Utility of Procalcitonin for Diagnosis of Superimposed Infections in Patients With Acute Heart Failure

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Respiratory infections are well-known precipitant factors for heart failure decompensations. Nevertheless, the diagnosis of life-threatening infections, such as pneumonia, is challenging. Pneumonia and acute heart failure often display overlapping clinical findings and, in other cases, more accurate infection-related findings are missing. In recent years, procalcitonin has emerged as a promising tool for early and accurate diagnosis of pneumonia and, interestingly, for guiding antibiotic therapy in patients with acute heart failure. We discuss two cases of acute heart failure with high procalcitonin on admission and different clinical outcomes. In this setting, procalcitonin may be a useful tool for guiding antibiotic therapy. Further controlled studies are warranted.

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KEY WORDS

Procalcitonin • Acute heart failure • Concomitant infections • Procalcitonin-guided therapy

Acute heart failure (HF) represents the primary cause of hospitalization in elderly people.[1] It is well established that infections are recognized precipitating factors for HF decompensation.[2] In contemporary data including 48,612 admissions for acute HF, both pneumonia and respiratory processes were present in 35% of cases.[3] Nevertheless, diagnosis of relevant infections, especially pneumonia, in patients with HF is challenging, because infections and HF-related symptoms and signs often overlap.[4] In addition, it is not infrequent that, in some representative subgroups of patients (such as elderly people and highly comorbid patients), infection-related findings are subclinical or even missing. In

this scenario, an early and accurate diagnosis of life-threatening bacterial infections is supported by the ominous prognosis observed when both conditions are present and there is the need for an additional therapeutic approach.[5,6]

Within the available diagnosis armamentarium, plasma levels of procalcitonin (PCT), an upregulated protein in infectious states, has been used as a biomarker for determining the severity of the infections and for guiding antibiotic therapy.[7] In patients with acute dyspnea, PCT has emerged as a promising tool to differentiate between acute HF and superimposed pneumonia. Furthermore, recent studies have suggested that PCT may play a crucial role in guiding antibiotic therapy in patients with acute HF.[4,8,9] In the following cases, we describe two clinical acute HF scenarios in which PCT assessment was useful for clinical decision-making.

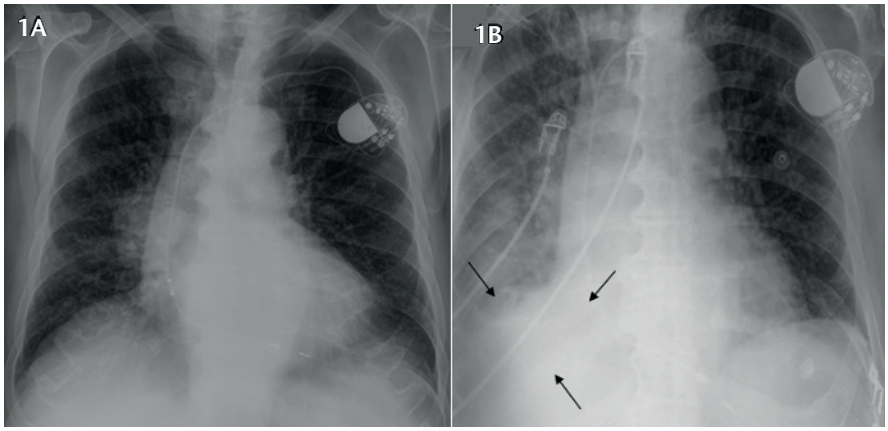

Figure 1. **(A)** Chest radiograph on admission reveals mild interstitial lung edema and no signs of pneumonia. **(B)** Chest radiograph on the fourth day shows focal parenchymal abnormality related to consolidation of the right lower lobe suggesting pneumonia (*black arrows*).

