Introduction

Procalcitonin (PCT) a peptide precursor of the hormone calcitonin, is produced by the parafollicular cells (C cells) of the thyroid and by the neuro-endocrine cells of the lung and the intestine [1]. PCT level has been shown to rise in response to proinflammatory stimulus [2], especially of bacterial origin and in this case, it is produced mainly by the cells of the lung and the intestine [3]. Measurement of PCT can be used as a marker of severe sepsis caused by bacteria and generally grades well with the degree of sepsis. PCT is used increasingly as a marker of bacterial infection, with PCT >2 ng/mL advocated as an indicator to initiate antibiotics in patients with presumed infection. However, not every elevated PCT is an infection.

Case: 49 year-old women presented in July with fever, nausea, vomiting, confusion, headache, light-headedness, neck stiffness and abdominal pain for one day. Her past medical, family and social history were non-contributory. Examination revealed fever (99.5 °F), tachycardia (pulse 115/min) and dry oral mucosa.

Labs showed high white blood cell (WBC) count-18,000/mm$^3$, PCT-145.88 ng/mL, Aspartate transaminases (AST) -560 units/L, Alanine transaminases (ALT) -213 units/L and Alkaline phosphatase (ALP)-201 units/L. She was hydrated and antibiotics started after drawing blood cultures and lumbar puncture. Urinalysis, Computed Tomography (CT) scan of head, lumbar puncture, chest X-ray and CT scan of abdomen and pelvis were non-contributory. Blood cultures and viral meningitis panel was negative. Next day, she became afebrile, WBC dropped to 11,300/mm$^3$, PCT-92.3 ng/mL, AST-57 units/L, ALT-86 units/L and ALP-111 units/L. She reported being in the sun, the entire preceding day, while moving to new apartment in 95 °F heat and not drinking any fluids. She was diagnosed with heat stroke, hydrated and antibiotics stopped. She responded well and was discharged next day.

Discussion: She had highly elevated PCT without any infectious etiology. Her PCT trended downwards the next day, thus correlating with PCT's half-life of 25-30 hours. Heatstroke usually presents clinically with systemic inflammatory response syndrome and can have elevated PCT and transaminases. Thus, in patients with high PCT, clinicians should be equally vigilant for non-infectious inflammatory etiologies.

Not Every Rise in Procalcitonin is Infection
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Abstract

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Discussion: She had highly elevated PCT without any infectious etiology. Her PCT trended downwards the next day, thus correlating with PCT’s half-life of 25-30 hours. Heatstroke usually presents clinically with systemic inflammatory response syndrome and can have elevated PCT and transaminases. Thus, in patients with high PCT, clinicians should be equally vigilant for non-infectious inflammatory etiologies.

Case Report

A 49 year old lady, who recently shifted her home to Kalamazoo town, presented in month of July with complaints of nausea, 5 episodes of non-bloody vomiting, confusion and light-headedness for one day, accompanied by pain in head and neck, 6/10 in intensity, gradual in onset, non radiating, stiffening, relieved by massaging and increased by movements. The pain was accompanied by neck stiffness and photophobia. She also complained of dull diffuse abdominal pain, 5/10 in intensity, gradual in onset, non radiating, non-localized to any quadrant, without any association with meals/constipation/diarrhea. She had chills and a documented fever of 102 °C before arriving at our hospital. She denied any blurring of vision, aural/nasal discharge, cough, chest pain, shortness of breath, diarrhea, constipation, weakness or numbness in limbs. She denied any falls, loss of consciousness, head trauma, history of travel. Her past history was significant for carcinoid tumor status post right hemicolectomy and appendectomy and hysterectomy. On examination, her blood pressure was 109/82 mm Hg, pulse 115/min, oral temperature 99.5 °F (37.5 °C) and respiratory rate of 16/min. She was well built and nourished but was distressed due to pain. Her physical
examination was unremarkable except for a midline scan in abdomen and a diffuse tenderness in lower abdominal area. Her labs were significant for high white blood cell (WBC) count 18,000/mm³, PCT level was 145.88 ng/mL, Aspartate transaminases (AST)–560 units/L, Alanine transaminases (ALT)-213 units/L, Alkaline phosphatase (ALP)–201 units/L. Otherwise, complete blood count and metabolic panel was unremarkable. C-reactive protein was elevated to 10.2 mg/dL. Erythrocyte sedimentation rate was elevated to 36 mm/hr. Her computed tomography (CT) scan of head did not show any mass lesion or acute hemorrhage. Lumbar puncture was done, blood cultures drawn and she was started on Vancomycin and Ceftriaxone and well hydrated. Her lumbar puncture was unremarkable. Cerebrospinal fluid (CSF) serology was negative for syphilis, Lyme antibodies, California encephalitis, Eastern Equine encephalitis, St Louis encephalitis, Western Equine encephalitis, Herpes simplex virus (HSV) 1 and HSV-2, Measles, Mumps, Varicella Zoster, Adenovirus, Influenza type A and B, Coxsackie A and B, Cytomegalovirus and West Nile virus. Her blood cultures came back negative. Her chest X-ray and CT abdo pelvis with contrast did not show any acute abnormality. Urinalysis was remarkable for 2+ bacteriuria but cultures only showed 25,000-50,000 colonies/cc of normal urogenital flora. Hepatitis panel was negative for Hepatitis A and Hepatitis B antigen and was positive for only Hepatitis C antibody. Peripheral smear revealed neutrophilic leukocytosis with left shift. Her antibiotics were stopped after she turned afebrile the next day. Her WBC dropped to 11.3 next day and other markers started trending down with PCT to 92.3 ng/mL, AST–57 units/L, ALT–86 units/L and ALP falling to 111 units/L. On further questioning, she admitted that she was out in the sun all day moving to her new apartment and did not drink plenty of fluids. She was diagnosed with heat stroke and well hydrated. The patient responded well and was discharged the next day.

Discussion

Thus, our patient had highly elevated PCT without an underlying infectious etiology. In serum, PCT has a half-life of 25 to 30 hours. Heatstroke is a life-threatening illness with a complex pathophysiology sharing some similarities with sepsis [7]. Patients with heatstroke usually present clinically with systemic inflammatory response syndrome (SIRS) criteria with up to 58% of heatstroke patients having elevated PCT values, without any specific infection and these values seemed to correlate with a more critical illness [8]. A meta-analysis of 18 studies found that PCT distinguished sepsis from nonseptic systemic inflammation poorly (sensitivity of 71 percent and specificity of 71 percent) [9]. Heatstroke could represent a non-septic pathway for PCT synthesis. Some studies reported an elevated plasma level of inflammatory cytokines (tumor necrosis factor a (TNF-α), interleukin-1a, interferon-a) in classic heatstroke [8]. The TNF-α precedes PCT detection in serum after endotoxin injection in normal subjects and injection of TNF-α can stimulate PCT synthesis in animal models [8]. It is hypothesized that sepsis and heatstroke share TNF-α as a common inducer of PCT [8] which could cause PCT to rise in non-infectious inflammatory states. Thus, clinicians should have high index of suspicion for diagnosis of heat stroke in appropriate clinical setting and have open mind for diagnosis of non-infectious inflammatory conditions in presence of elevated PCT.

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