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A lethal mimicker of acute gastroenteritis

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The patient was a 53-year-old lady who had been referred by a private general practitioner for gastroenteritis and hypotension. She presented with diarrhoea twice followed by dizziness and repeated vomiting. She was found hypotensive by the private doctor and was transferred to the emergency department by ambulance.

The initial vital signs recorded by the ambulance crew were blood pressure 73/45mmHg and pulse rate 102/min, so fluid resuscitation was commenced. She had no other chronic illness except a history of ovarian mucinous borderline malignancy with total hysterectomy and bilateral salpingo-oophorectomy performed 20 years ago.

By the time she reached hospital, her vital signs were as follows:

- Blood pressure: 105/61 mmHg
- Pulse: 112/min
- SpO2: 95% on room air
- Temp: 36.4°C
- Glasgow Coma Scale: E4V5M6

Physical examination revealed that she was dehydrated. There was no rash. Her abdomen was soft and nontender. Digital rectal examination showed loose brownish stool and no blood or melena.

Bedside ultrasound was performed by the attending doctor and the findings included:

- No intraperitoneal free fluid
- No abdominal aortic aneurysm
- Collapsed inferior vena cava
- Empty bladder and no hydronephrosis

However, there was no documentation of any findings regarding to cardiac contractility as well as any pericardial effusion, cardiac tamponade or right heart strain.

Her point-of-care blood test revealed blood glucose of 17.1mmol/L and haemoglobin of 11.5g/dL. The venous blood gas analysis revealed pH 7.29, pCO_2 6.2 kPa, pO_2 3.1 kPa, bicarbonate 22.8 mmol/L and base excess -4. The findings showed mild metabolic acidosis. Electrocardiogram was unremarkable except sinus tachycardia. Chest X-ray and CT brain were also unremarkable.

She was managed in the resuscitation room for the provisional diagnosis of dehydration and hypovolemic shock. She was treated with a 1L intravenous bolus of 0.9% sodium chloride. However, the response to the initial intravenous fluid therapy was poor. Her blood pressure further dropped to 86/53mmHg and her pulse rate was 102/min despite fluid resuscitation was continued. She was admitted to the medical ward for gastroenteritis with hypovolemia. The doctor did not consult the intensive care unit at that time.

How to approach a patient with shock?

Shock is a state of circulatory failure, leading to end-organ hypoperfusion with resultant tissue hypoxia. It is often suspected in patients with

hypotension, tachycardia (or sometimes bradycardia in cardiogenic shock), altered mental status or cool clammy skin. However, the clinical features can be non-sensitive or non-specific, so a high index of suspicion should be maintained to look out for compensated shock. Some patients, especially children, may have an intense tachycardia response as compensation before hypotension develops.

The four classes of shock include cardiogenic, obstructive, hypovolemic, and distributive. History and physical examination alone may not be sufficient to determine the etiology of shock, and point-of-care ultrasound (PoCUS) is a useful tool that can increase the diagnostic accuracy when combined with clinical evaluation.

Table 1. Etiologies of different types of shock

Types	Etiologies
Cardiogenic	Rate / rhythm (e.g., bradycardia) LV or RV failure (e.g., MI, myocarditis) Valves (e.g., papillary muscle or cordae tendinae rupture) Toxins (e.g., BB, CCB)
Obstructive	Tension pneumothorax Cardiac tamponade Pulmonary embolism Outflow obstruction (e.g., HOCM) Dynamic hyperinflation
Distributive	Sepsis (cardiogenic in late phase) Neurogenic (e.g., SCI) Endocrine (e.g., adrenal insufficiency) Medications (e.g., sedation) Anaphylaxis
Hypovolemic	Haemorrhage Gastrointestinal loss Renal loss Skin loss (e.g., burn) Other third space loss or low intake

