E-ISSN: 2708-1508
P-ISSN: 2708-1494
Impact Factor (RJIF): 5.39
IJCRS 2025; 7(2): 264-268
www.casereportsofsurgery.com
Received: 21-07-2025
Accepted: 25-08-2025

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Acute Gangrenous Appendicitis Following Recent Laparoscopic Cholecystectomy: A Rare Postoperative Diagnostic Challenge

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DOI: https://www.doi.org/10.22271/27081494.2025.v7.i2d.230

Abstract
Acute appendicitis developing shortly after an elective laparoscopic cholecystectomy is an exceedingly rare clinical occurrence and poses a significant diagnostic challenge. Postoperative right upper or right-sided abdominal pain is often attributed to biliary complications such as bile leak, retained ductal stones, or subhepatic collections, making appendicitis a less likely consideration. The overlap of symptoms between postcholecystectomy syndrome and acute appendicitis further complicates timely recognition.
Hyperbilirubinemia has recently been recognized as a reliable biochemical marker for complicated appendicitis, particularly in gangrenous or perforated cases, due to endotoxin-mediated hepatocellular dysfunction. We present a case of acute gangrenous appendicitis occurring one week after an uneventful laparoscopic cholecystectomy, highlighting the diagnostic difficulties in differentiating biliary from appendiceal pathology in the early postoperative period. The case underscores the importance of maintaining a broad differential diagnosis and considering appendicitis even in patients with recent abdominal surgery presenting with atypical right-sided pain and elevated bilirubin levels.

Keywords: Acute Gangrenous Appendicitis; Laparoscopic Cholecystectomy; Postoperative Complications; Hyperbilirubinemia

Introduction
Appendectomy and laparoscopic cholecystectomy are among the most commonly performed emergency and elective surgical procedures worldwide. The coexistence or sequential occurrence of these two pathologies is well documented; however, the development of acute appendicitis shortly after an elective cholecystectomy is exceptionally rare. Most postoperative abdominal pain within days following laparoscopic cholecystectomy is typically attributed to complications such as bile leakage, retained common bile duct stones, abscess formation, or port-site infections. The possibility of a new-onset intra-abdominal inflammatory process unrelated to the biliary system, such as acute appendicitis, is seldom considered and therefore often overlooked.
This diagnostic pitfall is further amplified by the clinical overlap between postcholecystectomy syndrome and early appendicitis. Patients may present with nonspecific right-sided abdominal pain, nausea, and low-grade fever—symptoms that can easily be misinterpreted as residual biliary irritation, bile duct spasm, or subhepatic abscess formation. Both conditions may show mild to moderate elevations in inflammatory markers and hepatic enzymes, leading to further diagnostic ambiguity. Radiologic imaging becomes indispensable in such scenarios to avoid unnecessary delays in diagnosis and management.
A particularly relevant laboratory clue in such cases is hyperbilirubinemia, which has emerged as a reliable biochemical marker of complicated appendicitis. Several studies have demonstrated that elevated total bilirubin levels correlate strongly with gangrenous or perforated appendicitis [1]. The proposed mechanism involves endotoxemia caused by Gram-negative bacteria, primarily *Escherichia coli* and *Klebsiella spp.*, which release lipopolysaccharide (LPS) endotoxins into the circulation. These endotoxins impair hepatocellular uptake and canalicular excretion of bilirubin, leading to intrahepatic cholestasis [2]. Thus, hyperbilirubinemia may serve as an early and sensitive indicator of complicated infection, even before radiologic signs of perforation become apparent.
The combination of recent biliary surgery, nonspecific right-sided abdominal pain, and

hyperbilirubinemia may therefore create a diagnostic paradox. Surgeons and clinicians may instinctively attribute these findings to residual or recurrent biliary pathology rather than a new, distinct intra-abdominal process. This overlap underscores the importance of maintaining a broad differential diagnosis and considering acute appendicitis even in the early postoperative period following laparoscopic cholecystectomy.

In this report, we present a rare case of acute gangrenous appendicitis occurring one week after an uncomplicated laparoscopic cholecystectomy, emphasizing the diagnostic challenges related to symptom overlap, laboratory findings, and the potential role of hyperbilirubinemia as a biochemical marker of complicated disease. Early recognition and timely surgical intervention are crucial to prevent morbidity in such atypical postoperative presentations.

