Despite promising results of ECMO treatment, randomized clinical trials are needed for approval of this method. The same is reported on the proning effect [10]. Supportive care includes fluids, antibiotics, corticosteroids, prostaglandins, nitric oxide, prostacyclin, exogenous surfactant administration, lisofylline, ketoconazole and N-acetylcysteine. According to other reports, ceftriaxone, azithromycin, vancomycin and levofloxacin were preferred for treating co-infection and superinfections with *Escherichia coli*, *Streptococcus pneumoniae* and *Staphylococcus aureus* in patients with swine flu. To keep the patient as dry as possible, fluids should be applied cautiously except cases of sepsis. In most patients, pressors must be added to maintain peripheral perfusion. To date, activated protein C has not been proven to be effective [3, 4]. The patient in the presented case received cefuroxime and ciprofloxacin as well as difluconazole. Dopamine and norepinephrine were also administered because of hypotension. Intravenous methylprednisolone was maintained. No significant improvement was achieved. It seems possible that optimization of general supportive care is crucial for better outcome in such cases.

REFERENCE

- Jain S, Kamimoto L, Bramley AM, Schmitz AM, Benoit SR, Louie J, et al. Pandemic Influenza A (H1N1) Virus Hospitalizations Investigation Team. Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. *N Engl J Med.* 2009; 361(20): 1935–44.
- Jaber S, Conseil M, Coisel Y, Jung B, Chanques G. ARDS and influenza A (H1N1): patients' characteristics and management in intensive care unit. *Ann Fr Anesth Reanim.* 2010; 29(2): 117–25.
- British Infection Society, British Thoracic Society, Health Protection Agency. Pandemic flu: clinical management of patients with an influenza-like illness during an influenza pandemic. Provisional guidelines from the British Infection Society, British Thoracic Society and Health Protection Agency in collaboration with the Department of Health. *Thorax* 2007; 62 (Suppl 1): 1–46.
- Jain R, Dahnogare A. Pharmacological Therapy for Acute Respiratory Distress Syndrome *Mayo Clin Proc.* 2006; 81(2): 205–212.
- Zambon M, Vincent JL. Mortality rates for patients with acute lung injury/ARDS have decreased over time. *Chest.* 2008; 133(5): 1120–7.
- Henzler T, Meyer M, Kalenka A, Alb M, Schmid-Bindert G, Bartling S, et al. Image Findings of Patients with H1N1 Virus Pneumonia and Acute Respiratory Failure. *Acad Radiol.* 2010; 17(6): 681–685.
- Busi Rizzi E, Schinin V, Ferraro F, Rovighi L, Cristoforo M, Chiappetta D, et al. Radiological findings of pneumonia in patients with swineorigin influenza A virus (H1N1). *Radiol Med.* 2010; 115: 507–515.
- Urso R, Bevilacqua N, Gentile M, Biagioli D, Lauria FN. Pandemic 2009 H1N1 virus infection associated with purpuric skin lesions: a case report. *J Med Case Reports.* 2011; 5(1): 132.
- Ferguson ND, Frutos-Vivar F, Esteban A, Anzueto A, Alia J, Brower RG, et al. Mechanical Ventilation International Study Group. Airway pressures, tidal volumes, and mortality in patients with acute respiratory distress syndrome. *Crit Care Med.* 2005; 33: 21–30.
- Davies A, Jones D, Bailey M, Beca J, Bellomo R, Blackwell N, et al. Extracorporeal membrane oxygenation for 2009 influenza A(H1N1) acute respiratory distress syndrome. *JAMA* 2009; 302: 1888–1895.