LV: left ventricle; RV: right ventricle; MI: myocardial infarction; BB: beta blockers; CCB: calcium channel blockers; HOCM: hypertrophic obstructive cardiomyopathy; SCI: spinal cord injury

To evaluate for undifferentiated shock in the emergency department, the Rapid Ultrasound for Shock and Hypotension (RUSH) exam can be performed after clinical assessment. The RUSH exam is quick and easy to perform and can assess some of the key anatomical structures involved in the causes of, or compensation for, different types of shock. The original RUSH exam consists of several key elements using the HIMAP mnemonic: heart, inferior vena cava (IVC), Morrison's pouch/Extended Focused Assessment with Sonography in Trauma (E-FAST), aorta, and pulmonary.[2,3] (Table 2) Now the protocol also conceptualizes the evaluation of the cause of shock by focusing on three aspects, namely the pump (cardiac evaluation), tank (volume status assessment) and pipes (circulation system assessment). (Table 3) Findings on PoCUS and physical examination can then be integrated for the bedside classification for shock evaluation.

Table 2. The HI-MAP approach of RUSH exam

Heart	Is there a pericardial effusion? How is the global contractility? Is there right ventricular strain?
IVC	Is the IVC full or collapsed?
Morrison pouch	Is there a haemoperitoneum or pleural effusion?
Aorta	Is there an aortic aneurysm or dissection?
Pulmonary	Is there a pneumothorax? Is there interstitial edema?

IVC: inferior vena cava, AAA: abdominal aorta aneurysm, DVT: deep vein thrombosis, RV: right ventricle

Table 3. The RUSH exam findings using the "pump, tank & pipe" concept

RUSH exam	**Pump**	**Tank**	**Pipe**
Hypovolemic shock	Hyperdynamic	Small or collapsing IVC Peritoneal or pleural fluid	AAA or aortic dissection
Distributive shock	Hyperdynamic (early sepsis) Poor contractility (late sepsis)	Normal or small IVC Pleural or peritoneal fluid	Normal
Obstructive shock	Cardiac tamponade RV strain	Large, non-collapsing IVC Absent lung sliding	DVT
Cardiogenic shock	Poor contractility	Large, non-collapsing IVC B-lines Pleural effusion	Normal

However, while the above approach works well for subjects with a single mechanism of shock, it may be less useful for patients with a combined or multifactorial shock. Septic shock is an example in which there are multiple etiologies that can contribute to hemodynamic compromise, including intravascular volume depletion, cardiac dysfunction, and peripheral vasodilation. It is important to know that a patient with sepsis may have concomitant hypovolemia due to gastrointestinal volume loss, reduced fluid intake, tachypnea, sweating, as well as capillary leak leading to loss of intravascular volume.[4] On the other hand, sepsis may also give rise to cardiogenic shock due to myocardial dysfunction in the late phase.

It is not uncommon for patients with an underlying infection to present with poor intake or gastrointestinal fluid loss. If the unstable hemodynamics of these patients do not improve after the hypovolemia has been corrected (which can be ascertained by repeating assessment of the IVC diameter and collapsibility), sepsis should be considered as the cause of the persistent shock state. Studies have shown that early RUSH exam is less sensitive for septic shock or shock with mixed etiologies.[5] Therefore, the clinician may miss the diagnoses especially when the underlying infection is not correctly identified.

There is also no single diagnostic tool for sepsis. Several screening tools have been developed for early identification of sepsis, including the Sequential Organ Failure Assessment (SOFA), Quick Sequential Organ Failure Assessment (qSOFA), and the National Early Warning system (NEWS). However, these tools are only useful for patients already suspected to have an infection. They cannot be used for diagnosing sepsis and are not useful for differentiating septic shock from other types of shock.

Therefore, the clinician should carefully look for any clinical signs and symptoms of an infection in patients presenting with shock, and bear in mind that some infections may not present with fever or may have a non-specific presentation.

