



## Nosocomial Pneumonia Induced by Short Mechanical Ventilation in an Infection-Prone Diabetic Patient who Underwent Cardiac Arrest due to Allergic Coronary Spasm

Maeda H<sup>1</sup>, Takeguchi F<sup>2</sup>, Kurata A<sup>3</sup> and Yoshida K<sup>1\*</sup>

<sup>1</sup>Department of Forensic Medicine, Tokyo Medical University, Japan

<sup>2</sup>Department of Nephrology, Tokyo Medical University, Japan

<sup>3</sup>Department of Molecular Pathology, Tokyo Medical University, Japan

### Abstract

Ventilator-associated pneumonia (VAP) refers to nosocomial pneumonia occurring more than 48 hours of mechanical ventilation (MV). An elderly diabetic woman experienced cardiac arrest due to allergic coronary spasm upon piperacillin injection for postoperative endophthalmitis. She had a history of systemic anaphylactic reaction to a penicillin antibiotic. Catecholamine infusion and MV recovered her from cardio-pulmonary arrest within 15 minutes. Shortly thereafter, electrocardiogram showed ST changes reflecting severe left ventricular anterior wall ischemia. She was extubated before transfer to a university less than 3 hours after the cardio-pulmonary resuscitation. Echocardiography shortly post-transfer demonstrated full recovery of cardiac contractility. She was alert and presented no particular symptoms on day 2. Early on day 3, however, pneumonia was diagnosed from dyspnea, reduced O<sub>2</sub> saturation, and pulmonary hypo-opacities, and progressed to death with sepsis on day 8. This case presents a unique type of pneumonia induced by brief MV, in contrast with the 48 hour's requirement of MV for VAP. Retrospectively, serum procalcitonin after the successful resuscitation showed septic level, and would provide potential usefulness in the antibiotic administration for prevention of the pneumonia evoked by brief MV in infection-prone patients.

### OPEN ACCESS

#### \*Correspondence:

Ken-ichi Yoshida, Department of Forensic Medicine, Tokyo Medical University, 6-1-1 Shijuku, Shinjuku-ku, 160-8402 Tokyo, Japan, Tel: 81-3-3351-6141; Fax: 81-3-3353-7672; E-mail: [kenyoshi@tokyo-med.ac.jp](mailto:kenyoshi@tokyo-med.ac.jp)

Received Date: 19 May 2016

Accepted Date: 13 Jul 2016

Published Date: 19 Jul 2016

#### Citation:

Maeda H, Takeguchi F, Kurata A, Yoshida K. Nosocomial Pneumonia Induced by Short Mechanical Ventilation in an Infection-Prone Diabetic Patient who Underwent Cardiac Arrest due to Allergic Coronary Spasm. *Ann Clin Case Rep.* 2016; 1: 1039.

**Copyright** © 2016 Yoshida K. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Keywords:** Acute coronary syndrome; Anaphylaxis; Cardiac arrest; Coronary spasm; Procalcitonin; Tryptase; Ventilator-associated pneumonia

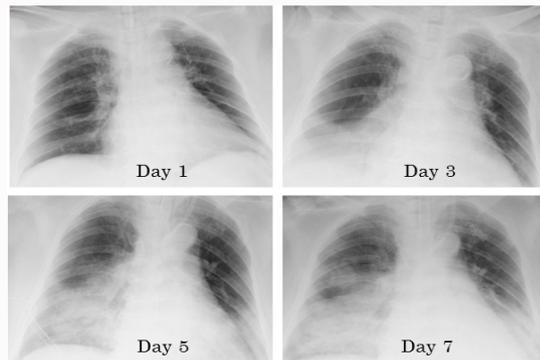
### Introduction

Ventilator-associated pneumonia (VAP) refers to nosocomial bacterial pneumonia that develops after more than 48 hours of MV, with high (24~50%) mortality rate [1,2]. Patients with diabetes mellitus are thought to be susceptible to infections, but a review on 84 clinical studies negated diabetes as an independent risk factor for VAP [3]. More than 48 hours of MV is known to predispose patients to VAP [2]. Meanwhile, allergic coronary spasm (Kounis syndrome) is characterized by allergen-mediated coronary spasm through mast cell-derived vasoconstrictors, and we confirmed the diagnosis by post-autopsy measurement of tryptase levels in the serum sampled shortly after resuscitation and kept frozen [4].

