

# Bile Cast Nephropathy Caused by Obstructive Pancreatic Carcinoma and Failed ERCP

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## ABSTRACT

Bile cast nephropathy is an often overlooked condition of acute renal injury in the setting of high serum bilirubin. While the exact pathophysiology remains unknown, possible mechanisms of renal injury are tubular obstruction from bile casts, direct toxicity from bile acids, and decreased renal perfusion due to hemodynamic changes. We present a patient with hyperbilirubinemia as a result of common bile duct obstruction due to pancreatic adenocarcinoma who developed anuric acute renal injury. Urine analysis showed bile casts that were highly suggestive for bile cast nephropathy. The patient underwent hemodialysis and bile drainage with full restoration of renal function.

## INTRODUCTION

Bile cast nephropathy is an often overlooked condition of nephrotoxicity associated with hyperbilirubinemia. Although the exact pathophysiological mechanism is unknown, direct toxicity of bile casts to the nephron and tubular obstruction are hypothesized mechanisms.<sup>1</sup> Because of the rarity of the disease, there are no universally applied treatment guidelines, and the prevalence is likely greater than previously recognized.<sup>2</sup>

## CASE REPORT

A 64-year-old white man with a history of well-controlled diabetes mellitus presented with a 4-week history of progressive jaundice, dark-colored urine, and light-colored stools. He reported weight loss of 20 kg in the preceding 5 months. Family history was negative for liver or kidney disease. He reported no alcohol, tobacco, or drug use. On physical examination the patient was jaundiced and alert; no other abnormalities were reported. Abdominal ultrasound (US) revealed intra- and extrahepatic bile duct dilatation, with a common bile duct (CBD) of 16 mm and a hypoechoic lesion in the pancreas. Subsequent computed tomography confirmed these findings, revealing a mass of 34 mm in the pancreatic head suspect for pancreatic carcinoma. The patient was referred to our hospital for a pancreaticoduodenectomy.

