

# Vancomycin Resistant Enterococcus in Infected Walled Off Necrosis: Possible Causation & Management

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Received Date: February 20, 2024 | Accepted Date: May 13, 2024 | Published Date: May 27, 2024

**Citation:** Mason Winkie, Katherine M. Cooper, Joseph Daniel, Jeeva Subramanian, Prashanth Rau, (2024), Vancomycin Resistant Enterococcus in Infected Walled Off Necrosis: Possible Causation & Management, *International Journal of Clinical Case Reports and Reviews*, 17(3); DOI:10.31579/2690-4861/404

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## Abstract:

Peri-pancreatic fluid collections are frequently encountered by clinicians caring for patients who recover from acute or chronic pancreatitis. Although these fluid collections are common, the type of collection and resulting complications can significantly affect patient mortality. We present a 29-year-old female who originally presented with acetaminophen toxicity secondary to pain management for interstitial edematous pancreatitis (IEP) complicated by renal failure. The patient later developed intermittent fevers with concern for an underlying infection and was ultimately found to have walled-off necrosis (WON) infected by an uncommon hepatobiliary pathogen previously isolated in a urine culture despite asymptomatic bacteriuria.

## Background:

Acute pancreatitis (AP) is divided into two categories: IEP and necrotizing pancreatitis (NP). Fluid collections are a common sequela for both subtypes. In IEP, fluid collections include acute peripancreatic fluid collections (APFCs) and pseudocysts (PC). Fluid collections in NP include acute necrotic collections (ANCs) and walled-off necrosis (WON) (1). All associated AP fluid collections carry an increased risk for infection, but speed and degree of management varies depending on the collection type (2).

## Objective:

To report a case of AP complicated by a miscategorized fluid collection later determined to be WON with superimposed vancomycin resistant enterococcus (VRE) and discuss a unique approach to anti-microbial therapy selection.

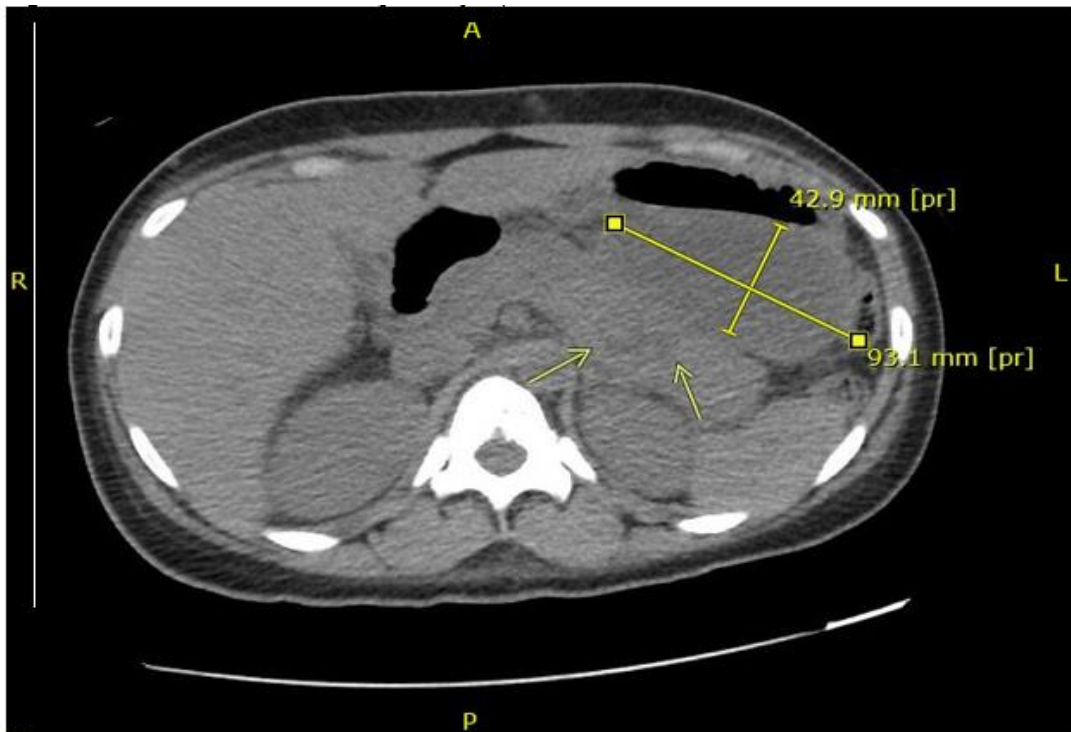
**Key words:** Acute pancreatitis; acute necrotic collections; walled-off necrosis; necrotizing pancreatitis

