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The Sepsis Look-Alike: A Rare Presentation of Hypercalcemia

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Abstract:

Hypercalcemia is a clinically significant metabolic derangement that commonly arises from primary hyperparathyroidism and malignancy. However, its atypical presentations can mimic life-threatening conditions such as ***sepsis****, leading to diagnostic delays and inappropriate early management. The objective of this observational case-based study was to examine the diagnostic challenges posed by severe hypercalcemia presenting with features resembling sepsis, including tachycardia, hypotension, altered mental status, and leukocytosis. A patient admitted during the study period presented with fever, dehydration, tachycardia, and elevated inflammatory markers, raising a strong suspicion for sepsis. However, persistent symptoms despite broad-spectrum antimicrobials prompted further evaluation. Laboratory testing revealed markedly elevated serum calcium levels, metabolic alkalosis, suppressed parathyroid hormone levels, and evidence of dehydration-induced acute kidney injury. Imaging studies aided in excluding infectious sources, ultimately shifting the diagnosis from presumed sepsis to* ***hypercalcemia crisis****. The patient's clinical condition improved significantly following aggressive intravenous hydration, calcitonin, bisphosphonates, and correction of electrolyte imbalances, confirming hypercalcemia as the primary pathology. This case reinforces that* ***hypercalcemia can clinically masquerade as sepsis****, sharing features such as tachycardia, hypotension, fever, leukocytosis, and acute kidney injury. Misdiagnosis may lead to delayed or inappropriate interventions, including unnecessary antibiotics. Early identification of hypercalcemia requires maintaining a high index of suspicion, particularly when sepsis-like symptoms persist despite adequate antimicrobial therapy. Routine electrolyte screening, renal profiling, and evaluation of parathyroid hormone levels are essential in such scenarios. This study emphasizes the critical need for clinicians to consider metabolic abnormalities as potential sepsis mimickers, thereby avoiding misdiagnosis and guiding appropriate treatment.*
Keywords: ***Hypercalcemia, Sepsis mimicker, Metabolic emergency, Calcium crisis, Diagnostic challenge***

Introduction:

Hypercalcemia is a relatively common metabolic abnormality encountered in clinical practice, most frequently caused by **primary hyperparathyroidism** and **malignancy** (1). Despite its prevalence, hypercalcemia can present with diverse and often non-specific symptoms, making diagnosis challenging, especially in emergency settings. Severe hypercalcemia, if untreated, may progress to a life-threatening state termed **hypercalcemic crisis**, which may imitate other serious systemic illnesses including sepsis, systemic inflammatory response syndrome, and dehydration-related shock (2). The overlapping clinical features between hypercalcemia and sepsis make differentiation difficult. Symptoms of hypercalcemia such as fever, tachycardia, hypotension, anorexia, nausea, vomiting, altered mental status, and renal impairment parallel

many classical presentations of sepsis (3). This creates a complex diagnostic picture and may lead to early misclassification as an infectious process. Studies have documented that sepsis-like presentations of hypercalcemia frequently result in excessive or prolonged use of antibiotics until metabolic evaluations reveal the underlying pathology (4). Additionally, hypercalcemia may cause leukocytosis and elevated inflammatory markers such as CRP, further mimicking systemic infection (5). In resource-limited settings or busy emergency departments, where rapid decisions are necessary, metabolic disorders like hypercalcemia may be overlooked. Malignancies, especially solid tumors with bone metastasis, hematological malignancies, and parathyroid abnormalities often present with severe hypercalcemia (6). Hypercalcemia-induced dehydration causes prerenal azotemia and contributes to clinical deterioration, sometimes fulfilling criteria for septic shock (7). Although rare, **hypercalcemia presenting as a sepsis look-alike is a recognized but under-reported clinical phenomenon** (8). Early recognition is essential because the management of hypercalcemia differs significantly from that of sepsis. Hypercalcemia requires prompt **aggressive hydration, diuretics, calcitonin, bisphosphonates, and identification of the causative pathology**, while sepsis necessitates antimicrobials, source control, and hemodynamic support (9). Delay in identifying hypercalcemia can worsen renal injury, prolong hospitalization, and increase morbidity. This study aimed to describe a case where hypercalcemia closely resembled sepsis, discuss the diagnostic challenges, examine overlapping clinical features, and highlight the significance of maintaining differential diagnoses when evaluating patients with sepsis-like presentations.

