

WebM&M

Morbidity and Mortality Rounds on the Web

Spotlight

A Missed Bowel Perforation – the Importance of Diagnostic Reasoning



Agency for Healthcare Research and Quality
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Source and Credits

- This presentation is based on the September 2023 AHRQ WebM&M Spotlight Case
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 - CME credit is available
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Objectives

At the conclusion of this educational activity, participants should be able to:

- Describe the steps in diagnostic processing.
- Identify strategies to reduce diagnostic errors.
- Define the most current definition of sepsis.
- Explain the importance of early sepsis recognition.
- Formulate differential diagnoses for an acute abdomen.
- Identify factors that place a patient at higher risk for death after abdominal surgery for a bowel perforation.

A MISSED BOWEL PERFORATION – THE IMPORTANCE OF DIAGNOSTIC REASONING

A case highlighting describing how the failure to identify a brewing abdominal process led to fulminant sepsis with rapid clinical deterioration and eventual demise.

Case Details (1)

- A 58-year-old woman admitted to the cardiac unit a few days earlier for volume overload developed tachycardia to 110 bpm and tachypnea to 20 breaths/min overnight, with diarrhea and a mildly distended abdomen.
- Her bedside nurse acknowledged a Sepsis Alert through the electronic health record (EHR), prompting screening for sepsis with a chemistry panel, a complete blood count, a lactic acid level, and blood cultures.
- Within the hour, the results revealed mild leukocytosis ($12,500/\text{mm}^3$), hyponatremia (119 mmol/L), and an elevated lactic acid level of 2.7 mmol/L.
- The nurse contacted the provider on call, who cautiously ordered a 250-milliliter saline bolus, believing that hypoperfusion and hypovolemia from diuresis explained the elevated lactic acid.

Case Details (2)

- A repeat lactic acid level four hours later was 5.1 mmol/L.
- The bedside nurse then called the rapid response team (RRT), which observed a more distended abdomen, but with normal mentation.
- Further workup ensued, including a chest radiograph, repeat blood cultures, and urinalysis.
- The on-call cross-covering provider remained reluctant to consider sepsis and did not evaluate the patient at the bedside. Instead, focused on the history of diuresis, diarrhea, and fluid restriction, they ordered blood products and albumin to increase oncotic pressure and expand intravascular volume.

Case Details (3)

- The following morning, vital signs revealed hypotension to 65/43 mmHg, worsening tachycardia to 131 bpm, and tachypnea to 24 breaths/min.
- The primary team ordered cefepime but was still reluctant to provide aggressive fluid hydration given the patient's clinical history of volume overload.
- The intensive care unit (ICU) team was contacted, but two hours later, the patient developed pulseless cardiac arrest requiring resuscitation and emergency intubation.
- She was then transferred to the ICU, where she was hypothermic to 33.9°C, leukopenic to 2,800/mm³, and anemic with a hemoglobin of 6.4 mg/dL. With continued hypotension and tachycardia, she was diagnosed as having septic shock and disseminated intravascular coagulation (DIC).

Case Details (4)

- Antibiotics were broadened with the addition of vancomycin and metronidazole, and vasopressor support was provided with norepinephrine.
- The acute care surgery team was contacted, but given the patient's instability and grave prognosis, she was deemed not a surgical candidate.
- The family decided to withdraw care and the patient died the following afternoon.
- A few days later, her ascitic fluid cultures grew *Enterococcus fecalis*, *Enterococcus casseliflavus*, yeast, *Bacteroides fragilis*, and anaerobic gram-positive rods, and her autopsy later confirmed perforated bowel.

A MISSED BOWEL PERFORATION – THE IMPORTANCE OF DIAGNOSTIC REASONING

THE COMMENTARY

By Leah Timbang, MD MPH, Voltaire R. Sinigayan, MD,
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BACKGROUND

Background (1)

- This is an unfortunate case describing the failure to identify a brewing abdominal process, which over the span of hours led to fulminant sepsis with rapid clinical deterioration and eventual demise.
- The patient's ascitic fluid cultures and autopsy findings confirmed bowel perforation, but this diagnosis was never explicitly considered.
- It is not entirely clear what happened, but aggressive diuresis with concurrent diarrhea, possibly in the setting of mesenteric ischemia or infectious colitis, could have triggered a perforation.
- Applying root-cause-analysis (RCA) methodology, we can appreciate the complexity of the case and identify provider-level and system-level gaps that led to delayed diagnosis. RCA will guide this commentary with a focus on diagnostic failure, failure to identify and target early sepsis, and then failure to pursue source control with surgical intervention after the source of sepsis was identified.

