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Severe Acute Global Respiratory Failure Treated with Non Invasive Ventilation: Role of Presepsin as an Early Marker of Sepsis

Barzaghi F^{1*}, Oggionni E², Piluso M², D’Arcangelo F², Parachini L², Nadalin M¹, Pagani S², and Scarpazza P²

¹School of Medicine and Surgery, University of Milano Bicocca, Respiratory Unit, San Gerardo Hospital, Monza, Monza, Italy

²Division of Respiratory Diseases with Intermediate Respiratory Intensive Care Unit, Vimercate Hospital, Vimercate, Monza e Brianza, Italy

*Corresponding author:

Francesca Barzaghi,
Respiratory Diseases and Respiratory Intermediate
Care Unit, Vimercate Hospital, via SS. Cosma e
Damiano 10 20871 Vimercate (MB), Via Gondar 6C,
20900, Monza (MB), Italy, Tel: +39 039 665 7269;
E-mail: f.barzaghi1@campus.unimib.it

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Presepsin; Sepsis; Respiratory failure; Non invasive ventilation; Respiratory intermediate care unit

1. Abstract

1.1. Introduction

In poly pathological patients an early diagnosis of respiratory failure is often difficult. Frequently, poly pathology does not allow intubation and intensive care unit (ICU) treatment with invasive mechanical ventilation (IMV). Non-invasive ventilation (NIV) and admission to respiratory intermediate care unit (RICU) may be the only option in these cases. Presepsin, a new predictive marker of systemic infection, appears particularly useful for early diagnosis, treatment and prognosis of sepsis.

1.2. Case

A 73-year-old man with a previous history of ischemic heart disease undergoing coronary artery bypass grafting (CABG), residual constrictive pericarditis, previous multiple hospitalizations for heart failure (CHF), autoimmune hemolytic anemia on chronic steroid therapy and cognitive impairment arrived to the Emergency Department (ED) in acute global respiratory failure with severe acidosis; he was normothermic, radiological imaging showed aspecific diffuse parenchymal thickening and traditional inflammatory markers (white blood cell - WBC - count and serum level of C-reactive protein - CPR - and procalcitonin - PCT) were in normal range, but blood tests revealed a marked elevation in the value of presepsin. Intensivist’s evaluation concluded for a do-not intubate (DNI) status and the patient was admitted to RICU. The combined

treatment with NIV, broad-spectrum antibiotics and dopamine resulted in a progressive improvement of the clinical, laboratoristic and radiological parameters and the subsequent discharge of the patient to home in satisfactory general condition.

1.3. Conclusions

Elevated presepsin level was found to be an early predictor of severe sepsis, after preceding other laboratory or clinical signs of infection. NIV in RICU and medical therapy allowed the successful treatment of a severe global respiratory failure in a DNI patient.

2. Introduction

Sepsis is a rapidly evolving condition characterized by high mortality that must be promptly recognized and treated [1].

The evolution of medicine permits the survival of poly pathological patients with DNI status that, in life-threatening conditions, cannot be treated in intensive care units (ICU) [2]. In these cases, a crucial role can be played by RICU [3], which allows an alternative treatment with NIV combined with continuous monitoring of vital parameters [4].

In addition, it is often difficult in these poly pathological patients to make an immediate clinical and radiological differential diagnosis that distinguishes an inflammatory origin from an acute heart failure [5], that in many cases could coexist.

Presepsin is a new predictive marker of systemic infection [6]. Values below 200 pg/ml exclude septic conditions, while values

greater than or equal to 1000 pg/ml are indicative of high risk of progression of systemic infection and mortality at 30 days, comparable to a SOFA (Sequential Organ Failure Assessment) score greater than or equal to 8 [7, 8] even though the measurement of the widely known inflammatory biomarkers (CRP, WBC, PCT) is initially negative [9].

3. Case

G.V. is a 73-year-old man with a previous history of chronic ischemic heart disease; in consequence of an anterior myocardial infarction he had been subjected to angioplasty and coronary stenting at the age of 54 years and, at the age of 67 years, he underwent coronary artery bypass (BPAC) for unstable angina. Four years later a constrictive pericarditis of possible post-pericardiotomy origin complicated by multiple episodes of heart failure was diagnosed. His medical history also included cognitive impairment (MMSE 18/30), hypertension and type-2 diabetes mellitus.

In May 2021 the patient has been admitted to cardiology department for a severe new episode of heart failure in constrictive pericarditis; after transferring to cardiac surgery, the possibility of pericardial decortication was excluded. During hospitalization, diagnosis of autoimmune hemolytic anemia (Coombs positive) was made, then systemic steroid therapy (Prednisone 50 mg/day) was started.

