CLINICAL VIGNETTE

Atypical Presentation of Acute Gangrenous Cholecystitis

Susan D. Leonard, MD

Case Report

An 80-year-old female with history of hypertension, hyperlipidemia, hypothyroidism, and gout, was hospitalized for altered mental status and slurred speech. Evaluation was negative for acute stroke or any other neurologic process. During her hospitalization, she had a rising leukocytosis, eventually up to 27K, but no clear source of infection including negative urine, blood and CSF bacterial and fungal cultures. She had no abdominal pain, fever, nausea, vomiting. She had lost ten pounds over the last year due to change in diet, without anorexia or abdominal discomfort. During the evaluation of leukocytosis, CT abdomen and pelvis unexpectedly showed gangrenous gallbladder with perforated cholecystitis. During this time, she continued to deny any abdominal symptoms, and her main symptom was altered mental status with persistent leukocytosis. She remained afebrile and repeat exam was negative for Murphy's sign. The patient eventually underwent laparoscopic subtotal cholecystectomy. Her slurred speech resolved, dysphagia improved and her diet was advanced to regular. After stabilization in the hospital, she was eventually discharged to a skilled nursing facility for rehabilitation.

Discussion

Acute cholecystitis is characterized by inflammation of the gallbladder. Gangrenous cholecystitis (GC) is a more severe complication of acute cholecystitis, resulting from ductal obstruction, leading to vascular insufficiency, epithelial injury, and increased gallbladder wall tension.[1,2] This advanced form of gallbladder inflammation is associated with high morbidity and mortality.[1,3] Factors that increase risk of gangrenous cholecystitis include male gender, age >45, cardiovascular disease, diabetes and leukocytosis.[3] Some extreme cases may present with negative Murphy's sign due to denervation from the gangrenous injury.[4]

Furthermore, cholecystitis can present atypically, especially in the elderly without any classic symptoms. Geriatric patients are more difficult to evaluate because of increased frailty, co-existing diseases, variability of symptoms, and sometimes a limited ability to provide reliable history.[4,5] The older population also has a higher risk for disease necessitating surgical treatment and complications.[6] There may be no obvious clinical, laboratory, or imaging modality that can definitively diagnose the condition.[4,5]

A review of the literature demonstrated various examples of atypical presentations of cholecystitis. Parker and colleagues performed a retrospective cross-sectional review of emergency room records, chart and surgical operative reports of patients over 65 years, who were determined at surgery to have acute cholecystitis.[7] One-hundred and sixty eight patients' medical records were reviewed and many did not have the classic symptoms, abnormal laboratory or imaging results. Eight patients that presented to the emergency room did not have abdominal pain, ninety-four were afebrile, and sixty-nine had normal white blood cell counts. Although ultrasonography was diagnostic for the majority, eight patients had normal results on imaging studies.[7]

Another series presented eight cases with GC and found half of the patients with abdominal pain and half with nausea and vomiting.[1] Only one patient was febrile and two were hypertensive, but otherwise all remained hemodynamically stable. Six patients had negative Murphy's sign and lack of abdominal symptoms, and only three had leukocytosis and elevated inflammatory markers. The liver function enzymes were within normal range. One unique example included the atypical presentation of gangrenous cholecystitis with the sole complaint of intractable hiccups. The hiccups were caused by sudden diaphragmatic and intercostal muscle contractions following laryngeal closure.[8] Since hiccups have a neurologic reflex comprised of midbrain pathways, the patient with intractable hiccups likely had irritation involving the reflex arc due to gallbladder inflammation.[1,8]These patients with atypical presenting symptoms also lacked specific findings on physical exam and laboratory testing. Furthermore, delayed evaluation and hospital admission were critical criteria for developing GC.[7] Although leukocytosis may not always be present, the higher degree of elevated white blood cell count correlated with the severity of infection. One study showed that a WBC >17K/mm3 was a predictor for progression to GC.[9]

Lastly, imaging is critical in the diagnosis of acute cholecystitis and gangrenous cholecystitis.

Ultrasonography shows heterogeneous or striated thickening in the gallbladder with pericholecystic fluid collections.[10] Intraluminal membranes with desquamative gallbladder mucosa can be specific, but may not be common. CT findings may show gas in the wall or lumen, intraluminal membranes, irregular wall, or pericholecystic abscesses.[10] These examples illustrate

that classic symptoms and objective data for acute cholecystitis may not be present in the geriatric population and heightened awareness is necessary to correctly diagnose the condition.