DIAGNOSTIC FAILURE

Diagnostic Failure (1)

This patient was initially admitted to the cardiac care unit with symptoms suggesting volume overload, presumably heart failure, and this initial diagnosis likely had a powerful impact on the failure to consider alternative diagnoses. Useful frameworks to examine the features and failures in diagnostic processing have been developed, and can be divided into four steps:

1. Hypothesis generation
2. Framing the patient's problem
3. Gathering and processing information, such as findings on the clinical examination and laboratory testing
4. Verifying the diagnosis by making sure that competing hypotheses can be reasonably excluded.¹

Diagnostic Failure (2)

- Cognitive biases can adversely affect the diagnostic process and reflect the use of heuristics, or mental shortcuts, to identify patterns quickly and to facilitate timely decision-making. Over 32 common errors in diagnostic reasoning have been identified, including three that may have operated in this case:
 - the sunk costs phenomenon – *“the more clinicians invest in a particular diagnosis, the less likely they may be to release it and consider alternatives”*;
 - anchoring – *“the tendency to perceptually lock onto salient features in the patient’s initial presentation too early in the diagnostic process, failing to adjust this initial impression in light of later information”*; and
 - confirmation bias - *“the tendency to look for confirming evidence to support a diagnosis rather than look for disconfirming evidence to refute it, despite the latter often being more persuasive and definitive.”*¹
- In this case, **anchoring** on fluid overload or heart failure likely led to neglecting nonconforming data such as diarrhea and a mildly distended abdomen. **Confirmation bias** led to misinterpretation of the patient’s hyponatremia and elevated lactate as evidence of overdiuresis in the setting of heart failure, rather than underlying sepsis. These biases likely contributed to missed opportunities for the on-call clinician to perform a bedside examination when it was warranted.

Diagnostic Failure: The Missing Bedside Examination (1)

- When doctors recall cases in which they missed a diagnosis, they frequently report performing an incomplete bedside examination.²
- This association between faulty bedside assessment and diagnostic error was corroborated in a systematic review of medical malpractice cases, in which failure to perform an adequate history or physical examination contributed to 42% of all missed diagnoses, and to almost 70% of missed cancer diagnoses.²

Diagnostic Failure: The Missing Bedside Examination (2)

- In this case, it is unclear whether findings suggesting a serious underlying abdominal process were missed at admission.
- Did diuresis-induced hypotension cause mesenteric ischemia and perforation, or did inflammatory colitis precipitate volume overload?
 - Indeed, infection has recently been described “as a common, though under-recognized, precipitating factor of acute heart failure.”³
 - Therefore, that this patient may have had a “brewing” abdominal infection at admission that was missed because physicians focused on another acute process (i.e., acute decompensated heart failure).
- There was failure in the fourth step in the diagnostic process, verifying the diagnosis by ruling out competing alternative hypotheses, due to failure to perform a bedside exam when multiple red flags for an “acute abdomen” became apparent: elevated lactate level, hyponatremia, and hypotension.

Diagnostic Failure: The Missing Bedside Examination (3)

- Beyond the cognitive biases outlined above, systems-level factors may also have played a role.
- One particularly common factor is high physician workload.⁴ Questions to consider when analyzing workload:
 - How many patients was the physician covering?
 - Were they also responsible for intensive care patients?
 - Were they at the end of their workweek or workday?
- All these factors can contribute to overwork and affect the diagnostic process.

Diagnostic Failure: The Missing Bedside Examination (4)

- Other organizational and environmental factors that play an important role in diagnostic error include:
 - Reimbursement structures that discourage consultation
 - Incomplete medical records
 - Cultural and language barriers with patients
 - Communication barriers between doctors
 - Lack of back-up in community hospital settings.⁴
- The rapid response nurse was called, but it is unclear whether the patient's worsening abdominal distention was communicated to the physician.
- However, the mere fact that the rapid response team was called should have been perceived as a red flag that warranted in-person assessment by a physician.
 - Indeed, a Japanese study found that delayed diagnosis of gastrointestinal perforations was significantly associated with examination only by non-physician practitioners.⁵

Diagnostic Failure: Reducing Diagnostic Error (1)

- System-level interventions to reduce diagnostic errors may include caps on the number of patients assigned to each physician and nurse, or sequential or concurrent bedside evaluation with the rapid response team.
- Several prospective studies have demonstrated that provider-specific feedback and disease-specific education improve diagnostic accuracy.¹
 - For example, providing emergency department (ED) physicians with intensive, real-time feedback on the outcomes of discharged patients decreased their rate of adverse events.¹
 - A regional program to educate primary care physicians on the clinical presentation of subarachnoid hemorrhage resulted in more timely diagnosis of this life-threatening syndrome.¹
 - Authors have suggested reducing diagnostic errors through a renewed emphasis on teaching the bedside examination, deliberate feedback loops, and debiasing interventions to recognize and avoid using inappropriate heuristics¹