Case Presentation

A 39-year-old woman was admitted for elective laparoscopic cholecystectomy due to ultrasound-confirmed gallstone disease. Preoperative clinical and laboratory evaluations were unremarkable. A standard four-port laparoscopic cholecystectomy was performed according to the American technique. The critical view of safety was established, and Calot's triangle structures were securely clipped and divided. The procedure was uneventful, and the patient was discharged 24 hours postoperatively.

On postoperative day 6, she presented with acute abdominal pain. The pain had begun two days earlier in the epigastrium and migrated to the right lower quadrant. She reported loss of appetite, nausea, vomiting, and fever up to 38°C. On examination, she had marked tenderness in the right iliac fossa with rebound and guarding.

Laboratory tests revealed:

- WBC: 17.7 × 10^9/L
- NLR: 12.2
- CRP: 100.75 mg/L
- Total bilirubin: 38.7 μmol/L

Given her recent cholecystectomy, ultrasound and contrast-enhanced CT were performed to rule out biliary complications. Imaging excluded fluid collection in the gallbladder bed and biliary dilatation but showed a thickened appendix with luminal obstruction and pelvic fluid.

Emergency appendectomy was indicated. Intraoperatively, the appendix appeared gangrenous with perforation. The specimen measured 9.5 × 1 cm with mesoappendix up to 1.5 cm. The serosa was dull with fibrinopurulent deposits. The lumen was dilated and filled with hemorrhagic coprolithic material.

Histopathology confirmed acute gangrenous appendicitis with transmural necrosis, fibrinopurulent periappendicitis, and reactive lymphoid follicles. [Fig 1-2.] Microbiological cultures from the appendiceal lumen yielded *Pseudomonas aeruginosa*, *Klebsiella pneumoniae ssp. pneumoniae*, and *ESBL-positive Escherichia coli*.

The postoperative course was uneventful, and the patient was discharged in good condition.

Discussion

The present case emphasizes the complex interplay between microbial ecology, host response, and therapeutic intervention in the development of complicated appendicitis following laparoscopic cholecystectomy. Postoperative abdominal pain in such a setting is easily misattributed to biliary pathology; however, the timing and biochemical findings in this patient—especially the presence of hyperbilirubinemia—highlighted a systemic inflammatory process consistent with complicated appendicitis rather than biliary dysfunction.

Timing of Appendectomy and Diagnostic Considerations: The early postoperative period following cholecystectomy represents a diagnostic blind spot, as abdominal discomfort and laboratory abnormalities are often interpreted as residual effects of surgery. In this case, right lower quadrant pain developed within days of cholecystectomy, delaying consideration of appendicitis. Such delay is clinically significant: even brief postponement of surgical intervention can allow progression from early inflammation to gangrenous disease. This underscores the need for high clinical suspicion and prompt imaging in postoperative patients presenting with new or shifting abdominal pain, even when recent surgery may confound interpretation.

Microbial Profiles in Complicated Appendicitis: Complicated appendicitis differs microbiologically from its uncomplicated counterpart. While *Escherichia coli* remains the dominant isolate across both forms, complicated disease typically involves polymicrobial infection, incorporating *Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterococcus spp.,* and anaerobes such as *Bacteroides fragili.* These organisms possess diverse virulence factors, including β-lactamase production, biofilm formation, and enhanced endotoxin release potential. The presence of *ESBL-producing Enterobacteriaceae* and multidrug-resistant (MDR) strains correlates strongly with severe inflammation and tissue necrosis [3, 4].

This polymicrobial synergy promotes extensive mucosal invasion, impaired clearance, and increased intraluminal pressure, facilitating bacterial translocation and endotoxin dissemination. In contrast, uncomplicated appendicitis often exhibits a restricted, mono-bacterial flora dominated by *E. coli* with limited virulence potential and self-limiting mucosal involvement.

Endotoxin Release and Systemic Inflammatory Pathways: The pathogenic hallmark of complicated appendicitis lies in lipopolysaccharide (LPS) endotoxin release from Gram-negative bacterial membranes. Under normal conditions, LPS is embedded within the outer membrane and sequestered from host immune recognition. When bacterial integrity is compromised—by immune-mediated killing, ischemia, or antibiotic-induced lysis—large quantities of free LPS are released into the circulation [5, 6].

