Arch Rheumatol 2024;39(1):133-135
doi: 10.46497/ArchRheumatol.2024.9940

LETTER TO THE EDITOR

Is procalcitonin elevation always an indicator of bacterial infection?

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Adult-onset Still's disease is a systemic inflammatory disorder with fever, arthritis, and rash.[1] Although the etiology is not known, some viral (rubella, echovirus, Epstein-Barr, cytomegalovirus) and bacterial *(Yersinia enterocolitica, Mycoplasma pneumoniae)* factors have been accused.[2] It is difficult to diagnose and can be diagnosed by excluding other causes, such as malignancy, collagen tissue disease, and infection. It is very difficult to distinguish from bacterial infections, especially since it is accompanied by fever and rashes, elevated C-reactive protein (CRP), erythrocyte sedimentation rate, and leukocytosis.

Procalcitonin (PCT) is a prehormone of calcitonin normally secreted by thyroid C cells in response to hypercalcemia. Since it was determined that PCT, whose serum level is low under normal conditions, increases in bacterial infections and does not increase significantly in systemic viral and immunological diseases, it has been used as a marker, particularly in the detection of bacterial infections.[3]

A 28-year-old female patient applied to the emergency service in the middle of August with fever, joint pain, swelling, abdominal pain, and skin rash. The patient, who stated that her complaints started about 10 days ago, gave birth five months ago. No complications developed after delivery. The patient's white blood cell count (WBC) was 9.06 K/uL, CRP was 304.1 mg/L, aspartate aminotransferase was 173 U/L, and alanine transaminase was 103 U/L on admission to the emergency department. Urine culture showed no growth. Abdominal tomography and posteroanterior chest X-ray was evaluated as normal. The patient was given three days of ceftriaxone 1 g two times a day intramuscular treatment and was referred to the infectious diseases outpatient clinic.

When the patient, whose complaints did not go away, applied to the infectious diseases outpatient clinic, the analyzes were as follows: WBC, 14.57 K/uL; CRP, 37.8 mg/L;PCT, 0.72 ng/mL. Consequently, the patient was given five days of cefdinir 600 mg orally two times a day and called for control. The patient, who applied to the hospital again five days later, had a fever of 38.7°C and was hospitalized for further examination and treatment. The PCT value had increased, and the ferritin value was four times the normal value. Blood and urine cultures were negative, *Brucella* screening was negative, and viral markers, such as those for hepatitis virus and Epstein-Barr virus, were negative. The chest radiograph was evaluated as usual. An empiric treatment of meropenem 1 g three times a day was started. No signs of infective endocarditis were detected in the echocardiography performed by the cardiology department. The patient was referred to the rheumatology outpatient clinic due to arthritis in the right knee and left ankle, and adult Still's disease was considered. Methylprednisolone

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Received: March 20, 2023
Accepted: March 22, 2023
Published online: February 01, 2024

Citation: Ecesoy V, Ecesoy H. Is procalcitonin elevation always an indicator of bacterial infection? Arch Rheumatol 2024;39(1):133-135. doi: 10.46497/ArchRheumatol.2024.9940.

Table 1. Laboratory data of the patient

	1. Application (ER)	2. Application (infectious diseases)	3. Application (inpatient)	Steroid treatment Day 5	Steroid treatment Day 15
WBC (K/uL)	9.06	14.57	10.17	8.23	24.34
CRP (mg/L)	304.1	379.8	367.3	23.1	11.0
ESR (mm/h)			141	19	14
AST (U/L)	173		614	26	20
ALT (U/L)	103	94	297	60	38
Ferritin (ng/m)			>1,650	943	416.6
Procalcitonin (ng/mL)		0.72	5.83	0.28	0.05

ER: Emergency room; WBC: White blood cell count; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; AST: Aspartate aminotransferase; ALT: Alanine transaminase.

500 mg/day was intravenously administered for five days. As of the second day, the patient's fever decreased, and the rashes that appeared with the fever disappeared. At the end of the fifth day, all blood results of the patient decreased (Table 1). The patient was discharged with 60 mg peroral methylprednisolone. At the follow-up two weeks later, there was no arthritis, no fever, and the rash did not recur. All blood results of the patient were within normal limits or very close to normal. The patient was advised to gradually decrease the methylprednisolone dose and was called for control.

Although PCT is the precursor of calcitonin secreted from the medullary C cells of the thyroid gland, studies have shown that PCT levels are high in patients with thyroidectomy without calcitonin secretion during severe bacterial infections.[4,5] The PCT-secreting nonthyroid tissue is not known, but it is thought to be leukocytes, neuroendocrine cells, and lungs.[6] In a study with monkeys by Nijsten and Olinga,[7] it was shown that PCT is of liver origin and the liver produces large amounts of PCT after stimulation of human liver tissue with tumor necrosis factor alpha (TNF-α) or interleukin (IL)-6. These studies show that PCT can be secreted as a result of endotoxins or cytokines (e.g., IL-6, TNF-α, and IL-1β) not only from the thyroid but also from various tissues.[8]

Although PCT is a marker often used in the detection of bacterial infections, it can also increase inflammatory processes, as seen in this case. In some cases, it can reach quite high numbers, such as >35.[9] A similar conclusion was reached in the case presented by Fayed et al.[10] There are many publications showing that PCT is elevated outside of bacterial infections. For example, a recently published observational study found increased PCT in patients with post-COVID-19 (coronavirus disease 2019) multisystem inflammatory syndrome.[11] Yu et al.[12] found that the main cause was rhabdomyolysis in a patient who was followed up with the assumption of sepsis and whose PCT values increased considerably. PCT was found to be high in the acute period of Kawasaki disease in children, particularly in those who were resistant to intravenous immunoglobulin therapy.[13]

In conclusion, the fact that the CRP value is quite high in patients who apply to the infectious diseases outpatient clinic with symptoms of fever and arthritis and the accompanying high PCT causes physicians to make decisions in favor of a bacterial infection. Inflammatory diseases, such as Still's disease, need to be considered, specifically in patients with multiorgan involvement whose cultures are negative and who do not respond to antibiotic therapy, even if the PCT is high. Better recognition of the disease will make it easier to diagnose.

Patient Consent for Publication: A written informed consent was obtained from patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept: V.E., H.E.; Data collection and/or processing: H.E.; Analysis and/or interpretation, critical review: V.E., H.E.; Literature review, writing the article: V.E.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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