## Case Report:

A 29-year-old female with a medical history of alcohol use disorder, recent ED admission for IEP, and mesenteric vein thrombosis (on anticoagulation) presented to the hospital for severe abdominal discomfort with excessive acetaminophen usage. Basic laboratory evaluation revealed aspartate aminotransferase > 15,000 and acute kidney injury (AKI) inciting concern for acetaminophen toxicity. The patient was admitted to the ICU for multi-system organ failure secondary to unintentional overdose versus severe pancreatitis. She was managed with a N-acetylcysteine drip, fluid resuscitation, and renal replacement therapy (RRT). After 1 week in the ICU, her renal function, abdominal pain, and overall clinical status improved allowing transfer to the floor hospital medicine service.

On hospital day 15, the patient experienced recurrent abdominal pain, intermittent fevers, and increasing leukocytosis. Intravenous vancomycin and piperacillin/tazobactam were started pending infectious work-up.

Urinalysis revealed 1+ leukocyte esterase and 31 leukocytes. VRE (<50,000 CFU) was isolated on reflex urine culture, however, this asymptomatic bacteriuria was not considered the infectious source given the absence of urinary symptoms. A CTA/P was obtained to evaluate for an intra-abdominal pathology, though the study was ordered without contrast due to the patient's recent AKI and need for RRT. The CT identified a heterogeneously dense pancreas with a poorly defined 4 x 9 x 9 cm fluid collection near the lesser sac of the stomach and the pancreas body (Figure 1). A contrast study was recommended for better characterization, but this was deferred given the lack of a mature fluid collection which would benefit from procedural intervention. Based on the CT, antimicrobial coverage was narrowed to ceftriaxone and metronidazole to target the likely intra-abdominal infection presumed to be an APFCs or early PC in the setting of the patient's previously identified IEP.

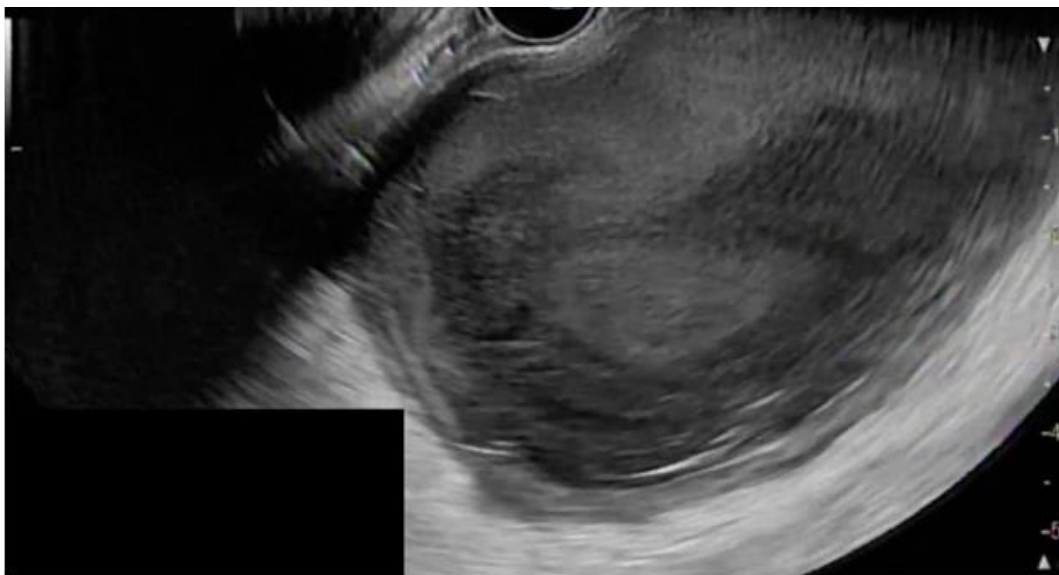


**Figure 1:** Non-Contrast CT after Hospital Day 15

Newly identified 4.6 x 9.4 x 9.1 cm fluid within the lesser sac not present at time of admission. Additionally, a heterogeneously dense area was identified within the pancreas that was concerning for necrosis although indeterminate without contrast.

