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Digoxin Toxicity with Nonspecific Symptoms in an Elderly Dialysis Patient: A Diagnostic Challenge in the Emergency Department

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Abstract

Digoxin toxicity is often difficult to recognize in elderly patients with renal failure because symptoms are vague and frequently overlap with common acute conditions. We describe an 81-year-old woman on chronic haemodialysis who presented with progressive asthenia, psychomotor slowing, fever, and altered mental status, initially suggesting sepsis. Laboratory tests showed mild hyperkalemia and metabolic acidosis, while imaging and cultures revealed no acute findings. Incomplete medication history delayed suspicion, but markedly elevated serum digoxin levels (>5 ng/mL) confirmed toxicity. Administration of digoxin-specific antibody fragments followed by haemodialysis led to progressive clinical improvement. This case highlights the need to consider digoxin toxicity in high-risk patients with nonspecific symptoms and emphasizes the importance of early recognition and antidote therapy to prevent severe complications.

Keywords: Acute Digoxin Intoxication; Renal Failure-Associated Drug Accumulation; Haemodialysis Patient Presentation; Altered Mental Status in Digitalis Toxicity; Digoxin-Fab Antibody Therapy; Diagnostic Pitfalls in Elderly Patients.

Introduction

Digoxin remains in use for the management of atrial fibrillation and heart failure, but its narrow therapeutic index and complex pharmacokinetics make toxicity a persistent clinical problem, particularly in the emergency setting.[1–3] Chronic digoxin intoxication is now more frequent than acute overdose and typically develops insidiously in patients with multiple comorbidities, polypharmacy, and fluctuating renal function [1,4]. Clinical manifestations are often nonspecific and may include gastrointestinal, neurological, visual, and cardiovascular symptoms, while electrocardiographic changes and arrhythmias, although common, are not pathognomonic [1-3]. As highlighted by recent consensus recommendations, the diagnosis of digoxin toxicity is therefore based primarily on clinical suspicion, supported but not definitively ruled in or out-by serum digoxin levels, which do not consistently correlate with the severity of poisoning [1,2].

Elderly patients with chronic kidney disease (CKD) represent a particularly vulnerable population. Reduced renal clearance, age-related changes in volume of distribution, and frequent drug-drug interactions markedly increase the risk of digoxin accumulation and toxicity, even at conventional doses [1,4-6].

Population-based studies in older adults with CKD have shown that higher starting doses are associated with an increased risk of hospital admission for digoxin toxicity, reinforcing the need for cautious dosing and close monitoring in this group [4,5]. Case-based literature further illustrates how digoxin intoxication may be overlooked or misattributed in frail, multimorbid patients,

especially when they present with vague constitutional symptoms or altered mental status [6].

Risk is further amplified in patients on chronic hemodialysis, in whom digoxin elimination is substantially reduced and dialysis itself does not effectively remove the drug [1,7]. Several case reports describe haemodialysis patients presenting to the emergency department with nonspecific symptoms such as confusion, weakness, or presumed sepsis, in whom digoxin toxicity was only recognized after a detailed medication review or measurement of serum level [7,8]. In this context, early recognition of potentially life-threatening features such as significant hyperkalemia, high-grade atrioventricular block, or malignant ventricular arrhythmias is crucial, as international consensus identifies prompt administration of digoxin-specific antibody fragments as the mainstay of therapy [1,3,9,10]. Real-world registry data confirm that DigiFab® is highly effective and generally safe in reversing severe digoxin toxicity, although its use may still be under-recognized or delayed in clinical practice [9,10].

Against this background, we report the case of an elderly hemodialysis patient presenting to the emergency department with fever, altered mental status, and nonspecific symptoms, in whom digoxin toxicity represented an important and initially unsuspected diagnostic challenge.

Case Presentation

An 81-year-old woman with a past medical history significant for chronic heart failure, permanent atrial fibrillation, iatrogenic hypothyroidism, and end-stage renal disease on thrice-weekly hemodialysis, was brought to the emergency department (ED) due to a progressive decline in her general condition. Over the preceding three to four weeks, according to her relatives, she had experienced increasing asthenia, fluctuating confusion, and intermittent disturbances in visual fields described as “dark areas” and difficulty focusing. She had undergone an ophthalmologic examination during this period, which did not reveal structural ocular abnormalities, and the symptoms were initially attributed to fatigue or age-related visual changes.