In this patient, the initial clinical picture and ultrasound findings were compatible with hypovolemic shock. However, there was a paradoxical response to intravenous fluid therapy. Ultrasound examination should be repeated, to recheck the fluid status and to look for an alternative explanation of the hypotension. It is also important to check if the degree of vomiting and diarrhea is commensurate with the persistent shock, so other differential diagnoses can be considered in the early stage.

Progress of the patient

Upon admission to the medical ward, she remained afebrile initially, and her blood pressure improved to 93/54mmHg. She had persistent tachycardia with pulse up to 130 bpm and her electrocardiogram showed the "S1Q3T3" pattern. She was therefore arranged Computed Tomography Pulmonary Angiogram (CTPA), which did not reveal any pulmonary embolism. Her blood results revealed leukocytosis (white cell count 14.6 x 10^9/L), impaired renal function (creatinine 164umol/L) and hyperglycemia (random glucose 34.7mmol/L). There was also deranged liver function (elevated alkaline phosphatase 342U/L, elevated total bilirubin 25umol/L, normal alanine transaminase), which could be due to cholestasis secondary to sepsis.

She remained hypotensive and developed a kick of fever afterwards. She was given repeated boluses of intravenous fluid and dopamine infusion for the suspected septic shock. Intravenous (IV) piperacillin/tazobactam was given, and insulin infusion was started. The patient was then transferred to the intensive care unit for further management. Computed Tomography (CT) of Abdomen and Pelvis was done in view of the uncertain source of sepsis. (Figure 1 & 2)

Figure 1. CT Abdomen & Pelvis (axial) showing gas collection and renal parenchyma necrosis in the left kidney (white arrow) due to EPN, as well as distended gall bladder (black arrow) due to septic cholestasis

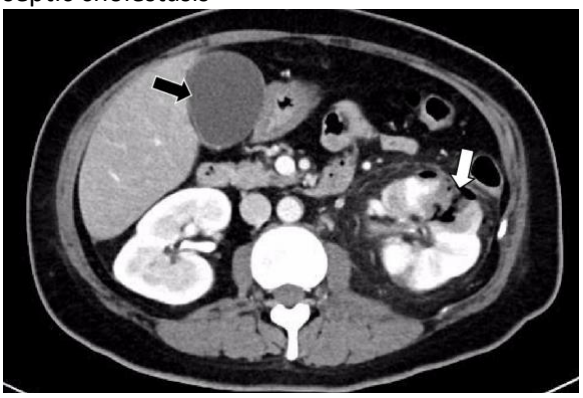
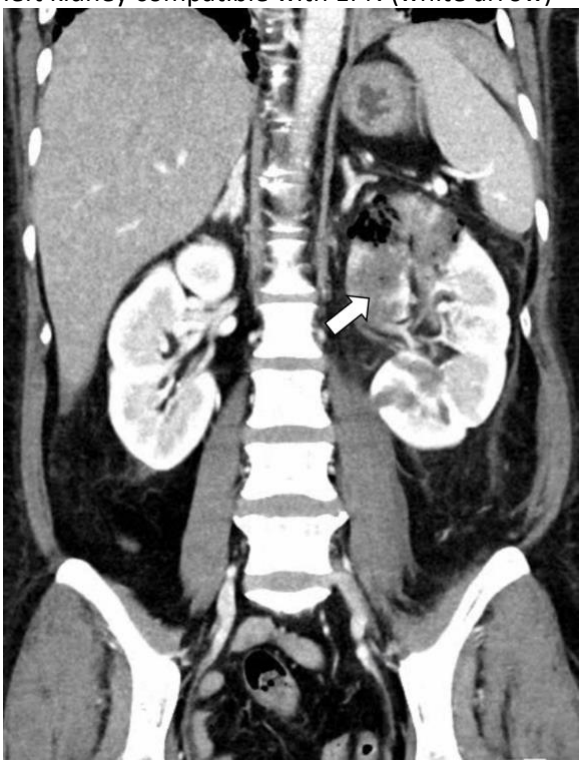


Figure 2. CT Abdomen & Pelvis (coronal) showing similar features at the superior pole of left kidney compatible with EPN (white arrow)



The CT scan showed swollen left kidney with perinephric stranding. There were gas densities at the renal parenchyma extending into the perinephric spaces, as well as hypo-enhanced patches in the renal parenchyma representing necrosis. The diagnosis was emphysematous pyelonephritis (EPN).

