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Serum Procalcitonin Levels in Pulmonary Coccidioidomycosis

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Introduction

Procalcitonin (PCT) is a glycoprotein precursor of the hormone calcitonin, which has emerged as a valuable biomarker in clinical medicine. It is particularly useful distinguishing bacterial infections from viral infections and is produced by various tissues in response to inflammatory stimuli. Synthesis is significantly elevated in bacterial infections, while remaining low in viral infections.[1,2] As an acute-phase reactant, procalcitonin is often used to help clinicians make more accurate diagnoses, differentiating between bacterial and viral causes of infection. This impacts treatment decisions, especially in antibiotic use.[3]

In patients with bacterial infections, particularly those with systemic involvement such as sepsis or pneumonia, procalcitonin levels can rise sharply, often correlating with the severity of the infection.[2,4] Conversely, in viral infections, such as those caused by influenza or respiratory viruses, procalcitonin levels typically remain within normal or low ranges.[5] This differential response is thought to arise due to the distinct inflammatory pathways activated by bacterial and viral pathogens, with bacterial infections generally eliciting a stronger proinflammatory response.

The clinical utility of procalcitonin has been widely studied, particularly in the context of unnecessary antibiotic usage. Elevated PCT levels support need for antibiotics in bacterial infections, while lower levels suggest antibiotics may not be required, thus improving antibiotic stewardship and reducing risk of antimicrobial resistance.

The current evidence for use of PCT as a marker to help diagnose fungal infection or differentiating that from other infections is not yet adequate, due to a lack of randomized controlled trials. Sakata et al. initially reported the relationship between serum procalcitonin levels and primary coccidioidomycosis in 2014. They included a small number of patients who had symptoms within 8 weeks, without a relationship between elevated procalcitonin and coccidioidal infection.[6] Our presentation may help determine whether there is an association between serum procalcitonin levels and primary pulmonary coccidioidomycosis.

Methods

This retrospective review analyzed the Valley Fever Institute database between 2017 and 2021. This was approved by the Kern Medical Institutional Review Board. The literature search was conducted on PubMed and Google scholar using search terms: coccidioidomycosis; community-acquired pneumonia; and procalcitonin levels. Coccidioidomycosis (cocci) infection was confirmed by serology, sputum or broncho-alveolar lavage microbiology, and radiological evidence of pneumonia. Bacterial infections were excluded after reviewing sputum and blood culture results.

A total of 74 patients' records were included in this study. Fifty-two patients had an acute cocci infection and 22 patients had chronic infection. Acute infection was defined as a new symptomatic primary pulmonary coccidioidomycosis less than six weeks duration. Chronic infection was defined as a previously proven coccidioidomycosis infection or pneumonia with symptoms of six or greater weeks. The first value of the procalcitonin assay was considered as positive using a cutoff of > 0.10 μg/L. IRB approval was obtained # 18039.

Results

Of all patients with acute pulmonary coccidioidomycosis infection 34 patients (65.38%) had a positive test for procalcitonin as compared to 12 patients (54.54%) amongst the chronic pulmonary coccidioidomycosis patients. The odds ratio of 1.57 suggests a greater incidence of positive procalcitonin among acute patients. However, as the p-value was 0.3811, did not reach statistical significance.

Discussion

Coccidioidomycosis, a fungal infection caused by *Coccidioides* species, is endemic to specific regions of North and South America, particularly the southwestern United States, Mexico, and parts of Central and South America. Pulmonary coccidioidomycosis is the most common manifestation, with symptoms ranging from mild respiratory illness to severe pneumonia, and in some cases, disseminated disease.[7] Diagnosing pulmonary coccidioidomycosis typically involves a combination of clinical evaluation, radiographic findings, and microbiological testing, including culture or serology for *Coccidioides* spp. However, the diagnostic process can be challenging, especially in the early stages of infection or in immunocompromised patients, where cocci symptoms may overlap with other bacterial and viral respiratory illnesses.[7]

Although procalcitonin is primarily used to assess bacterial infections, recent studies suggest that PCT levels may also be elevated in certain fungal infections, including coccidioidomycosis. A few reports have documented the presence of elevated serum PCT levels in patients with pulmonary coccidioidomycosis, suggesting that it may serve as a complementary diagnostic marker. The elevation in PCT levels in fungal infections, including coccidioidomycosis, may be due to the inflammatory response triggered by fungal pathogens, particularly in patients with significant tissue damage or with secondary bacterial infections complicating the fungal disease.[8] Some studies suggested that procalcitonin levels may reflect the severity of disease, with higher levels associated with more severe pulmonary involvement or the presence of disseminated coccidioidomycosis.[6]

While procalcitonin is a useful biomarker for bacterial infections, its role in fungal infections such as pulmonary coccidioidomycosis remains an area of ongoing research. One limitation of PCT in fungal infections is a relative lack of specificity. Elevated PCT levels are not exclusive to bacterial infections and can be observed in other conditions, including sepsis, trauma, and systemic inflammatory responses to fungal infections.[9] In summary, procalcitonin remains a valuable biomarker in distinguishing bacterial infections from viral infections, particularly in the context of lower respiratory illnesses. However, its utility in fungal infections, such as pulmonary coccidioidomycosis, requires further investigation. While PCT levels may be elevated in some patients with pulmonary coccidioidomycosis, it should not be relied upon as a sole diagnostic marker. A multifaceted approach that combines clinical presentation, microbiological testing, and other biomarkers will continue to be needed for accurate diagnosis and management of complex respiratory infections.

Limitation

The limitation of this study includes the retrospective design involving a single community hospital resulting in limited power. Difficulties excluding concomitant bacterial infection, makes it challenging to determine whether elevated procalcitonin level is a result of inflammation or directly caused by the fungal infection and represents another limitation.

Conclusion

This limited power study found procalcitonin did not have clinical value in diagnosing pulmonary coccidiomycosis or differentiating between acute or chronic form of the infection.

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