FAILURE TO IDENTIFY AND TARGET EARLY SEPSIS

Failure to Identify and Target Early Sepsis (1)

- Sepsis is the body's overwhelming systemic response to an infection that if left unchecked, can lead to decreased tissue perfusion, organ dysfunction, and eventual death.
- A 1991 consensus conference developed an initial definition that focused on the then-prevailing view that sepsis resulted from a host's systemic inflammatory response syndrome (SIRS) to infection.⁶
- A minor update followed in 2001,⁷ but in 2014, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine convened a task force of 19 critical care, infectious disease, surgical, and pulmonary specialists to undertake a comprehensive reassessment.
 - In this most recent iteration, known as Sepsis-3, sepsis was redefined as “life threatening organ dysfunction caused by a dysregulated host response to infection”.⁸ Organ dysfunction can be represented by an increase in the Sequential Organ Failure Assessment (SOFA) score of 2 points or more.⁸
 - Septic Shock was also redefined as “hypotension not responsive to fluid resuscitation,” with the added requirement for vasopressors to maintain a mean arterial pressure (MAP) \geq 65 mmHg and a lactate of >2 mmol/L.⁸

Failure to Identify and Target Early Sepsis (2)

- In the patient above, strict application of the Sepsis-3 definition would miss the diagnosis of sepsis until she was in florid septic shock.
- Perhaps the first indication the patient was in early sepsis was the elevated lactate level.
 - Lactate is often used in conjunction with screening, but it is so non-specific as to be more useful for prognostication and severity assessment.
 - The on-call physician erroneously believed that volume overload alone could cause lactate elevation. However, a lactate level $>2\text{mmol/L}$ in the setting of sepsis is associated with increased risk of inpatient mortality,⁹ making bedside assessment of the patient essential.

Failure to Identify and Target Early Sepsis (3)

- Early recognition continues to be important for survival of patients with sepsis.^{10,11}
- If recognized early, effective treatment can be initiated with survival as high as 80%, even with septic shock, according to a retrospective cohort study involving 14 intensive care units in the US and Canada.¹²
- And yet, approximately 1 in every 3 hospital deaths are associated with sepsis, which continues to be the leading cause of inpatient hospital deaths.¹¹
- As discussed in a previous [PSNet WebM&M commentary](#), clinician bedside assessments are truly essential for a timely and correct diagnosis, and should be used in conjunction with bedside markers and laboratory assessments, not in lieu of those data.

Failure to Identify and Target Early Sepsis (4)

- If sepsis is recognized early, providers can initiate early life-saving treatments and management.¹²
- According to guidelines, immediate administration of antibiotics within the hour of sepsis recognition is recommended.¹³
 - For every hour antibiotics are delayed, progression to septic shock increases by 8% and mortality increases by 4-9%.^{12,13}
- In addition to antibiotic therapy, the sepsis guidelines recommend at least 30ml/kg of IV crystalloid fluid be given within the first 3 hours of resuscitation for sepsis induced hypoperfusion or septic shock.¹⁴
 - Even in clinical settings where volume overload was an issue, there was a slight mortality benefit with bundled therapy that included the 30ml/kg volume requirement.¹⁵

Failure to Identify and Target Early Sepsis (5)

- Would early diagnosis, treatment, and management have made a difference in this case?
 - In 2019, Kahn and colleagues reported that New York's state-mandated protocolized sepsis care was associated with a greater decrease in sepsis mortality than was observed in control states that did not have sepsis regulations.¹⁶
 - Townsend and colleagues reported that compliance with the SEP-1 recommended bundle of care was associated with lower 30-day mortality.¹⁷
 - There is debate on the utility of the individual components of bundled care and whether the all-or-none approach is practical.
- Once sepsis was recognized the patient in this case was transferred to the ICU and received guideline-directed treatments. However, given the abdominal source of sepsis, it is doubtful whether the patient would have survived without a surgical intervention. Even with surgery, the mortality rate is still 30-50%, and even higher at 70% if the patient had a perforation and diffuse peritonitis as seen in this patient.¹⁸

MANAGEMENT OF BOWEL PERFORATION

Management of Bowel Perforation (1)

- Focusing on the patient's abdominal signs and symptoms, the differential diagnosis for abdominal distention and diarrhea includes infectious, inflammatory, neoplastic, and vascular etiologies.
 - It is uncertain whether this patient had an underlying infectious process, such as infectious colitis leading to toxic megacolon.
 - Another possible etiology for this patient's bowel perforation is mesenteric ischemia. Atrial fibrillation (not described here) and heart failure would put her at risk for an embolus to a mesenteric artery thus leading to bowel ischemia and eventual perforation.
- In this case, cross sectional computed tomography (CT) imaging at the onset of her abdominal symptoms would have been very helpful.