An endoscopic ultrasound (EUS) (Figure 2) was performed one week later and showed a fluid collection thought to be consistent with a peri-gastric PC. Needle aspiration of the cyst revealed turbid and purulent fluid, which was sent for culture. A cystogastrostomy was created using a lumen-apposing metal stent (LAMS) with subsequent drainage of purulent fluid. After drainage was complete, necrotic tissue was identified with diagnosis of NP and WON. Despite drainage and antibiotic coverage for typical

intra-abdominal infections, the patient continued to experience low grade fevers, pain, and persistent leukocytosis. Ultimately, the culture from the WON isolated VRE and antibiotics were transitioned to IV Daptomycin based on the susceptibility profile from the previously isolated urine culture. In time, the VRE of the WON demonstrated the same sensitivity profile as the VRE from the urine culture. An endoscopic guided necrosectomy was performed five days after the cystogastrostomy creation at which time the LAMS stent was removed. After the single necrosectomy and daptomycin treatment, the patient subsequently experienced improvement in all symptoms and was deemed safe for discharge.



**Figure 2:** Endoscopic Ultrasound Image of Fluid Collection

Endosonographic ultrasound demonstrated a 8 x 5 cm single compartment hypoechoic and septated lesion.

## Discussion:

While there are case reports of pancreatitis complicated by VRE enteritis, pancreatitis with VRE infected necrosis is not discussed in the literature [3, 4]. To our knowledge, this is the first case report demonstrating successful treatment of VRE infected WON, a rare complication in a young patient with acute necrotizing pancreatitis.

The decision to start antibiotics in patients with pancreatitis is complicated as systemic inflammatory response occurs even without infection. As such, professional guidelines recommend against the routine use of antibiotics for AP [5]. Our patient had a complicated hospitalization for presumed acetaminophen toxicity in the setting of recurrent pancreatitis and was initially improving prior to the onset of new fever. The timing of her fever raised concern for an infected peripancreatic fluid collection, originally thought to be an APFC or early PC in the setting of the patient's previously identified IEP and inadequate imaging. Conversely to AP, antibiotic therapy is always recommended for proven infected and necrotic pancreatitis, though first line treatment is endoscopic drainage and debridement. However, it is recommended to wait  $\geq 4$  weeks for these procedures to allow for the fluid collection to mature. Given the high mortality rate associated with infected necrotic pancreatitis (upwards of 30%), necessitates antimicrobial coverage prior to culture data [6]. In these cases, broad spectrum antibiotics that penetrate pancreatic tissue are recommended for use including carbapenems, quinolones, ureidopenicillins, and metronidazole [7]. The overall prognosis appeared poor when the patient did not improve despite standard of care with cyst drainage and antibiotics. However, transitioning to IV daptomycin based on susceptibilities of urine VRE resulted in successful control of her infection.

Here, we would like to highlight that the clinical relevance of the patient's previous urine culture. Prior to full speciation of the enterococcus from the pancreatic culture, IV daptomycin was chosen based on antimicrobial sensitivities from the urine VRE. It is generally accepted that culture positive bacteremia is not a pre-requisite for distant seeded infections (e.g., septic arthritis after dental work). In these cases, transient bacteremia results in invasion of closed spaces or vulnerable tissue. In our patient, it is highly likely that transient bacteremia occurred due to VRE translocation from the urinary tract and led to infection of the WON. This rationale was used when initiating daptomycin prior to full susceptibility information being available from the speciated WON aspirate, which proved to be a successful strategy resulting in the patient's rapid clinical improvement.

Our case is the first to suggest patients with VRE asymptomatic bacteriuria and infected peri-pancreatic fluid collections may benefit from expanded antibiotic consideration especially when diagnostic modalities are limited. Through this case, we want to emphasize two points. Firstly, daptomycin was demonstrated to have pancreatic fluid penetration and could be considered for patients with infected pancreatitis in the

appropriate clinical context. Next, asymptomatic bacteriuria, considered unnecessary to treat, can still cause transient bacteremia and translocation [8]. This possibility proposes that urine cultures may provide predictive value for infections in suspected peri-pancreatic fluid collections and can be used to guide therapy (eg. similar to how nasal testing for staphylococcus aureus is used to guide antibiotics in skin and soft tissue infections) even before procedural intervention is undertaken.

## Financial Disclosures/Conflicts of Interest

This work was not supported by any funding source. The authors have no conflicts of interest to disclose.

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