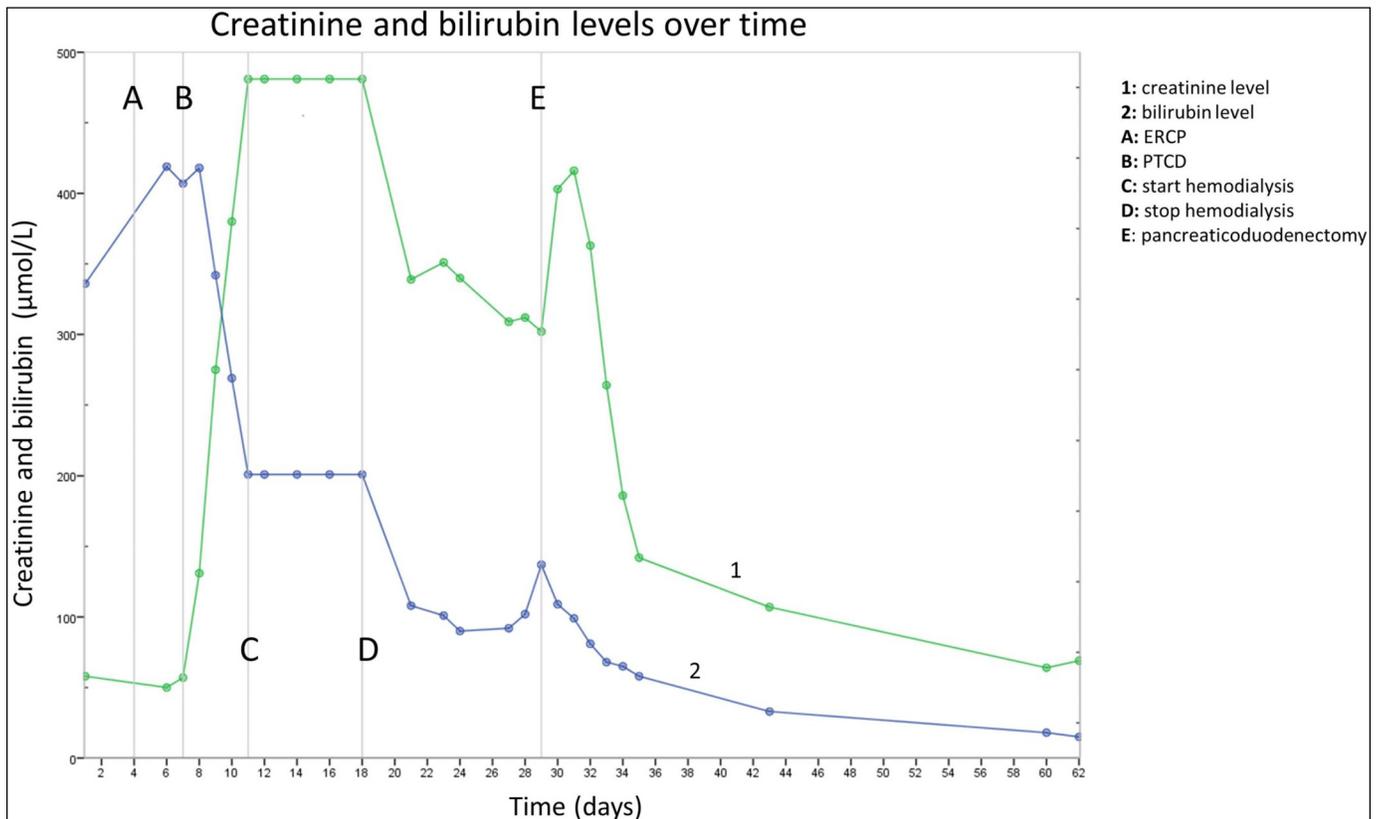
Laboratory results at the time of presentation (day 1) showed total serum bilirubin 336  $\mu\text{mol/L}$ , aspartate aminotransferase 46 U/L, gamma-glutamyltransferase 140 U/L, alkaline phosphatase 446 U/L, sodium 138 mmol/L, potassium 3.7 mmol/L, creatinine 58  $\mu\text{mol/L}$ , and creatinine clearance  $>60$  mL/min. On day 4 after presentation, an endoscopic retrograde cholangiopancreatography (ERCP) visualized a distal stenosis of the CBD. Biopsy and brush of the CBD revealed adenocarcinoma. Due to tumor obstruction, cannulation of the CBD during ERCP was not successful. On day 5, the patient developed cholangitis. Antibiotic therapy with cefuroxime was started, and percutaneous transhepatic bile duct drainage was performed on day 7. The patient received tobramycin once after the drainage procedure for fever and chills. The total bilirubin level at that time was 407  $\mu\text{mol/L}$ . Blood cultures

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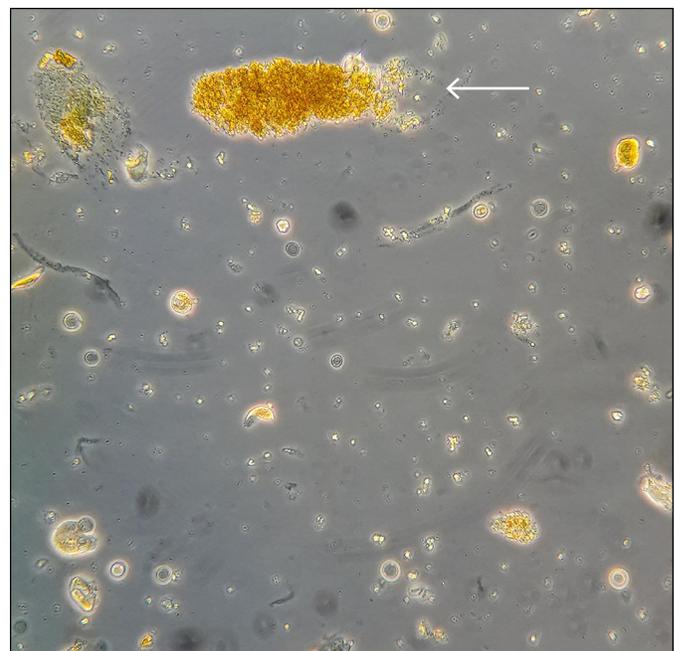
**Figure 1.** Creatinine and bilirubin levels over time.