We found a new type of pneumonia induced by brief (<3 hours) MV in response to the cardiac arrest due to allergic coronary spasm, though VAP requires more than 48 hours of MV. Serum procalcitonin (PCT) levels in the early days of admission have been shown to be useful in the prevention of VAP [5]. In this case, retrospective analysis revealed the rise of PCT to a septic level in the serum sampled 3 hours after the resuscitation, when there was neither symptoms of pneumonia, nor abnormal CRP level. Here, we the dangerous nosocomial pneumonia induced by brief tracheal intubation and MV for cardiopulmonary resuscitation in an infection-prone and diabetic patient, and potential usefulness of PCT in the preventive antibiotic medication for such pneumonia.

### Case Presentation

An obese small woman (Body Mass Index 37.4, calculated from 154cm of height and 70.4Kg of body weight) in her mid-sixties had a long-term history of diabetes complicated with renal failure (nephropathy and left nephrectomy), cataract, and leg gangrene. Four years ago she had



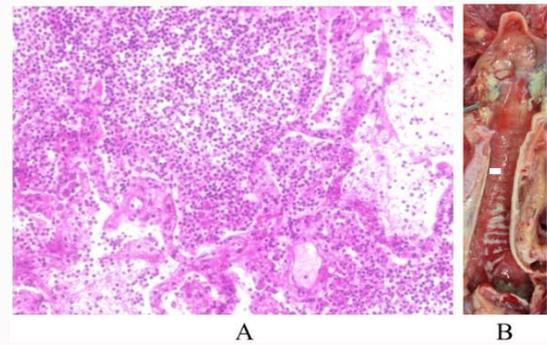
**Figure 1:** Temporal change in chest radiographs presenting pneumonia.

undergone left below-the-knee amputation and had started regular dialysis and insulin therapy. In the meantime, hospital admissions were repeated for bedsore infections and pneumonia. One week before the day of the accident, intraocular lens was implanted for cataract. In the morning of the accident, she was diagnosed of unilateral endophthalmitis complicated with the lens implantation, and prescribed with piperacillin, although her medical interview sheet attached to her medical record had documented her history of systemic allergy to penicillin. Eight minutes after the start of piperacillin infusion, she experienced cardiac-pulmonary arrest. She was injected with adrenalin (1 mg × 4), and received MV through an endotracheal tube, but not defibrillation before successful resuscitation within 10–15 minutes. Meanwhile, infusion of dopamine and noradrenalin was required for more than one hour until blood pressure was stabilized. Electrocardiography (ECG) demonstrated a remarkable ST depression in precordial leads, reflecting severe ischemia due to left anterior descending artery (LAD) spasm. A laboratory examination approximately 90 minutes after resuscitation revealed increased aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) levels, renal failure, leukocytosis (11320/mm<sup>3</sup>), and hyperglycemia. After extubation, she was transferred to a university intensive care unit (ICU) approximately 3 hours post-resuscitation. Echocardiography confirmed a normal (60%) ejection fraction shortly after the admission.

On day 2, she became fully conscious and could eat independently. Early on day 3, her blood oxygen saturation (SpO<sub>2</sub>) were maintained at 92~93%, but suddenly dropped when she rapidly raised her upper body on the bed. A chest radiograph revealed reduction in the bilateral pulmonary opacities, particularly in the right lower lobe (Figure 1), consistent with coarse crackle on auscultation. Despite of non-invasive positive pressure ventilation using positive end-expiratory pressure (PEEP) mode, SpO<sub>2</sub> was declined to 90~91%. She was also estimated to suffer from heart failure, and underwent continuous hemodiafiltration and continuous infusion of pressor agents.

At am 0:00 on day 4, deterioration of the respiratory failure was demonstrated by the great reduction in pO<sub>2</sub> (58.5mmHg). With the decrease in the pulmonary opacities, the CRP level and WBC counts increased greatly from day 4. Gram-negative bacteria were detected in the sputum but not in the blood.

Data from the EV100 critical care monitor (Edwards Lifesciences, Irvine, CA) suggested peripheral vasodilation. Together with hyperthermia, these findings support the development of sepsis from pneumonia. Retrospectively, the patient fulfilled the new (2016) diagnostic criteria for sepsis conferred by the combined semi-



**Figure 2:** Microscopic finding on lobar pneumonia.

(A) Hematoxylin-eosin staining.