On 14th October 2021 he was transported to the ED in a soporous conscious state (GCS = 9), tachypnoic (RR=44/min) with severe global respiratory insufficiency (hemogasanalysis in spontaneous breathing with FiO₂ 45%: pH 7.07, pO₂ 41 mmHg, pCO₂ 123 mmHg, HCO₃- 36 mmol/L, Lac 2.8 mmol/L, SatO₂ 63%, P/F 91), APACHE II (Acute Physiology and Chronic Health Evaluation II) score = 33 (corresponding to 78.6% of predicted mortality) and SOFA score = 9, with radiological imaging of diffuse parenchymal thickening (Figure 1), 36°C body temperature, hypertension (BP 186/114 mmHg), tachycardia (HR 140 bpm, sinus rhythm), increased NT-proBNP (2684 pg/mL with normal values 50-194). Traditional inflammatory serum markers were negative (WBC 4.62 x 10¹²/L with normal formula, CRP 7.4 mg/L with normal values 0-8, PCT 0.45 ng/mL with normal values 0-0.5) against a marked elevation of presepsin (3200 pg/mL). The intensivists indicated a DNI status by reason of the numerous copathologies and the patient from ED was directly admitted to RICU.

He arrived to the ward on the same day tachycardic (sinus tachycardia HR 110/min), tachypnoic (RR 30/min), normothermic with ongoing amines (dopamine 5 gamma/kg/min) for onset of hypotension (BP 80/40 mmHg), stopped furosemide infusion (40mg/24 hours started in ED) and continuous NIV (Monnal T75 ventilator PSV mode: PS 14 cmH₂O, PEEP 5 cmH₂O, FiO₂ 45%), as well as broad-spectrum antibiotic therapy (Piperacillin/Tazobactam 4/0.5

g administered every eight hours) based on presepsin level. The hemogasanalysis with NIV FiO₂ 45% improved (pH 7.26, pO₂ 89 mmHg, pCO₂ 65 mmhg, HCO₃- 29 mmol/L, Lac 3.4 mmol/L, SatO₂ 96%, P/F 198).

In the morning of the next day (15th October), fever occurred and a marked increase of all inflammatory biomarkers (Figure 2 and 3) appeared in blood test (CRP 241.8 mg/L, PCT 34.4 ng/mL, WBC 12.18 x 10¹²/L) manifesting a septic shock picture. On chest X-ray, signs of vascular congestion were reduced and, after four hours from last hemogasanalysis, blood gas values further improved (hemogasanalysis with NIV FiO₂ 45%: pH 7.55, pO₂ 79 mmHg, pCO₂ 52 mmHg, HCO₃ 45 mmol/L, Lac 2 mmol/L, SatO₂ 95%, P/F 176). Also the consciousness enhanced (GCS 15) and NIV was set from continuous to cycles. The following onset of atrial fibrillation (AF) with high ventricular response but at the same time the progressive normalization of blood pressure values, due to sepsis control (on 16th October: CRP 158 mg/L and PCT 20 ng/mL; 17/9 CRP 77 mg/L and PCT 11 ng/mL), allowed firstly a dosage reduction, then the rapid suspension of dopamine. For AF the patient started the antiarrhythmic therapy with amiodarone and low molecular weight heparin (EBPM) at anticoagulant dosage then shifted to a new oral anticoagulant (Dabigatran 150 mg/die x2).

The echocardiocolordopplergraphy showed: a normal size left ventricle with parietal thickness, akinesia in apical septum and apex and apical inferior dyskinesia with slightly reduced global systolic function (EF 45-50%); paradoxical septal movement and significant variability of transmitral pattern and aortic flowmetry with respiratory acts as in constrictive pericarditis; dilated (22 mm) and poorly collapsible vena cava; slight biatrial enlargement; right ventricle of normal size; minimal mitral and tricuspid regurgitation.

In the following days, persistent AF/atrial flutter despite amiodarone therapy made electrical cardioversion necessary in order to restore sinus rhythm.

The patient progressively improved until complete weaning from NIV, normalization of inflammatory serum markers (CRP 1.9 mg/L as shown in Figure 2, PCT 0.29 ng/mL as shown in Figure 3, WBC 7.68 x 10¹²/L) and respiratory gas exchanges (hemogasanalysis in ambient air: pH 7.50, pO₂ 81 mmHg, pCO₂ 43 mmHg, HCO₃- 34 mmHg, Lac 0.8 mmol/L, SatO₂ 97%, P/F 386). The last radiological imaging only showed the known left pleural scarring (Figure 4). The sinus rhythm at electrocardiogram (ECG) was stable and the NT-proBNP values significantly reduced (from 2685 pg/mL to 592 pg/mL).

The patient was discharge to home after 16 days of hospitalization.