Conclusion

Acute cholecystitis is a disease process that can lead to severe complications including gangrenous cholecystitis. Diagnosis of GC is challenging especially in the elderly because the atypical symptoms can lead to missed diagnoses, surgical delays, and increased risk for complications, morbidity and mortality. The classic symptoms of abdominal pain and fever may not be present, or may be masked by vague symptoms such as altered mental status, anorexia, or failure to thrive. This case illustrates a unique example of how atypical symptoms presented in a geriatric patient with only mental status changes and worsening leukocytosis. Her symptoms initially seemed more neurologic, but was later attributed to acute gangrenous cholecystitis. The discussion reviews of other case studies illustrating non-classic manifestations of the illness in the older population. In conclusion, increased vigilance for more subtle indicators of acute cholecystitis are necessary, and should prompt further investigation to avoid delays or misdiagnoses of this illness.

REFERENCES

1. **Safa R, Berbari I, Hage S, Dagher GA**. Atypical presentation of gangrenous cholecystitis: A case series. *Am J Emerg Med*. 2018 Nov;36(11):2135.e1-2135.e5. doi: 10.1016/j.ajem.2018.08.039. Epub 2018 Aug 17. Review. PubMed PMID: 30146394.
2. **Önder A, Kapan M, Ülger BV, Oğuz A, Türkoğlu A, Uslukaya Ö**. Gangrenous cholecystitis: mortality and risk factors. *Int Surg*. 2015 Feb;100(2):254-60. doi: 10.9738/INTSURG-D-13-00222.1. PubMed PMID: 25692427; PubMed Central PMCID: PMC4337439.
3. **Girgin S, Gedik E, Taçyildiz IH, Akgün Y, Baç B, Uysal E**. Factors affecting morbidity and mortality in gangrenous cholecystitis. *Acta Chir Belg*. 2006 Sep-Oct;106(5):545-9. PubMed PMID: 17168267.
4. **Dhir T, Schiowitz R**. Old man gallbladder syndrome: Gangrenous cholecystitis in the unsuspected patient population. *Int J Surg Case Rep*. 2015;11:46-49. doi: 10.1016/j.ijscr.2015.03.057. Epub 2015 Apr 18. PubMed PMID: 25917175; PubMed Central PMCID: PMC4446664.
5. **Indar AA, Beckingham IJ**. Acute cholecystitis. *BMJ*. 2002 Sep 21;325(7365):639-43. Review. PubMed PMID: 12242178; PubMed Central PMCID: PMC1124163.
6. **Contini S, Corradi D, Busi N, Alessandri L, Pezzarossa A, Scarpignato C**. Can gangrenous cholecystitis be prevented?: a plea against a "wait and see" attitude. *J Clin Gastroenterol*. 2004 Sep;38(8):710-6. PubMed PMID: 15319657.
7. **Parker LJ, Vukov LF, Wollan PC**. Emergency department evaluation of geriatric patients with acute cholecystitis. *Acad Emerg Med*. 1997 Jan;4(1):51-5. PubMed PMID: 9110012.
8. **Chang FY, Lu CL**. Hiccup: mystery, nature and treatment. *J Neurogastroenterol Motil*. 2012 Apr;18(2):123-30. doi: 10.5056/jnm.2012.18.2.123. Epub 2012 Apr 9. PubMed PMID: 22523721; PubMed Central PMCID: PMC3325297.
9. **Merriam LT, Kanaan SA, Dawes LG, Angelos P, Prystowsky JB, Rege RV, Joehl RJ**. Gangrenous cholecystitis: analysis of risk factors and experience with laparoscopic cholecystectomy. *Surgery*. 1999 Oct;126(4):680-5; discussion 685-6. PubMed PMID: 10520915.
10. **Bennett GL, Rusinek H, Lisi V, Israel GM, Krinsky GA, Slywotzky CM, Megibow A**. CT findings in acute gangrenous cholecystitis. *AJR Am J Roentgenol*. 2002 Feb;178(2):275-81. PubMed PMID: 11804880.