Materials and Methods：

This observational case-based study was conducted in the Department of Internal Medicine, RAMA Medical College Hospital and Research Centre, Pilkhuwa, Hapur, from 22 December 2023 to 27 May 2024. The study focused on a patient presenting with high-grade fever, tachycardia, hypotension, dehydration, and altered mental status, features that initially raised suspicion for sepsis. Ethical approval was obtained prior to data review. A structured protocol was followed for patient evaluation. Upon admission, routine blood investigations including complete blood count, serum electrolytes, renal function tests, liver function tests, inflammatory markers (CRP, ESR, procalcitonin), arterial blood gas analysis, urinalysis, and blood cultures were conducted. Radiological imaging included chest X-ray and abdominal ultrasonography to search for any infectious source. The initial working diagnosis was sepsis of unknown origin, and broad-spectrum intravenous antibiotics were initiated according to hospital guidelines. Despite 48 hours of treatment, the patient's symptoms persisted with worsening dehydration and rising serum creatinine. This non-responsiveness prompted expanded metabolic evaluation. Serum calcium was measured, revealing a markedly elevated level (>14 mg/dL), suggestive of severe hypercalcemia. Additional evaluations included serum ionized calcium, parathyroid hormone, 25-hydroxy vitamin D, 1,25-dihydroxy vitamin D, serum phosphate, and alkaline phosphatase. Electrocardiography was performed to detect hypercalcemia-associated conduction abnormalities. Clinical correlation with metabolic results indicated hypercalcemia as the primary cause of the patient's deteriorating condition. The patient was then shifted from sepsis protocol to hypercalcemia management protocol. Treatment included aggressive intravenous hydration with isotonic saline, intravenous calcitonin for rapid reduction of calcium levels, and bisphosphonates for sustained control.

Renal function was closely monitored, and diuretics were cautiously used after adequate hydration. Daily serum calcium levels were measured for monitoring therapeutic response. Blood and urine cultures eventually returned negative, ruling out infection. Imaging studies showed no abnormalities consistent with infectious pathology. Detailed evaluation for malignancy was initiated, including CT scans and serum tumor markers, according to standard hypercalcemia evaluation algorithms (10). Follow-up assessments showed progressive improvement in mental status, stabilization of blood pressure, reduction in heart rate, and gradual recovery of renal function. The patient responded well to therapy, confirming severe hypercalcemia as the primary diagnosis.

Results:

The patient initially presented with symptoms strongly suggestive of sepsis: fever (101°F), tachycardia (128 bpm), hypotension (90/60 mmHg), dehydration, and altered mental status. Laboratory findings included leukocytosis, elevated CRP, and mild metabolic alkalosis. Initial renal parameters suggested prerenal acute kidney injury. Antibiotic therapy was initiated but yielded no clinical improvement. Subsequent metabolic testing revealed significantly elevated serum calcium (>14 mg/dL) with suppressed parathyroid hormone levels, confirming non-parathyroid hypercalcemia. Ionized calcium levels were markedly high, and renal impairment was attributed to dehydration from hypercalcemia-induced polyuria. All infectious workup including blood cultures was negative. Imaging studies revealed no sepsis source. After hydration, calcitonin, and bisphosphonate therapy, the patient demonstrated rapid clinical improvement, confirming hypercalcemia as the true underlying cause of the sepsis-like presentation.

Discussion:

Hypercalcemia can present with symptoms resembling sepsis, causing diagnostic confusion and leading to unnecessary or prolonged antibiotic therapy (4,5). Shared clinical features such as fever, tachycardia, hypotension, renal impairment, and leukocytosis create a misleading clinical picture. This case emphasizes the importance of considering metabolic disturbances like **hypercalcemia crisis** when sepsis treatment fails to produce improvement. Early calcium testing in sepsis-like conditions can help avoid misdiagnosis and improve patient outcomes.

Conclusion:

This study highlights a rare but clinically important presentation of hypercalcemia mimicking sepsis. The case demonstrates that hypercalcemia can produce systemic manifestations that strongly resemble infectious processes. Persistent symptoms despite antibiotics should prompt metabolic evaluation, particularly serum calcium testing. Early recognition and timely management with hydration, calcitonin, and bisphosphonates can prevent complications and reduce morbidity.

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