(B) Macroscopic findings on bronchitis.

qualitative evaluation of respiratory (pO<sub>2</sub>), coagulation (platelet counts), hepatic (bilirubin), cardiovascular (mean blood pressure), neuronal (Glasgow Coma Scale), and renal (creatinine) dysfunctions. The pulmonary opacities and aeration difficulty worsened with time. Cephalexin, a cephalosporin antibiotic, was administered after confirmation of its safety.

### Autopsy findings

The heart (440g) showed hypertrophy with a thickened right ventricular (RV) wall (0.4 cm), compared with the normal thickness of the left ventricle (LV, 1.5 cm) and septum (1.5 cm), but no ventricular dilatation was identified. The distal LAD showed 90% stenosis, the left circumflex artery was very thin with 70% stenosis, while the right coronary artery showed mild stenosis. Histology showed diffuse and severe myocardial fragmentation and waviness, reflecting hypercontraction and hyperextension, respectively. Lipid infiltration was remarkable in the LV as well as the RV. We found neither plaque erosion nor rupture in the LAD, the culprit artery for the coronary spasm.

The lungs showed severe consolidation (left, 955 g; right, 1035 g), with histological findings of acute lobar pneumonia (Figure 2A), but no hyaline membrane formation, edema, or fibrosis. Bronchial mucosal reddening supported bronchitis (Figure 2B). The left kidney had been removed. The right kidney (135 g) showed severe glomerular and arteriolar sclerosis, with hematoma and grayish amorphous deposits in the pelvis. Histology of the spleen (190 g) showed a small focal abscess.

We evaluated myocardial injury, anaphylaxis (allergic coronary spasm), and bacterial infection by measurements of troponin T, tryptase and PCT, respectively, in the sera frozen shortly after the resuscitation and ICU admission, respectively (Table 1). The troponin level was high at ICU admission. However, the lack of histological findings of coagulation necrosis or leukocyte infiltration excluded the possibility of myocardial infarction. Together with the high serum levels of AST and LDH, we think that reperfusion of the arrested (ischemic) heart was the primary cause of the increase in the serum levels of troponin T. Meanwhile, the high serum tryptase level and the ischemic ECG findings in the LAD-region shortly after resuscitation support the diagnosis of allergic coronary spasm as the cause of cardiac arrest.

Serum PCT levels were 0.13 and 2.59 ng/mL, respectively, shortly after resuscitation and ER admission, respectively, whereas serum CRP was normal (0.22 mg/dL) at ER admission (Table 1). The PCT

level at ER admission was 5-times higher than the cutoff value (0.5 ng/mL) for the diagnosis of sepsis, despite the lack of septic symptoms.

## Discussion

High serum tryptase levels that reflect mast cell degranulation and anaphylaxis [6], as well as ischemic ECG changes in the region of LAD with 90% stenosis, supported allergic coronary spasm [4] as the cause of the cardiac arrest shortly after the piperacillin injection. Meanwhile, endophthalmitis was induced by the cataract surgery performed a week prior. The ophthalmologist injected piperacillin, although the patient had provided the history of systemic shock to penicillin in the medical record.

We measured the PCT in the serum that had been frozen after resuscitation and ER admission, and found its increase to a septic level after the ER admission (Table 1). The high PCT level, leukocytosis and tachycardia shortly after the ER admission were consistent with systemic inflammatory response syndrome, although the chest radiograph and serum CRP level were within normal range, and the patient was asymptomatic until early on day 3.

Given the extremely rare incidence (0.13%) after cataract surgery [7], the endophthalmitis would have reflected the patient's predisposition to bacterial infection, as demonstrated by the repeated hospital admissions for bedsores infections and pneumonia. Although the review on 84 clinical studies negated diabetes as a risk factor for VAP [3], our patient also had a long history of renal failure (due to diabetic nephropathy), and dialysis, the known risk factors for VAP [8]. Bacterial colonization in the aero digestive system and aspiration of contaminated secretions into the lower airway have been known to predispose patients to VAP [1], and would have underlain the endophthalmitis, as well as the multiple histories of bacterial infections.