In the 48 hours prior to admission, her condition worsened, with marked psychomotor slowing, reduced oral intake, and increasing somnolence. On arrival at the ED, she appeared soporous and minimally responsive, with a Glasgow Coma Scale score of 12 (E3V4M5). Vital signs were heart rate 95 bpm with irregular rhythm, respiratory rate 14/min, blood pressure 100/50 mmHg, temperature 38.5 °C, and oxygen saturation 98% on room air. Physical examination revealed no focal neurological deficits, no signs of trauma, and no overt signs of infection such as skin or soft-tissue abnormalities.

Initial laboratory tests demonstrated neutrophilia, anemia (hemoglobin 9 g/dL), mild hyperkalemia (5.59 mEq/L), metabolic acidosis (pH 7.31), elevated lactate (4.5 mmol/L), and creatinine 3.7 mg/dL, consistent with her baseline renal failure. Given the presence of fever, altered mental status, and metabolic derangements, a working diagnosis of possible sepsis was considered. Blood cultures, urinalysis, and procalcitonin were obtained, and the patient underwent total-body computed tomography, which showed no acute or focal infectious source.

Electrocardiography revealed atrial fibrillation with controlled ventricular response and nonspecific ST-T abnormalities without features typical of acute ischemia or digoxin effect. Supportive management with intravenous fluids and broad-spectrum antibiotics was initiated, resulting in only partial and transient improvement of her mental status.

During reassessment in the ED, attention was directed to her chronic therapy. Because the medication history provided by relatives was initially incomplete and the patient was unable to provide reliable information, the exact dosage and adherence to home medications-including digoxin-were initially unclear. Once her medication list was recovered, it became evident that she had been receiving digoxin despite advanced renal dysfunction and recent fluctuations in dialysis scheduling due to logistical issues.

Given the persistence of nonspecific symptoms, the absence of an identifiable infectious source, the presence of visual disturbances preceding admission, and her high baseline risk for drug accumulation, a serum digoxin concentration was obtained several hours after ED arrival. Results showed markedly elevated levels, exceeding 5 ng/mL, strongly suggestive of significant digitalis toxicity.

In light of the clinical presentation and laboratory findings, the patient was treated promptly with digoxin-specific antibody fragments (DigiFab®). Haemodialysis was subsequently performed to address metabolic derangements and support clinical stabilization. Over the following hours and days, she demonstrated a gradual improvement in mental status, regression of visual disturbances, and resolution of constitutional symptoms. She was admitted to the emergency medicine ward for continued monitoring, where she achieved progressive recovery without arrhythmic complications.

Discussion

Digoxin toxicity remains a challenging diagnosis, particularly in elderly patients with multiple comorbidities and impaired renal function. Although the overall use of digoxin has declined with the advent of alternative therapies for heart failure and atrial fibrillation, toxicity continues to be encountered in clinical practice and is often under-recognized in acute settings [1-3,11,15]. The narrow therapeutic index, dependence on renal clearance, and frequent

drug–drug interactions make older adults especially vulnerable to both chronic and acute-on-chronic intoxication [1-3,11].

In our patient, the combination of fever, altered mental status, metabolic acidosis and elevated lactate initially suggested sepsis or metabolic decompensation, in line with common differential diagnoses in frail dialysis patients. Similar to previously reported cases, digitalis toxicity presented with nonspecific neurological and constitutional symptoms, leading to an initial work-up for infection, stroke or metabolic encephalopathy rather than for drug intoxication [4,6-8,14]. Prodromal visual disturbances, as reported over the weeks preceding admission, are consistent with known but often overlooked manifestations of digoxin toxicity and may precede more evident cardiovascular signs [1,2,6].

Chronic kidney disease (CKD) is a key determinant of risk. Reduced renal clearance and altered volume of distribution significantly increase the probability of digoxin accumulation even at doses traditionally considered "safe" [1,4-6,12,13]. A large population-based study in older adults with CKD showed that prescribing >0.125 mg/day was associated with a higher 90-day risk of hospital admission for digoxin toxicity compared with ≤0.125 mg/day, underscoring the need for cautious dosing and close monitoring in this group[12]. Pharmacokinetic modelling in older patients with heart failure and CKD further supports the need for individualized lower dosing strategies to avoid overexposure [13].