Management of Bowel Perforation (2)

- Different locations of perforation along the gastrointestinal tract lead to different presentations.
- In this patient with abdominal distension, tachycardia and quick progression to septic shock, a gastric or proximal small bowel perforation from an ulcer should also have been considered.
 - The stomach and proximal small bowel contain erosive and acidic contents that can lead to more rapid onset of peritonitis and SIRS response.¹⁹
 - A multi-center retrospective study in Japan found that delayed diagnosis occurred in 31% of their perforated bowel cases from 2015 to 2019, which was a decrease from prior studies,⁵ presumably due to more timely access to CT imaging.
 - If CT had been obtained while the patient was still stable, a timely surgical consultation could have been performed.

MORTALITY RISKS ASSOCIATED WITH SURGERY

Mortality Risks Associated with Surgery (1)

- A retrospective analysis of patients with intestinal perforations undergoing emergent surgery found that feculent ascites and a SBP <100 mmHg were independent risk factors for postoperative mortality.¹⁸
- In other cohorts, the presence of sepsis was a negative prognostic factor for both small bowel²⁰ and colonic perforations.²¹
- Other identified risk factors include older age, presence of comorbidities,²² acute kidney injury, leukopenia, acidemia, hypothermia, decreased hematocrit level, and low P/F (PaO₂/FiO₂) ratio for mechanically ventilated patients.^{23,24}
- Taking these factors into account, the patient in this case had a very high risk of postoperative mortality.

Mortality Risks Associated with Surgery (2)

- In this patient's clinical course, the surgical team was involved very late, by which time she had gone into cardiac arrest, organ failure, DIC, and required vasoactive support. It was clear that the patient was dying, but it is more difficult to assess whether surgery would alter this patient's course.
- Many factors are considered when deciding whether or not to operate, including the patient's current clinical status and prognosis, comorbidities, quality of life, and preferences.
- Scoring systems have been created to assess risk, such as the NSQIP (National Surgical Quality Improvement Program) calculator, APACHE II (Acute Physiology and Chronic Health Evaluation II), and the MPI (Mannheim Peritonitis Index).²³
- Ultimately, the surgeon, patient, and family need to discuss whether surgery is futile.

DAMAGE CONTROL SURGERY FOR SEVERE ABDOMINAL SEPSIS

Damage Control Surgery for Severe Abdominal Sepsis (1)

- In the most severe instances, with generalized peritonitis and septic shock, the patient's compromised physiology may preclude primary definitive surgery.²⁵
 - An anastomosis or large anatomical reconstruction performed in this clinical situation would place the patient at risk for death or major postoperative complications; such patients are better served with an initial damage control laparotomy.²⁵
 - The principles of damage control surgery include abbreviating operative time to control blood loss and abdominal contamination, simultaneous physiologic resuscitation, and definitive surgical management at a later time.¹⁸
 - In septic shock, patients appear to benefit from a period of resuscitation before surgical intervention and sepsis source control¹⁶, and use of sepsis treatment bundles may decrease the risk of circulatory collapse during surgery and contribute to improved outcomes.^{25,26}

Damage Control Surgery for Severe Abdominal Sepsis (2)

- Correct patient selection is crucial to maximize the benefit of any operation; not offering surgery to a patient with severe abdominal sepsis may be fatal, as in this case, but overuse of surgery exposes patients to the risks of multiple operations, open abdomen management, and prolonged intensive care stay, negating potential benefits of the intervention.²⁵
- In this case, the surgical team concluded that the patient was “not a surgical candidate”, and care was withdrawn. It is not clear whether this evaluation occurred after adequate resuscitation or whether additional resuscitative efforts would have made any difference at that late time.

TAKE HOME POINTS

Take-Home Points

- Emphasis on the bedside examination and deliberate feedback loops to physicians may be the most effective way to improve diagnostic accuracy and timeliness.
- Biomarkers and risk scores should be used in conjunction with bedside assessments in patients with suspected sepsis, not in lieu of those assessments.
- When an unanticipated change in clinical exam or status occurs, one should broaden the differential to consider other diagnoses.
- An “acute abdomen,” with findings such as severe distension, absent bowel sounds, rebound tenderness and guarding, is a surgical emergency and warrants immediate consultation from a surgical team.
- Adequate resuscitation and initiation of a protocolized sepsis bundle may potentially improve the prognosis of patients in shock who undergo “damage control laparotomy” due to severe abdominal sepsis.

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