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Case Report

# A Case of Proximal Tubulopathy Due to Hyperbilirrubinemia

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## Abstract

Cholemic nephropathy, a rare renal disorder resulting from severe hyperbilirubinemia, poses a unique challenge for clinicians due to its varied manifestations. This condition stems from impaired bilirubin metabolism, often associated with hepatobiliary diseases. Unconjugated bilirubin, elevated in cholemic nephropathy, exerts toxic effects on renal tubular cells, causing acute kidney injury and proximal tubulopathy.

***Keywords:*** *Hyperbilirubinemia, Tubulopathy, Hypokalemia, Hypophosphatemia.*

## Introduction

Cholemic nephropathy, a relatively uncommon yet clinically significant renal disorder, is characterized by renal impairment secondary to severe hyperbilirubinemia. This condition arises from impaired bilirubin metabolism, often due to hepatobiliary diseases such as obstructive jaundice or cholestasis, or massive hemolysis. The elevated levels of unconjugated bilirubin can exert toxic effects on the renal tubular cells, leading to tubular dysfunction and nephropathy. Cholemic nephropathy is marked by a spectrum of renal manifestations, including acute kidney injury, proximal tubulopathy, and disturbances in electrolyte and uric acid homeostasis. The underlying mechanisms

involve the deposition of bilirubin pigment within the renal tubules, contributing to the pathophysiology of this unique renal disorder. As a result, understanding cholemic nephropathy is crucial for clinicians faced with patients exhibiting both hepatic and renal dysfunction. The following case underscores the importance of knowing the association between hyperbilirubinemia and proximal tubulopathy.

## Case Report

A 46-year-old female patient with sickle cell anemia was admitted to the hospital on December 30, 2023, presenting with a one-day history of knee pain. The pain intensified, and stabbing chest pain emerged, continuous, not associated with exertion, and unresponsive to rest. She denied fever, cough, or shortness of breath, despite the pain. The admission chest CT showed no abnormalities. Under admission for investigation, she developed fever, jaundice, abdominal pain, a decline in general condition, nausea, and vomiting. Laboratory findings indicated hyperbilirubinemia with a predominance of the direct fraction, dark urine, and kidney disease: improving global outcomes (KDIGO) stage 3 acute kidney injury (AKI), without the need for renal replacement therapy. Abdominal CT revealed a hepatomegaly, without other findings. Empirical treatment with ceftriaxone and metronidazole was initiated. A blood culture on January 1 detected the growth of Salmonella spp, leading to a modification of the antimicrobial regimen to chloramphenicol. The patient experienced weakness, tachycardia, and tachypnea, necessitating oxygen supplementation via nasal cannula. Laboratory tests demonstrated severe anemia due to hemolysis and moderate hypokalemia, prompting a blood transfusion and potassium repletion, and intensive care unit admission. To elucidate the cause of hypokalemia we proceeded to a comprehensive laboratory investigation with urinary and plasma electrolytes, osmolality and proteinuria assessment, due to the possibility of a tubulopathy. The evolution of some of the exams are shown in Table 1. In urinalysis we found out (Table 3.) high TTKG, high potassium to creatinine ratio, high fractional excretion of potassium (1, 2), high uric acid to creatinine ratio, high fractional excretion of phosphorus and high protein to creatinine ratio, denoting renal wasting of these electrolytes despite their low serum level, and the same about uric acid.

**Table 1:** Comprehensive laboratory findings.

| *Urine Sample* | Sample 1 | Sample 2 |
|---|---|---|
| *Glucose (g/L)* | 0 | 0 |
| *Potassium (mEq/L)* | 16 | 15 |
| *Phosphorus (mg/L)* | 167 | < 50 |
| *Sodium (mEq/L)* | 56 | - |
| *Uric Acid (g/L)* | 0,2 | - |
| *Creatinine (g/L)* | 0.26 | 0,29 |
| *Osmolality (mOsm/kg)* | - | 314 |
| *Protein (g/L)* | 0,1 | 0,2 |
| | | |
| *Serum Sample* | Sample 1 | Sample 2 |

| | | |
|---|---|---|
| *Serum Osmolality (mOsm/kg)* | - | 282 |
| *Serum Creatinine (mg/dL)* | 1,0 | 0,73 |
| *Serum Phosphorus (mg/dL)* | 1,9 | 3,5 |
| *Serum Uric Acid (mg/dL)* | 2,9 | 2,1 |
| *Serum Potassium (mEq/L)* | 2,9 | 2,8 |
| *Serum Total Billirubin (mg/dL)* | 37,0 | 8,0 |
| *Serum Uncojugated Billirubin* | 12,3 | 2,0 |
| | | |
| *Renal indexes* | Sample 1 | Sample 2 |
| *Protein/Creatinine ratio (mg/g)* | 384 | 689 |
| *Fractional Uric Acid Excretion* | 26,5% | - |
| *Uric Acid/Creatinine ratio (mg/g)* | 789 (> 600) | - |
| *Fractional Phosphorus Excretion* | 33,81% (> 15%) | - |
| *Fractional Potassium Excretion* | 21.22% (> 9%) | 13.49% (>9%) |
| *TTKG* | - | 4.8 (>4) |
| *Potassium/Creatinine ratio (mEq/g)* | 61,5 (>13) | 51,7 (>13) |

## Conclusion

All the findings described before denotes a proximal tubulopathy. In fact, there is descriptions in the literature of tubulopathy induced by hyperbilirubinemia (3-5). The interesting aspect of our case is that we were able to document the changes in urine that corroborate the proximal tubular dysfunction. Unfortunately, a renal biopsy was not possible in the occasion to confirm the presence of bilirubin casts.

## Approval

- Ethics approval and consent to participate: the patient consent and have signed a consent form.
- Consent for publication: described above.
- Availability of data and material: data is available in the tables described in the article. Further data may be requested as needed by anyone that may be interested.
- Competing interests: no competing interests to declare.

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## Authors' Contributions

Ho Yeh-Li supervised and was responsible for the idealization of the report. Lucas F Theotonio dos Santos wrote the final draft and conducted the research of literature. Julia Figueiredo Petrucci wrote the first draft and helped in the research of literature.

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