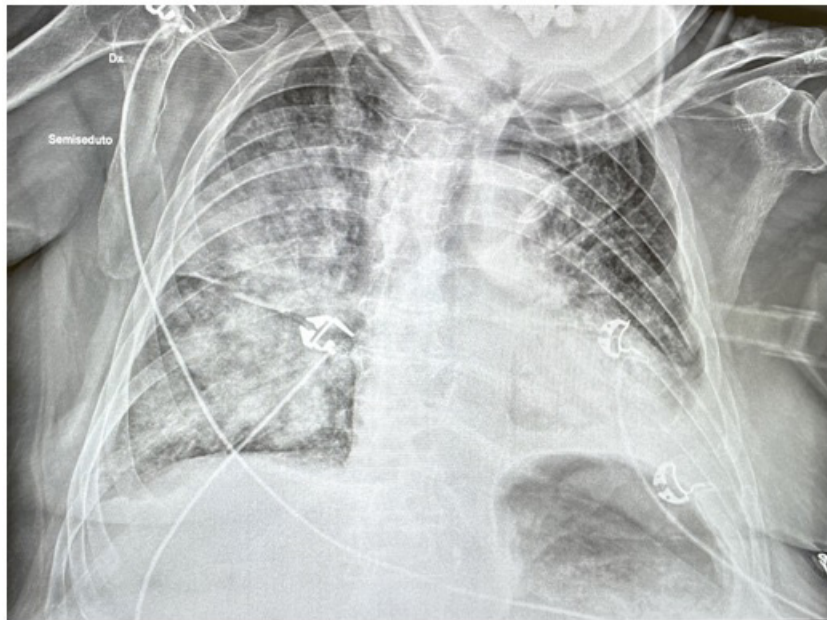


Figure 1: Chest X-ray taken at Emergency Department admission on 14th October: compact parenchymal thickenings involving the upper and lower lobes on the right and the left retrocardiac region. The left apical parenchyma is more aerated. Coexistence of thickening of the vascular pattern bilaterally as from overload. The thickenings have a slightly cottony appearance. Pleural scarring on the left.

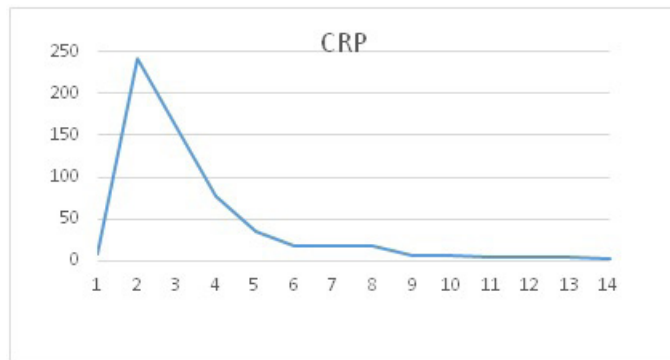


Figure 2: C-reactive protein (CPR) trend during 14 days of hospitalization.

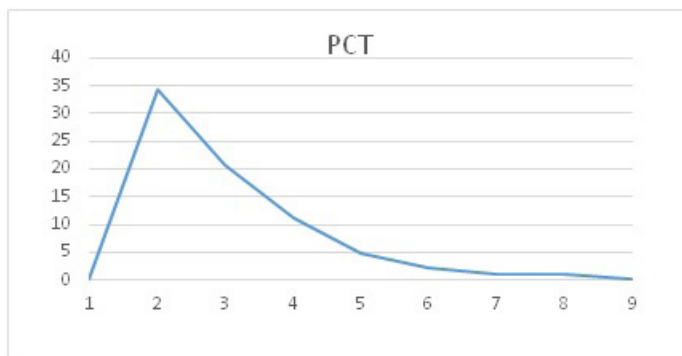


Figure 3: Procalcitonin (PCT) trend during 14 days of hospitalization.