The patient received an operation with left ureteral stent (Double J stent) insertion for drainage and was put on IV meropenem. The blood culture and urine culture later identified *Escherichia coli* as the pathogen, and meropenem was de-escalated to amoxicillin/clavulanate according to the antibiotic sensitivity result.

Her condition gradually improved, and her renal function returned to normal. Follow-up CT abdomen and pelvis was done three days later showed reduction in the previous hypo-enhanced patches and gas densities.

She also had newly diagnosed diabetes mellitus and was started on insulin therapy.

Emphysematous pyelonephritis

Emphysematous urinary tract infections include upper or lower urinary tract infection with gas formation, and may involve the bladder (cystitis), renal pelvis (pyelitis) and the kidney (pyelonephritis). Emphysematous pyelonephritis (EPN) is a serious acute necrotising infection of the kidney with high rate of morbidity and mortality.[6] The most relevant risk factor for this condition is diabetes mellitus, with up to >80% of the patients are diabetic, and it is also more common in females.[6,7,8] The left kidney is more commonly affected than the right one.[8] Obstructive uropathy is present in around 20% of patients.[7]

Escherichia coli is the most common organism, followed by *Klebsiella pneumoniae and Proteus*.[7,8] Polymicrobial infection is uncommon for EPN. The postulated explanation for gas accumulation is the production of hydrogen, carbon dioxide and nitrogen during fermentation of glucose and lactate by the microbial organisms.[9]

The symptoms of EPN may be indistinguishable from those in severe acute pyelonephritis. The

patient may present with fever, chills, flank or abdominal pain, nausea, and vomiting.

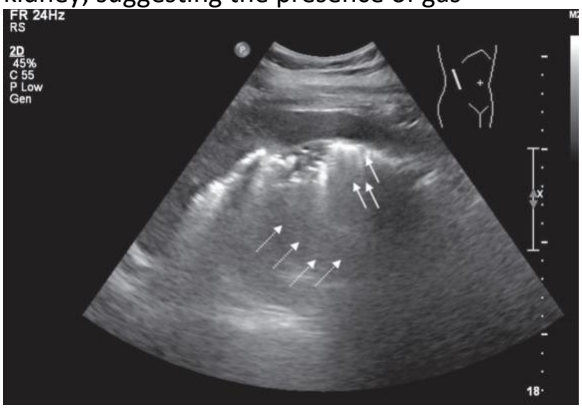
Physical examination may reveal costovertebral tenderness or rarely subcutaneous crepitus if the gas reaches the subcutaneous layer. It is noteworthy that some patients with acute pyelonephritis may present nonspecifically or with a picture similar to gastroenteritis, with symptoms including abdominal pain, vomiting and diarrhea.[10,11] It could be challenging to make the diagnosis without a high index of suspicion, especially if the patient does not present with fever or urinary symptoms. On the other hand, the gastrointestinal symptoms would render the EPN as a mimicker of acute gastroenteritis, delaying the diagnosis and definitive management.

