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YELLOW YELLOW DIRTY FELLOW- APPENDICITIS WITH CHOLESTASIS

General Surgery

Dr. Anil Kumar M.S, Professor, JSS Medical College and Hospital, JSS AHER, Mysore .

Dr. Girish Kumar N.M, Senior Resident, JSS Medical College and Hospital, JSS AHER, Mysore.

Dr. M.Srivats* Postgraduate, JSS Medical College and Hospital, JSS AHER, Mysore . *Corresponding Author

ABSTRACT

Acute Appendicitis, a common cause of acute abdomen, presents a diagnostic challenge when there is an atypical presentation. Awareness regarding peculiar presentations of common diagnosis such as acute appendicitis is paramount given its prevalence in the general population and the preventable nature of the morbidity and mortality associated with a delayed diagnosis. Here, we describe a case of 29 year old male with acute appendicitis and cholestatic jaundice due to sepsis, which resolved spontaneously post-appendectomy.

KEYWORDS

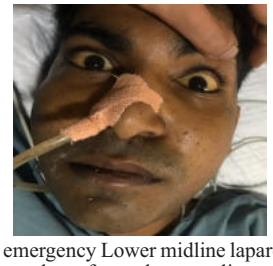
CASE REPORT

A 29 year old non-alcoholic and non-smoker patient presented to the Emergency department with pain abdomen since three days in the right lumbar and umbilical region, sudden onset, pricking type, gradually progressive in nature, non-radiating and associated with 3 episodes of non-bilious, non-blood stained vomitus containing food particles.

Patient gives history of sudden onset, progressive yellowish discoloration of sclera present since 3 days with no associated abdominal distension, discolouration of urine or bowel complaints No reported history of fever, anorexia, nausea, loose stools or constipation or previous episodes of similar complaints.

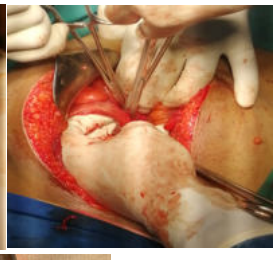
On Examination, Patient had tachycardia and was normotensive. There was deep icterus and no other signs of liver cell failure. Abdominal examination showed Tenderness over right lumbar and right iliac fossa with rebound tenderness and guarding present over right lumbar and iliac fossa, Hepatomegaly with liver span of 15 cm was noted clinically.

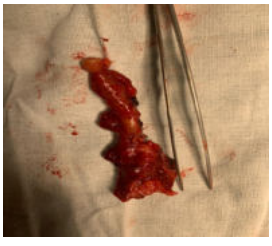
Investigations revealed Leucocytosis (total count: 23720 cells/cumm) with left shift (Neutrophilia: 85%) and peripheral blood smear showing Neutrophilia and toxic granules in neutrophils. Liver Function was deranged with conjugated hyperbilirubinemia with an increased total bilirubin- 9.34mg/dl, direct bilirubin – 7.26mg/dl and elevated alkaline phosphatase of 344 units/ml. Serum gamma glutamyl transferase was elevated (60 units/L) indicating cholestasis possibly induced by sepsis. Ultrasound abdomen showed inflamed appendix with adjacent inflammatory changes and collection of 30cc adjacent to base of appendix suggestive of possible ruptured appendix and abscess formation.



Patient underwent emergency Lower midline laparotomy and proceed in view of suspected perforated appendix causing peritonitis. Intraoperative finding of approximately 50-60cc of pus noted in the right iliac fossa, appendix was retrocaecal in position extending to right lumbar region in the right paracolic gutter plastered to posterior wall of caecum and proximal ascending colon. Rest of the visualised bowel loops were normal. Pus was drained, sent for analysis and elongated inflamed appendix with perforated tip with early mass formation noted in RIF and right lumbar region. Appendicular base was healthy and appendectomy was done and sent for histopathological examination. Gram negative organism Escherichia coli was isolated from the purulent collection and Histopathology of the appendix was reported as acute appendicitis with serositis and periappendicitis with a fecolith. Postoperatively serial Liver function tests showed a drastic spontaneous reduction in bilirubinemia as shown in **table no.1** along with a reduction in total count following source control.

Patient was treated in the post-operative period with IV antibiotics as per pus culture and sensitivity reports, analgesics (NSAID's) and supportive care with intravenous fluids. Patient had no febrile episodes, and repeat value of total leucocyte count on POD4 was 8440 cells/cumm with 62% Neutrophils indicating good sepsis control post-appendectomy and adequate response to treatment. Patient improved symptomatically and recovered well regaining normal bowel function and tolerating normal diet.