Once systemic, LPS binds to LPS-binding protein (LBP) and CD14, forming a complex that activates Toll-like receptor 4 (TLR4) on Kupffer cells, hepatocytes, and macrophages. This activation triggers NF-κB–mediated transcription of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), which drive hepatocellular dysfunction, inhibit bilirubin transporters (OATP1B1, OATP1B3, MRP2), and culminate in intrahepatic cholestasis. The resulting hyperbilirubinemia, therefore, reflects not only

hepatocellular stress but also the degree of endotoxemia and systemic immune activation.[Fig 3]

Paradoxical Impact of Preoperative Antibiotics: An important, yet underappreciated, factor in the evolution of complicated appendicitis is the timing and type of antibiotic exposure. β-lactam antibiotics act by disrupting bacterial cell wall synthesis, causing osmotic lysis in susceptible Gram-negative organisms. While bactericidal, this process can paradoxically amplify LPS release before surgical source control is achieved. The resulting surge in endotoxin concentration can transiently exacerbate systemic inflammation—manifesting as fever, tachycardia, and rising bilirubin—even as bacterial counts decline.

In contrast, in infections dominated by MDR or ESBL-producing strains, empiric β-lactam therapy is often ineffective. The bacteria remain intact, resulting in reduced acute LPS release but prolonged low-grade endotoxemia as the infection persists. This dynamic underlies a dual-pathway model of inflammation:

1. Susceptible-pathway appendicitis, where antibiotic-induced bacterial lysis provokes a rapid, endotoxin-driven cytokine storm.
2. Resistant-pathway appendicitis, characterized by chronic inflammation and sustained endotoxin leakage due to ineffective antimicrobial action.

Together, these mechanisms provide a unified framework explaining the paradoxical relationship between preoperative antibiotics, endotoxemia, and hyperbilirubinemia in complicated appendicitis.[Fig 4]

Integrating Pathophysiologic Models (Continuum, Dual-Entity, and Hybrid Perspectives): The evolution of complicated appendicitis has been interpreted through three complementary pathophysiologic frameworks that reflect both clinical observations and modern microbiological insights [7].

1. The Continuum Model: This classical model views appendicitis as a single progressive disease spectrum, beginning with simple catarrhal inflammation and advancing sequentially through suppurative, gangrenous, and eventually perforated stages. Disease severity, in this view, depends primarily on the duration of luminal obstruction and the resulting increase in intraluminal pressure, bacterial overgrowth, and ischemia. Delayed diagnosis or postponed appendectomy is therefore considered the key driver of complications. This model underlies the traditional surgical principle that "time equals progression" in acute appendicitis.
2. The Dual-Entity Model: In contrast, the dual-entity (or *two-pathway*) hypothesis proposes that uncomplicated and complicated appendicitis represent distinct pathophysiologic entities rather than sequential stages of the same process. Uncomplicated appendicitis arises from transient luminal obstruction and is often self-limiting or responsive to conservative antibiotic management. Conversely, complicated appendicitis results from polymicrobial or virulent infections, aggressive local invasion, and exaggerated host inflammatory response—features that are not necessarily preceded by an uncomplicated stage. This model is supported by recent microbiome analyses, which demonstrate distinct bacterial compositions and inflammatory cytokine profiles between uncomplicated and complicated forms.
3. The Hybrid Model: Contemporary evidence favors a hybrid model, integrating both viewpoints. According to this concept, uncomplicated and complicated appendicitis may originate from separate initial pathways, yet the clinical trajectory can overlap. Some uncomplicated cases may progress to complicated disease when factors such as delayed diagnosis, impaired immunity, or prior antibiotic exposure alter bacterial behavior or immune response. At the same time, some patients present de novo with highly virulent polymicrobial infections that bypass early inflammatory stages and manifest immediately as gangrenous or perforated appendicitis.

In essence, the hybrid model reconciles the apparent dichotomy between the continuum and dual-entity theories. It acknowledges that appendicitis is a heterogeneous syndrome—a dynamic interaction between host immunity, microbial virulence, and environmental factors—rather than a single linear disease. This understanding provides a more nuanced framework for interpreting atypical or postoperative presentations, such as the present case, where immune modulation and altered microbiota after recent cholecystectomy likely precipitated rapid evolution to gangrenous appendicitis.