Urinalysis can be used to identify pyuria to support the diagnosis of urinary tract infection, but computed tomography (CT) of the urinary system is required to diagnose EPN.[6] CT scan can not only detect gas accumulation but can also offer an accurate assessment on the extent of infection. Moreover, urinary tract obstruction associated with the infection can also be identified. Contrast scan is preferred, and the classical finding is a heterogeneous infected kidney embedded with hypodense abscesses containing fluid and gas.[12] EPN can be classified according to the CT scan findings using the Huang and Tseng classification:[7]

Class I: gas confined to collecting system
Class II: gas confined to renal parenchyma
Class IIIa: perinephric extension of gas or abscess
Class IIIb: extension of gas beyond Gerota fascia
Class IV: bilateral or EPN with solitary kidney

Conventional abdominal X-ray may also be used to detect abnormal gas shadows, which can be seen in around 30% of cases.[12] In situations where emergency CT scan is not readily available, PoCUS would also be a useful tool for ruling in the diagnosis in some suspected cases. Ultrasonography can identify an enlarged kidney with hyperechoic gas accumulation in the renal parenchyma or the collecting system. Gas bubbles on the ultrasound image are characterized by hyperechoic areas associated with ring down artefacts commonly known as dirty shadowing. (Figure 3) This finding should be carefully differentiated from the clean hypoechoic acoustic shadowing from a renal calculus.[13]

Figure 3. Ultrasound image showing multiple "ring-down" artefacts (arrows) with acoustic "dirty shadowing" (broken arrows) in the kidney, suggesting the presence of gas[22]



The initial management of an unstable patient of EPN with septic shock should begin with aggressive resuscitation including adequate intravenous hydration, early use of vasopressors and prompt administration of antibiotics together with frequent review of the hemodynamic response.[12] Insulin therapy should also be given for glucose control if necessary. The choice of empirical antibiotics should be broad-spectrum but should be tailored individually. The chosen regimen should target the most common pathogens mentioned above. Either beta-lactamase inhibitors or third generation cephalosporins may be given if the patient has a mild disease. However, given the increasing incidence of extended-spectrum beta-lactamase (ESBL) producing bacteria, carbapenems should be the agent of choice for high risk or critically ill patients.[14]

Urology consultation for surgical management is often necessary. Nephrectomy was once considered the optimal treatment for EPN, but early nephrectomy has been shown to be associated with a higher mortality.[6,15] It is therefore no longer considered the first line option and should only be reserved for patients who have failed other more conservative therapies.

The standard nowadays is a more conservative approach using percutaneous nephrostomy (PCN) or ureteric stent insertion as a drainage procedure. These can be performed even in the absence of urinary tract obstruction. There are case reports that some class I or class II patients can even achieve good outcomes when treated with antibiotics only.[16,17,18,19] However, it is shown that surgical decompression using a ureteral stent or PCN is associated with lower mortality when compared with antibiotic treatment alone.[20]

Risk factors for higher mortality have been identified, including sepsis, shock, confusion, thrombocytopenia, acute renal failure as well as Huang and Tseng class III-IV disease.[21] The presence of these risk factors may indicate more aggressive treatments or more invasive treatment modalities.[6]

Lessons to learn from the case:

1. **Beware of a multifactorial shock and suspect septic shock if hypotension does not improve after correction of hypovolemia**
2. **Consider alternative diagnoses when the severity of diarrhea and vomiting is not commensurate with the dehydration and shock**
3. **Do not be misled by the referring doctor without verifying the evidence**
4. **For a non-responder to IV fluid in suspected hypovolemic shock, consider inadequate volume replacement versus other etiologies**
5. **Clinico-pathological evaluation with PoCUS assessment using the "pump, tank, pipes" approach can elucidate the shock etiology, and it should be repeated (e.g., IVC assessment) in case of hemodynamic non-response**
6. **Sepsis does not always present with fever or localised symptoms of the infection**
7. **EPN may present with nonspecific symptoms mimicking gastroenteritis**
8. **For acute pyelonephritis, PoCUS can be used to look for abnormal gas in the kidneys, in addition to urinary obstruction or hydronephrosis**
9. **The management approach for EPN includes broad spectrum antibiotics and surgical decompression with ureteric stent insertion or percutaneous drainage**

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