MV for more than 48 hours is the known risk for VAP [2], but this case demonstrated that endotracheal intubation, for less than 3 hours, could have triggered lethal lobar pneumonia (Figure 1 and 2A) resulting from bronchitis in infection-prone patients who undergo cardiac arrest for a short duration (<15 minutes). The bronchitis was confirmed not only by the presence of gram-negative bacteria in the sputum (not in the blood), but also by the autopsy findings (Figure 2B).

The doctor's overlook of the patient's allergic history was thought to cause the piperacillin-induced allergic coronary spasm. However, since the patient's cardiac function was normalized by 3 hours after 10~15 minutes of resuscitation, we excluded the cardiac arrest as the direct cause of her death. Still, we inferred the contribution of the endotracheal intubation and MV to the pneumonia, sepsis, and death in this patient with putative upper airway bacterial proliferation. Consistent with the profile of our case, age (>60 years), co morbidities of renal failure, heart disease, pneumonia, sepsis, resuscitation >10 minutes predict poor prognosis in cases of cardiopulmonary resuscitation for in-hospital cardiac arrest [9].

There was an increase in serum PCT level to a septic level, but no chest radiographic opacity or rise in CRP 3 hours after the resuscitation, and 2.5 days before the clinical onset of pneumonia (day 3). It has been reported previously that PCT is a more sensitive and

specific blood marker for bacterial infection than CRP, leukocytosis, and hyperthermia in ICU patients [10]. Retrospectively, the high serum PCT level 3 hours post-resuscitation in the fully-recovered patient suggested the later onset of the pneumonia induced by brief MV. PCT increased much earlier than the appearance of signs and symptoms of pneumonia, and the increase in serum CRP. We recommend prophylactic administration of antibiotics in infection-prone and diabetic patients presenting with high serum PCT few hours after endotracheal intubation. However, sufficient cases with similar backgrounds are required to gain a solid evidence for the usefulness of the PCT for the initiation of antibiotic therapy.

## VAP Highlight

A diabetic patient had history of systemic anaphylaxis to penicillin antibiotic.

Piperacillin injection induced cardiac arrest due to allergic coronary spasm.

She was resuscitated within 15 min by catecholamine injections and mechanical ventilation.

Her cardiac function was normalized 3 hours after the resuscitation.

Serum procalcitonin level at the time predicted later onset of nosocomial pneumonia.

## References

1. Kollef MH. The prevention of ventilator-associated pneumonia. *N Engl J Med.* 1999; 340: 627-634.
2. Chastre J, Fagon JY. Ventilator-associated pneumonia. *Am J Respir Crit Care Med.* 2002; 165: 867-903.
3. Vardakas KZ, Siempos II, Falagas ME. Diabetes mellitus as a risk factor for nosocomial pneumonia and associated mortality. *Diabet Med.* 2007; 24: 1168-1171.
4. Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): a natural paradigm? *Int J Cardiol.* 2006; 110: 7-14.
5. Luyt CE, Guérin V, Combes A, Trouillet JL, Ayed SB, Bernard M, et al. Procalcitonin kinetics as a prognostic marker of ventilator-associated pneumonia. *Am J Respir Crit Care Med.* 2005; 171: 48-53.
6. Nishio H, Takai S, Miyazaki M, Horiuchi H, Osawa M, Uemura K, et al. Usefulness of serum mast cell-specific chymase levels for postmortem diagnosis of anaphylaxis. *Int J Legal Med.* 2005; 119: 331-334.
7. Gower EW, Lindsley K, Nanji AA, Leyngold I, McDonnell PJ. Perioperative antibiotics for prevention of acute endophthalmitis after cataract surgery. *Cochrane Database Syst Rev.* 2013; 15: CD006364.
8. Ranes JL, Gordon SM, Chen P, Fatica C, Hammel J, Gonzales JP, et al. Predictors of long-term mortality in patients with ventilator-associated pneumonia. *Am J Med.* 2006; 119: 897.
9. Schultz SC, Cullinane DC, Pasquale MD, Magnant C, Evans SR. Predicting in-hospital mortality during cardiopulmonary resuscitation. *Resuscitation.* 1996; 33: 13-17.
10. Oppert M, Reinicke A, Müller C, Barckow D, Frei U, Eckardt KU. Elevations in procalcitonin but not C-reactive protein are associated with pneumonia after cardiopulmonary resuscitation. *Resuscitation.* 2002; 53: 167-170.