DISCUSSION

Cumulative lifetime incidence of acute appendicitis is 7%[1] and mortality quoted variously as 0.17%[2] and 0.08%.[3] Appendiceal perforation is associated with a sharply increased morbidity (4% *vs* 12%[3]) and, subsequently a probable increased mortality although the analysis of such series may be small. There are no published datasets of mortality in appendiceal perforation with culture-positive sepsis, although given the high mortality of sepsis alone, it is suggested that this would further increase morbidity and mortality. Diagnosis of acute appendicitis has been enhanced with evolving diagnostic strategies, such as ultrasound, CT and laparoscopy. Despite these techniques, most helpful diagnostic factors are still clinical and biochemical.[4] Despite the prevalence of appendicitis, sepsis as a cause of cholestatic jaundice continues to be overlooked.[5] Hyperbilirubinaemia may precede positive blood cultures by 1–9 days in more than one-third of patients.[6]

Cholestatic hyperbilirubinaemia and its association with non-hepatic bacterial infection was first noted in 1837, [7] although more formal analysis dates from 1969 in Miller and Irvine's[8] prospective series of appendectomies. In their series, postoperative jaundice was correlated not with the position of the appendix, but rather with peritoneal

cultures positive for *E. coli*. They suggested that the bacterium might be systemically hepatotoxic. In 1840, an ex vivo demonstration by Utili et al.[9] that *E. coli* endotoxin led to a dose-dependent impairment of bile flow, not owing to reduced conjugation, hepatocyte damage or reduced hepatic perfusion. Subsequently, only two, non-English, articles have discussed acute appendicitis as a cause of cholestatic jaundice[10, 11] – *E. coli* again predominated. Cholestasis caused by other Gram-negative and some Gram-positive bacteria, and from other sources such as pneumonia, endocarditis, pyelonephritis, and soft tissue and pelvic abscesses have occasionally been reported, [12] but the literature is dominated by *E. coli* and peritonitis, suggesting that it is *E. coli*, regardless of originating viscus, and hepatic portal drainage, that are the significant factors.

Potential Mechanisms of cholestasis in sepsis, With regards to regulation of host defences against impending or active infections, the liver plays a central role providing a source of inflammatory mediators and is a major site of the removal of bacteria and endotoxins from systemic circulation. [14-15] Kupffer cells (KCs) of the liver make up 80%-90% of the fixed-tissue macrophages of the reticuloendothelial system (RES) take up bacteria, particles, and endotoxins (LPS) and release a variety of products on stimulation that are harmful to liver and cause liver injury, such as tumour necrosis factor, interleukin 1 and interleukin 6, superoxides, lysosomal enzymes, procoagulants, and platelet-activating factor.[15,16-18] Hepatic injury without biliary obstruction may accompany systemic infection in adults with pneumococcal pneumonia, streptococcal bacteraemia, salmonella infections (especially typhoid fever), and *Escherichia coli* bacteremia[20] ranging from mild reactive hepatitis to overt hepatocellular necrosis that usually resolves on appropriate treatment of bacteraemia.

Hepatocellular injury is not considered a frequent occurrence during extrahepatic bacterial infection. Most studies that reviewed liver histology in hyperbilirubinemia or hepatic abnormalities in bacterial infection have noted very mild to no inflammation. [21] The mechanism of hepatic injury depends on the underlying infection, yet most likely there is an unspecified toxin elaborated by the offending bacteria that ultimately leads to hepatocellular injury. [(20,21)]

Various investigations have confirmed the central role of endotoxemia in the genesis of cholestasis associated with sepsis. Direct invasion of the liver by bacteria is not a major cause of cholestasis or hepatic injury in most cases of septicemia. [18] Procoagulants released by activated Kupffer cells induce microvascular thrombosis and have been postulated to cause circulatory disturbance, which, in turn, could contribute to endotoxin induced hepatic injury. [18]

Cholestasis is a known complication of gram-negative bacterial infection, especially in infants. This syndrome is more frequent in the neonatal period and may account for as much as 33% of the cases of neonatal jaundice. [22] *Escherichia coli* is the most common pathogen isolated in most cases of sepsis associated with cholestatic jaundice. [21,23]

Pyelonephritis, peritonitis, appendicitis, diverticulitis, pneumonia, and meningitis are observed to present with jaundice in certain situations. The urinary tract is the most common site of infection associated with this syndrome, especially in the neonatal period. [23] Liver histology shows intrahepatic cholestasis with Kupffer cell hyperplasia and little or no evidence of cellular necrosis. Aside from cholestasis, liver histology reveals an almost normal hepatic parenchyma. [21] The features of the underlying infection usually dominate the presentation. [24] Jaundice and cholestasis are usually reversible and subside completely after resolution of the infection.

In our case, serial liver function tests and marker of infection such as total leucocyte count were found to have reduced spontaneously post appendectomy and source control. By removing the offending agent, the release of endotoxins and its subsequent effects such as cholestasis and associated inflammation were found to have reduced and prompt identification of an unusual presentation of a common condition was done and patient was managed accordingly.

Table No. 1: Comparison of Liver Function Test during the course of hospital stay

Parameter	At Admission	POD -2	POD-4
Total Bilirubin	9.34 mg/dl	4.28 mg/dl	2.59 mg/dl
Direct Bilirubin	7.26 mg/dl	3.39 mg/dl	2.04 mg/dl
SGOT	35 units/L	46 units/L	19 units/L
SGPT	31 units/L	31 units/L	16 units/L
Alkaline Phosphatase	344 units/L	237 units/L	160 units/L

CONCLUSION

Our patient represents an uncommon presentation of a common condition with considerable morbidity. Appendicular perforation with peritonitis and Gram negative sepsis has considerable mortality. It is therefore important that clinicians recognize the association between acute appendicitis and cholestatic jaundice and keep perforated viscus within the differential.

Prompt and appropriate surgical management of the condition with good sepsis control can help in providing adequate symptomatic relief and prevent morbidity and possible mortality in a preventable condition.

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