were positive for *Streptococcus pneumoniae* and *pseudomonas*, so the patient was treated with piperacillin/tazobactam. On day 8, his creatinine level increased (Figure 1). On the same day, a kidney US revealed no abnormalities. In the following days, renal function continued to deteriorate despite adequate fluid therapy. Blood pressure and diuresis were continuously adequate. Urine analysis revealed the presence of bile casts (Figure 2), bile pigments, and a normal percentage of dysmorphic erythrocytes with absence of leukocyte and erythrocyte casts. Having excluded renal and post-renal obstruction, and given the presence of bile casts in the urine, the diagnosis of bile cast nephropathy was made; we refrained from kidney biopsy. The patient underwent hemodialysis on day 11 and on day 19. After a total of five hemodialysis sessions, dialysis was discontinued because renal function had improved and the bilirubin level was declining (Figure 1). Pancreaticoduodenectomy was performed on day 28, and histopathology showed adenocarcinoma with clear margins. Renal function improved to normal within 3 months after hospital admission.

## DISCUSSION

Bile cast nephropathy is an often overlooked condition in which hyperbilirubinemia leads to acute renal injury. While the exact pathophysiologic mechanism of renal injury remains

unknown, several underlying factors may contribute.<sup>2,3</sup> Deposition of bile casts in the nephron, leading to tubular obstruction, is one possible mechanism.<sup>4</sup> The bile acid-



**Figure 2.** Urine analysis with the presence of a bile cast (arrow).

binding capacity of albumin is estimated to be in the range of 20 mg/dL. If albumin exceeds this level, bilirubin can accumulate, leading to cast formation and tubular obstruction.<sup>2,4-6</sup> Direct oxidative damage of renal tubular epithelial cell membranes is another proposed mechanism of renal injury. This is caused by the stimulation of oxygen-free radical production by excess bile acids.<sup>2,7-10</sup> In addition, sulfated bile salts inhibit the Na-H, Na-K, and Na-C pumps in the proximal tubules and in the loop of Henle, resulting in impaired cellular pH regulation and tubular injury.<sup>2,6,9,11</sup> Finally, bile salts have negative chronotropic and ionotropic effects. Peripheral vascular resistance is altered due to endotoxemia, hypoalbuminemia, and other mechanisms, all of which contribute to decreased renal perfusion.<sup>2,5,6</sup>

In our case, a pre-renal cause of acute kidney injury was unlikely because the patient was never hypotensive, and diuresis was adequate during his hospital stay. A post-renal cause of acute kidney injury was excluded because a kidney US revealed no hydronephrosis. The lack of proteinuria and no increased dysmorphic erythrocytes made glomerulonephritis less likely. Medications, including tobramycin, are known to cause tubulointerstitial nephritis. While this possibility cannot be completely ruled out, the patient had only one dose of tobramycin, and the urinary analysis lacked the characteristic leukocyte and erythrocyte casts. The improvement of renal function after the clearance of hyperbilirubinemia further supports the diagnosis of bile cast nephropathy. While kidney biopsy is the gold standard in the diagnosis of bile cast nephropathy, we refrained from this procedure because we were sufficiently confident of our diagnosis, and renal biopsy is associated with a small but clinically relevant risk of complications.

Currently, there are no accepted treatment guidelines for bile cast nephropathy, but reduction of bilirubin levels is essential. This can be achieved by relief of biliary obstruction, hemodialysis, or plasmapheresis.<sup>2</sup> It has been hypothesized that early reduction of bilirubin levels is most effective because extensive bile cast formation can delay recovery of renal function.<sup>1,4</sup> This may have been the case with our patient. While bilirubin had already started trending downward, creatinine levels were still high (Figure 1). Furthermore, bile sequestrants, such as cholestyramine and ursodeoxycholic acid, are less effective.<sup>6</sup>

Early recognition and treatment aimed at relieving the hyperbilirubinemia are key to preventing lasting kidney damage. Bile cast nephropathy is an under-reported diagnosis and should be considered in all patients with hyperbilirubinemia and kidney injury.

## DISCLOSURES

Author contributions: SEM van de Ven wrote and revised the manuscript. KV Pavlov, JJ Beutler, and RCH Scheffer revised the manuscript. RCH Scheffer is the article guarantor.

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Informed consent was obtained for this case report.

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