In the context of this case, the rapid onset of gangrenous appendicitis shortly after cholecystectomy supports the hybrid model. The patient likely developed de novo polymicrobial infection facilitated by postoperative immune modulation and antibiotic exposure, producing a fulminant inflammatory response consistent with the dual-pathway concept.

Clinical Implications: From a practical standpoint, the recognition of hyperbilirubinemia as a marker of complicated appendicitis and systemic endotoxemia can aid early diagnosis, particularly in postoperative patients where imaging findings may be confounded.[8] Understanding the microbiological diversity and paradoxical antibiotic effects reinforces the need for prompt surgical intervention and tailored antimicrobial coverage based on local resistance profiles. Furthermore, awareness of these mechanistic pathways underscores the importance of avoiding overreliance on empiric β-lactam therapy without concurrent source control.

Our patient's presentation with right iliac fossa tenderness, elevated inflammatory markers, and hyperbilirubinemia was consistent with complicated appendicitis. Hyperbilirubinemia has been increasingly recognized as a potential marker for complicated appendicitis, possibly due to bacterial endotoxemia and hepatocellular dysfunction.

The diagnostic role of CT in differentiating biliary complications from appendicitis was crucial in this case. While appendicitis after other abdominal surgeries has been reported sporadically, cases after recent laparoscopic cholecystectomy are extremely rare.

Histopathology and microbiological findings confirmed severe infection with multiple enteric pathogens, consistent with perforated gangrenous appendicitis. Prompt surgical intervention led to a favorable outcome.

This case highlights two important clinical lessons:

1. Acute appendicitis should be included in the differential diagnosis of acute abdomen even in the early postoperative period after laparoscopic cholecystectomy.
2. Biomarkers such as CRP, NLR, and bilirubin may help raise suspicion for complicated appendicitis, guiding timely imaging and intervention.

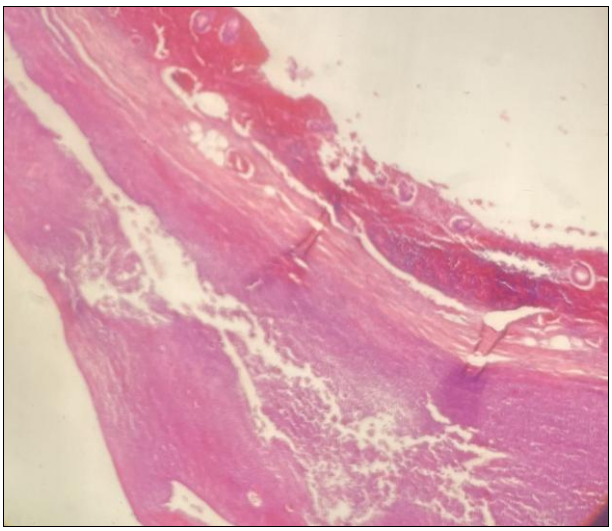

Fig 1: HE x40. Transmural acute inflammation and abscess

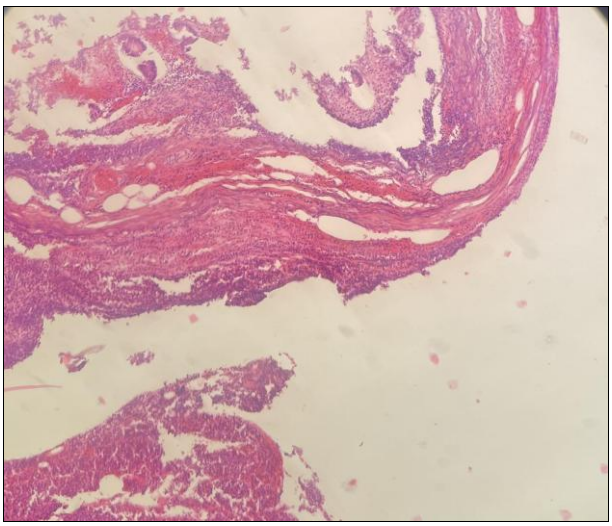

Fig 2: HE x100. Thinned wall with necrosis, hemorrhage and fibrinopurulent exudate