In hemodialysis patients, like our case, the situation is even more complex. Conventional haemodialysis and peritoneal dialysis are ineffective in removing digoxin, so small changes in dosing, adherence or intercurrent illness can precipitate toxicity [1,7,8,14,17]. Case reports of symptomatic digoxin toxicity in chronic haemodialysis patients describe very similar scenarios: progressive weakness, confusion or visual complaints, often initially attributed to infection or uremia, with toxicity only recognized after targeted measurement of serum levels [7,8,14,17].

Our case also highlights the central importance of an accurate medication history. Incompleteness of the drug list delayed suspicion, as frequently reported in older, cognitively impaired or dependent patients [6,11]. Consensus recommendations now explicitly emphasize early verification of digitalis use, especially in any high-risk patient presenting with unexplained neurological, gastrointestinal or cardiac symptoms [11].

Although serum digoxin concentrations do not correlate perfectly with clinical severity, markedly elevated levels strongly support the diagnosis when combined with a compatible clinical picture [1,2,11]. In our patient, levels >5 ng/mL, together with the chronic course and absence of alternative explanations, were highly suggestive of significant digitalis excess. Recent narrative reviews and consensus statements reaffirm that management decisions must be primarily clinical, and treatment with digoxin-specific antibody fragments should not be delayed while waiting for confirmatory levels in potentially life-threatening situations [1-3,11].

The administration of digoxin-specific Fab fragments remains the cornerstone of therapy for severe toxicity and has been associated with rapid reversal of dysrhythmias, improved hemodynamic and reduced mortality [3,9,10,11]. However, their use in patients with advanced renal failure raises specific issues. Because Fab-digoxin complexes are cleared renally, their elimination is significantly delayed in haemodialysis patients, with potential for rebound in free digoxin levels once equilibrium shifts [17]. Case reports describe the use of plasmapheresis in conjunction with Fab fragments to enhance removal of these complexes and prevent recurrent toxicity in patients with severely impaired renal function [17].

Traditionally, intermittent haemodialysis has been considered ineffective for digoxin removal; however, isolated reports suggest that continuous venovenous haemodialysis (CVVHD) may contribute to gradual reduction in serum digoxin levels in selected critically ill patients with acute kidney injury, particularly when Fab is unavailable [15]. In our case, haemodialysis was employed primarily for metabolic control and volume management rather than as a specific detoxification strategy, but it likely contributed to overall stabilization in the context of Fab therapy.

Recent registry data have clarified the prognostic impact of digoxin poisoning. In a large multicentre cohort, 7-day mortality was approximately 4-5%, rising to around 11% at 30 days, with higher risk among very elderly, dependent patients and those with cardiovascular or neurological manifestations at presentation [10,16].These findings reinforce that digitalis toxicity in older dialysis patients, such as the woman described here, is far from benign and warrants prompt recognition and aggressive management.

Taken together, our case underscores several key points:

1. High index of suspicion for digoxin toxicity is required in elderly CKD or hemodialysis patients presenting with subacute, nonspecific neurological or visual symptoms.

2. Medication reconciliation is crucial; incomplete drug histories are a frequent and avoidable cause of diagnostic delay.

3. Timely administration of digoxin-specific Fab fragments, guided by clinical severity rather than by levels alone, is essential to improve outcomes.

4. In patients with advanced renal dysfunction, careful post-Fab monitoring and, in selected cases, consideration of extracorporeal strategies such as CVVHD or plasmapheresis may be warranted to prevent rebound toxicity.

This case therefore adds to the growing body of literature illustrating how digoxin toxicity may masquerade as sepsis or metabolic encephalopathy in high-risk dialysis patients and highlights practical implications for early recognition and management in the emergency department.

Conclusion

This case illustrates the diagnostic complexity of digoxin toxicity in an elderly haemodialysis patient presenting with nonspecific and misleading symptoms. Visual disturbances, altered mental status, and subacute decline should prompt evaluation for digitalis toxicity, particularly in patients with renal impairment. Accurate medication reconciliation and early administration of digoxin-specific Fab fragments are essential for improving outcomes. Given the prognostic implications and potential for rebound toxicity in severe renal dysfunction, careful post-treatment monitoring is warranted.

Declarations

Contributors: All authors contributed to the clinical assessment, data collection, literature review and preparation of the manuscript. All authors have read and approved the final version.

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