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Case 1

A 71-year-old man with a history of hypertensive chronic HF was attended to in the emergency department for a 15-day history of progressive dyspnea, decreased diuresis, peripheral edema, and orthopnea. He also had a dry cough and no fever. Clinical characteristics are summarized in Table 1. No fever was identified and pulmonary auscultation revealed bibasilar crackles. Blood test results showed high N-terminal pro-brain natriuretic peptide (NT-proBNP) levels (25,607 pg/mL), hypokalemia, leukocytosis, neutrophilia, and mild renal failure (Table 1). The chest radiograph showed cardiomegaly and mild interstitial edema (Figure 1A). With the suspicion of a superimposed infection, his PCT level was measured (0.29 ng/mL). Transthoracic two-dimensional echocardiography showed a marked left ventricular hypertrophy, with preserved left ventricular ejection fraction and a moderate aortic regurgitation. After 8 hours of intravenous diuretic treatment and oxygen supplementation, the clinical situation improved and the patient was admitted with a diagnosis of acute HF. No antibiotic treatment was initiated.

On the fourth day after admission, the patient exhibited worsening heart and renal failure. Monitoring of temperatures revealed no fever since admission. At this time, an increase in PCT (0.40 ng/mL) and other acute phase reactants was observed and antibiotic therapy was started with intravenous levofloxacin. A chest radiograph showed right basal alveolar infiltrates suggesting pneumonia (Figure 1B) and the patient was transferred to the intensive care unit, where double intravenous antibiotic therapy (levofloxacin and meropenem) was initiated. At this time, blood culture and urinary antigen test results were positive for pneumococcus.

A new measurement of PCT levels on the sixth day revealed a continuous increase (0.99 pg/mL). In the following days, the patient suffered progressive systemic organ failure requiring vasoactive drugs and invasive mechanical ventilation. On the 21st day, the patient died.

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Case 2

An 84-year-old woman was seen in the emergency department for worsening shortness of

TABLE 1

Clinical Characteristics on Admission

	Case 1	Case 2
Physical Signs		
Systolic blood pressure (mm Hg)	115	101
Diastolic blood pressure (mm Hg)	78	68
Heart rate (beats/min)	60	77
Temperature (ºC)	36	37.1
Oxygen saturation (%)	88	94
Electrocardiogram	**Atrial Fibrillation**	**Sinus Rhythm. LBBB**
LVEF (%)	60	27
Laboratory Results		
Glucose (mg/dL)	113	142
Urea (mg/dL)	93	84
Creatinine (mg/dL)	1.44	1.01
Sodium (mmol/L)	152	141
Potassium (mmol/L)	2.5	4.4
CRP (mg/L)	23.1	66.1
GGT (U/L)	117	69
Leukocytes ($\times 10^9$/L)	12.34	9.63
Neutrophils ($\times 10^9$/L)	11.49	8.90
Lymphocytes ($\times 10^9$/L)	0.49	0.51
Monocytes ($\times 10^9$/L)	0.36	0.20
Hemoglobin (g/dL)	15.7	15
Procalcitonin (ng/mL)	0.29	1.83
NT-proBNP (pg/mL)	25,607	30,611
Arterial Blood Gases		
pO_2 (mm Hg)	43.10	59.2
pCO_2 (mm Hg)	45.70	37
pH	7.60	7.42

CRP, C-reactive protein; GGT, gamma-glutamyl transferase; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; pCO_2, partial pressure of carbon dioxide; pO_2, partial pressure of oxygen.

breath during the prior weeks. She had symptoms and signs of upper respiratory tract infection and had been receiving treatment with amoxicillin for 7 days. No prior fever during the past week was registered. Bibasilar crackles, rhonchus, and wheezing sounds were present in the pulmonary