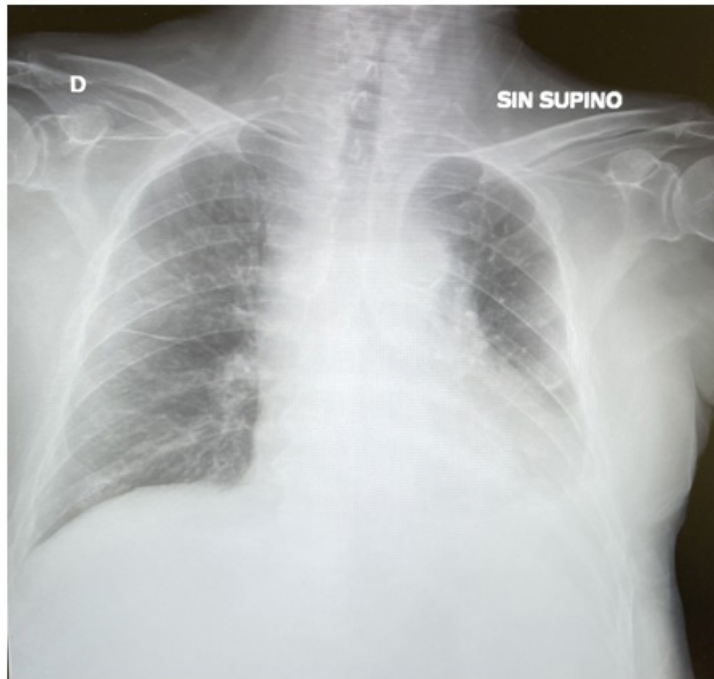


Figure 4: Chest X-ray on 23th October: Examination performed in a single projection in supine position. Improved parenchymal transparency bilaterally; known left costophrenic pleural scarring.

4. Discussion

Sepsis is the life-threatening failure of organs caused by a dysregulated host response to infection causing high rates of morbidity and mortality [10].

Early identification and strict monitoring of patients with sepsis is essential to alleviate the risk of multi-organ failure and to decrease mortality [11]. The available scoring systems such as Acute Physiology and Chronic Health Evaluation II (APACHEII) score [12] and Sequential Organ Failure Assessment (SOFA) scores [8] are predictive of hospital outcomes.

The sCD14-ST molecule, also known as presepsin, is a 13 kDa N-terminal fragment produced by cleavage of the soluble CD14 membrane marker/receptor protein after the recognition of bacterial lipopolysaccharide or other surface bacterial ligands, including gram-positive peptidoglycans, and the following host cell activation [13]. Higher levels were reported in the early stages of sepsis and they were correlated with severity [14] and prognosis [15]. The presepsin cut-off value of 1925 pg/mL is a predictor of ICU mortality in septic patients [16].

In our patient, normal values of traditional inflammatory serum markers at admission, the absence of fever and radiological opacities and a preexistent cardiovascular compromise did not allow a clear differential diagnosis between severe pneumonia and heart failure [5]; therefore, in the absence of an early increase in presepsin, a wrong diagnosis of a new severe acute heart failure could be made, delaying the beginning of antibiotic therapy and worsening the patient's prognosis.

A clear picture of septic shock, in fact, only emerged the day after

ED admission, presenting with marked hypotension, tachycardia and fever with elevation of traditional inflammatory biomarkers (CRP, PCT, WBC).

The early antibiotic treatment, starting on the basis of presepsin elevation, has been essential for the favorable clinical course.

An association with Linezolid was carried out on the basis of the preliminary report of positive blood culture for Gram-positive cocci (staphylo morphology), with subsequent definitive identification of methicillin-resistant *Staphylococcus hominis* sensitive to Linezolid; even if bacterial contamination could not be excluded, antibiotic therapy was continued in light of the good clinical course and the marked reduction of inflammatory biomarkers.

Another point we want to focus on is that, concerning respiratory gas exchanges, our patient was critical but, due to severe comorbidities, not eligible for treatment in intensive care unit (ICU) [17]. The DNI status led to the application of NIV even beyond the limits commonly reported in literature [4, 18] for both pH values (pH 7.07) and state of consciousness (GCS 9) at ED admission. NIV immediately performed in the ED and carried on in the RICU allowed a progressive and fast improvement of the hemogasanalysis values with the application of firstly continuous than intermittent ventilation until complete weaning [19]. The patient's soporous state (GCS 9) favored an indispensable excellent compliance during continuous NIV; with the improvement of consciousness's level (GCS 15) and of hemogasanalysis, ventilation was rapidly reduced and then discontinued.

The use of dopamine required for sepsis hypotension presumably facilitated the arrhythmic complication (AF then atrial flutter), but

the initial control of sepsis paradoxically favored the normalization of blood pressure values. Ventricular rate was controlled pharmacologically with amiodarone [20], electrical cardioversion, performed when the patient was hemodynamically stable and the inflammatory serum markers were off, finally restored sinus rhythm.

Among the numerous co-pathologies of the patient, we point out Coombs-positive autoimmune hemolytic anemia under chronic steroid therapy (Prednisone 50mg/day), which has probably favored the development of a severe bacterial infection [21]. On specialist hematologic indication, prednisone dosage was immediately reduced to 25 mg/day and an outpatient hematologic follow-up was scheduled.

5. Conclusions

Very high presepsin, APACHE II score and SOFA score values are predictive of high probability of mortality. The high initial presepsin level carried to the immediate introduction of antibiotic therapy. The DNI patient order pushed the NIV beyond the traditional indications reported in literature. Finally, the proper management in a specialistic intermediate care setting (RICU) by the pulmonologist, with a constant clinical and parametric monitoring, contributed to the favorable resolution of the case.

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