



## Elevated Serum Procalcitonin in the Setting of Anaphylactic Reaction: A Marker of Anaphylaxis

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### Abstract

Although Procalcitonin (PCT) serum level is still considered to be a highly specific and sensitive biologic marker that can be elevated in bacterial infection, it can be seen in noninfectious conditions such as multiple organ dysfunction syndrome, trauma, severe pancreatitis, rhabdomyolysis, hypovolemic and cardiogenic shock and burns. Our aim is to present a case report that highlights the fact that procalcitonin can be elevated in patients who are having an allergic reaction to medications, which emphasizes the importance that the physician should not depend solely on procalcitonin level in differentiating infectious from the non-infectious process, but it should be part of the integral clinical assessment.

**Keywords:** Procalcitonin; Anaphylaxis reaction; Sepsis

### Introduction

Procalcitonin is considered one of the acute phase reactants that can be elevated as part of the body's inflammatory response to pathogens [1-3], procalcitonin considered part of the supportive laboratory tests that guide to the diagnosis of sepsis [4]. However, procalcitonin can be elevated in many non-infectious conditions including inhalation injury, burns, pancreatitis, mechanical trauma, extensive surgery or heat stroke [2].

Our case will present elevated procalcitonin in a patient who is having an allergic reaction to a medication, which emphasizes the importance that clinicians should not depend solely on procalcitonin in differentiating infectious from non-infectious diseases.

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### Case Presentation

Our patient is a 71-year-old female with a past medical history of hypertension, Type II diabetes mellitus and adenocarcinoma of the lung status post resection and chemotherapy four years prior, presented to Jersey Shore University Medical Center with chest discomfort and shortness of breath.

She was found to be in acute congestive heart failure secondary to a hypertensive emergency. Blood pressure was normalized with intravenous Nitroglycerin and then oral lisinopril and amlodipine. Two days after was given the first-time dose of Hydrochlorothiazide (HCTZ), shortly after, patients started complaining of pruritus, shortness of breath and became diaphoretic. Vital signs including blood pressure were 124/54 mmHg, heart rate 106 beats/min, temperature 96.9 F, Respiratory rate 21 and pulse ox 92% on room air. Physical Exam of cardiovascular and lungs showed wheezing in bilateral lung fields with poor air entry, no crackles, no leg edema, no elevated JVD, normal heart sounds.

Initial procalcitonin level on admission was negative, repeat 3 h after onset of symptoms was 88 ng/mL (RR<0.5 ng/ml). Tryptase level was ordered and was 45 ng/mL (RR<11.4 ng/ml).

The patient was given a broad-spectrum antibiotic, epinephrine, prednisone, and antihistamine and transferred to the intensive care unit. Repeat procalcitonin level after 9 h was 329 ng/mL. The patient had an allergy to sulfa previously with similar reactions, the patient improved the second day and antibiotics were discontinued as all laboratory data and diagnostic imaging came back unremarkable for infection.

### Discussion

Procalcitonin is a 116 amino acid polypeptide precursor of calcitonin, which is produced in thyroid C cells [5]. In healthy humans, elevated levels of calcium, glucocorticoids, Calcitonin Gene-Related Peptide (CGRP), glucagon, gastrin, and B-adrenergic stimulation induce CALC-1 gene in C

cells of the thyroid to convert preprocalcitonin to procalcitonin and eventually calcitonin [6]. However, during a body's inflammatory response to certain pathogens, production of procalcitonin is altered directly by lipopolysaccharides and other toxic metabolites, or indirectly via inflammatory mediators such as IL-6 and TNF- $\alpha$  [6].

Sepsis is a syndrome, in which the body creates an exaggerated inflammatory response to an abnormal stimulus, commonly infection, which may cascade into severe multiorgan failure [3]. The annual incidence of sepsis is estimated to be 300 cases per 100,000 populations with an average annual cost of hospital care of approximately \$14 billion in the United States [7]. With prompt identification of sepsis, key improving outcomes, clinicians use diagnostic criteria comprised of physical exam findings, along with supportive laboratory data to guide management [3,7]. Criteria for Systemic Inflammatory Response Syndrome include Temperature  $>38$  C or  $<36$  C, Heart Rate  $>90$ /min, Respiratory Rate  $>20$ /min and White Blood Cell Count  $>12,000$  cells/uL or  $<4,000$  cells/uL [3,7]. Other screening criteria such as qSOFA has shown mixed evidence in their effectiveness for assessing sepsis. In the past decade, procalcitonin has increasingly been used to guide clinicians in deciding to give antibiotic therapy [4].

Procalcitonin elevation occurs within 2 h to 4 h of active bacterial infection, and peaks between 8 h to 24 h [2]. Low levels of serum procalcitonin are also useful for confirmation of viral infection, to safely discontinue antibiotics [2]. Procalcitonin has also been shown to be elevated in many non-infectious causes including inhalation injury, burns, pancreatitis, mechanical trauma, extensive surgery or heat stroke [2]. In these non-infectious causes of elevation, ranges of value and peak time may vary depending upon etiology [2]. There have also been case reports of elevated procalcitonin in the setting of different severity ranging from DRESS Syndrome to anaphylactic shock [8,9], implying its potential role as a marker. However, a case review of 8 different allergic reactions showed that only 3 of 8 cases have a significant elevation of procalcitonin [10].

In the case reported by Hiroyuki et al. [8] the patient developed an anaphylactic reaction to trimethoprim/sulfamethoxazole 12 days after starting therapy, like our patients, the patient had a marked elevation of procalcitonin and did receive antibiotic therapy for presumed sepsis. Cases reports of Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) Syndrome, a type of delayed allergic reaction, by Bonaci-Nikolic (2015) and Benoit et al. [9] showed patients with marked procalcitonin elevation. A study conducted by Sun-Young et al. [11] compared procalcitonin and C-Reactive Protein (CRP) to differentiate infection and drug hypersensitivity reactions. They showed that procalcitonin was a better marker than CRP to differentiate between infection and hypersensitivity

and that procalcitonin was normal in nearly 79% of patients with hypersensitivity [11]. Sun-Young et al. [11] did, however, show that the level of procalcitonin did have a positive correlation with the severity of the Allergic Reaction.

In the case reports study, clinicians tended to initiate antibiotic therapy with signs of SIRS and elevated procalcitonin [8,9,11]. From reviewing these cases, we believe that clinicians must be aware of alternate causes of procalcitonin elevation. Furthermore, with anaphylaxis having an overlapping presentation with possible sepsis, additional studies should be done to further evaluate the role of procalcitonin in the setting of hypersensitivity reactions.

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