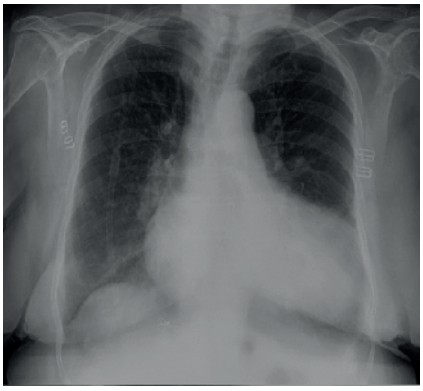
auscultation. The chest radiograph revealed interstitial edema without pleural effusion and no signs of pneumonia (Figure 2). Laboratory test results showed high levels of NT-proBNP (30,000 pg/mL), a normal leukocyte count, no electrolytic disturbances, and normal renal function. Characteristics on admission are presented in Table 1. Two-dimensional echocardiography showed severe left ventricular systolic dysfunction (27%). To rule out a relevant bacterial infection, her PCT level was measured (1.83 ng/ mL). At this time, intravenous antibiotic therapy was started with levofloxacin.

During admission, the patient showed a favorable clinical course with optimal response to diuretic and antibiotic treatment. Three days later, PCT and NT-proBNP levels decreased to 0.70 ng/mL and 10,711 pg/ mL, respectively. The patient was discharged on the seventh day without complications. After 6 months the patient remains stable (New York Heart Association class II/IV HF) without any new admissions.

Discussion

These two cases illustrate the potential utilization of PCT measurement to diagnose superimposed respiratory life-threatening infections in patients with acute HF. This issue is especially relevant due to the inaccuracy of traditional symptoms/signs and laboratory test results to distinguish the main cause of dyspnea. In both cases, the elevation of PCT levels preceded radiologic signs or unequivocal symptoms/signs of respiratory bacterial infection. In the first case, pneumonia was diagnosed 4 days later with catastrophic consequences. Conversely, in the second case, satisfactory results were obtained after an early antibiotic treatment administration guided by PCT values.

Figure 2. Chest radiograph on admission showing interstitial edema and no patterns of pleural effusion or consolidation.



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Some recent studies recommend the use of PCT values to unmask the source of acute dyspnea in the emergency department.[4,8,9] Maisel and colleagues showed that PCT level was more accurate than any other individual clinical variable for the diagnosis of pneumonia in patients presenting to the emergency department with shortness of breath, when applied to an unselected sample of patients with acute dyspnea.[8] In addition, this study also highlighted the potential utility of this biomarker for guiding antibiotic therapy in a subgroup of 568 patients with acute HF. In patients with PCT values higher than 0.21 ng/mL, antibiotic prescription was associated with better 90-day survival. Conversely, in those patients with PCT values lower than 0.05 ng/mL, an increased mortality was found when they were exposed to antibiotics. Likewise, another recent substudy has reported similar results.[10] Reinforcing previous evidence, our group has recently shown in an unselected cohort of 261 patients with acute HF and no active infection on admission that PCT levels were independently associated with higher risk of long-term mortality and recurrent admissions.[11]

Prior findings constitute a solid base for further more controlled studies aiming to unravel the clinical utility of PCT determination in patients with acute HF. A recently initiated study, the Improve Management of Heart Failure With Procalcitonin (IMPACT) trial (NCT02392689), seeks to randomly evaluate the effect of a PCT-guided arm on the risk of primary 90-day all-cause mortality in 792 patients with acute HF.

Conclusions

These two cases illustrate the potential clinical utility of PCT to optimize management of patients with AHF. Further controlled studies are warranted. ■

The authors declare no real or apparent conflicts of interest.

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MAIN POINTS

- Respiratory infections are well-known precipitants for heart failure decompensation.
- Diagnosis of life-threating infections such as pneumonia in acute heart failure patients is somewhat challenging.
- Procalcitonin has emerged as an accurate biomarker for the diagnosis of pneumonia in patients presenting to the emergency department with shortness of breath.
- In patients with acute heart failure, procalcitonin has also shown a potential utility for diagnosing superimposed bacterial infections and guiding antibiotic therapy.