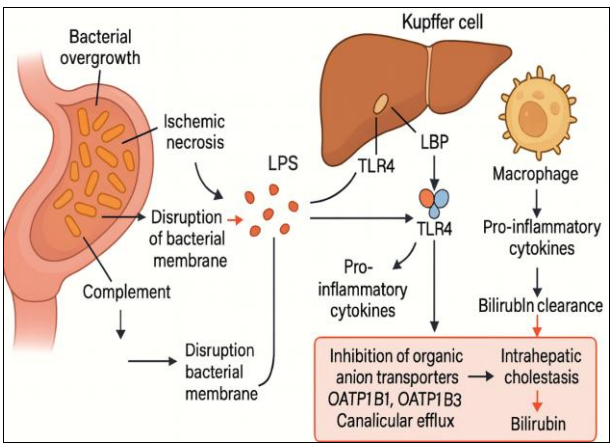

Fig 3: Mechanistic link between bacterial membrane disruption, lipopolysaccharide (LPS) release, and bilirubin metabolism.

Bacterial overgrowth and ischemic necrosis in the inflamed appendix lead to disruption of bacterial membranes through complement activation, releasing LPS into the portal circulation. LPS binds to LPS-binding protein (LBP) and activates Toll-like receptor 4 (TLR4) on Kupffer cells and hepatic macrophages, inducing the release of pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6). These cytokines suppress hepatocellular bilirubin clearance by inhibiting organic anion transporters (OATP1B1, OATP1B3) and canalicular efflux mechanisms, resulting in intrahepatic cholestasis and elevated serum bilirubin levels. This pathway links endotoxemia with hyperbilirubinemia observed in complicated appendicitis.

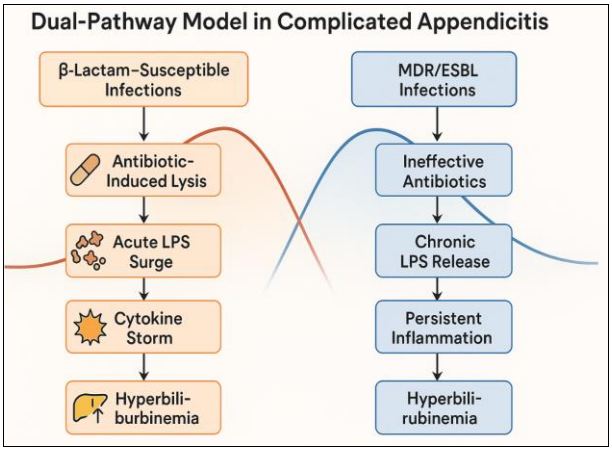

Fig 4: Dual-Pathway Model in Complicated Appendicitis.

Schematic illustration of two distinct but converging mechanisms leading to hyperbilirubinemia in complicated appendicitis

Left pathway (orange): In β-lactam–susceptible infections, antibiotic-induced bacterial lysis triggers an acute surge of lipopolysaccharide (LPS) release, provoking a cytokine storm that disrupts hepatic bilirubin clearance, resulting in acute hyperbilirubinemia.

Right pathway (blue): In multidrug-resistant (MDR) or extended-spectrum β-lactamase (ESBL)–producing infections, ineffective antibiotic action leads to chronic bacterial survival and sustained low-level LPS release. This persistent endotoxemia promotes prolonged inflammation and gradual bilirubin elevation.

Together, these two routes exemplify the dual-pathway model, highlighting how both acute lytic and chronic resistant processes contribute to the systemic inflammatory and cholestatic responses observed in complicated appendicitis.

Conclusion

Acute gangrenous appendicitis occurring shortly after laparoscopic cholecystectomy is rare but should be considered in patients presenting with postoperative acute abdomen. Prompt recognition, appropriate imaging, and timely surgical intervention are essential for preventing morbidity.

Conflict of Interest

Not available

Financial Support

Not available

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How to Cite This Article
Gelevski R, Jota G, Krsteska B, Andreevski V, Trenchikj B, Joksimovikj V. Acute Gangrenous Appendicitis Following Recent Laparoscopic Cholecystectomy: A Rare Postoperative Diagnostic Challenge. International Journal of Case Reports in Surgery. 2025;7(2):264-268.