Black and Blue

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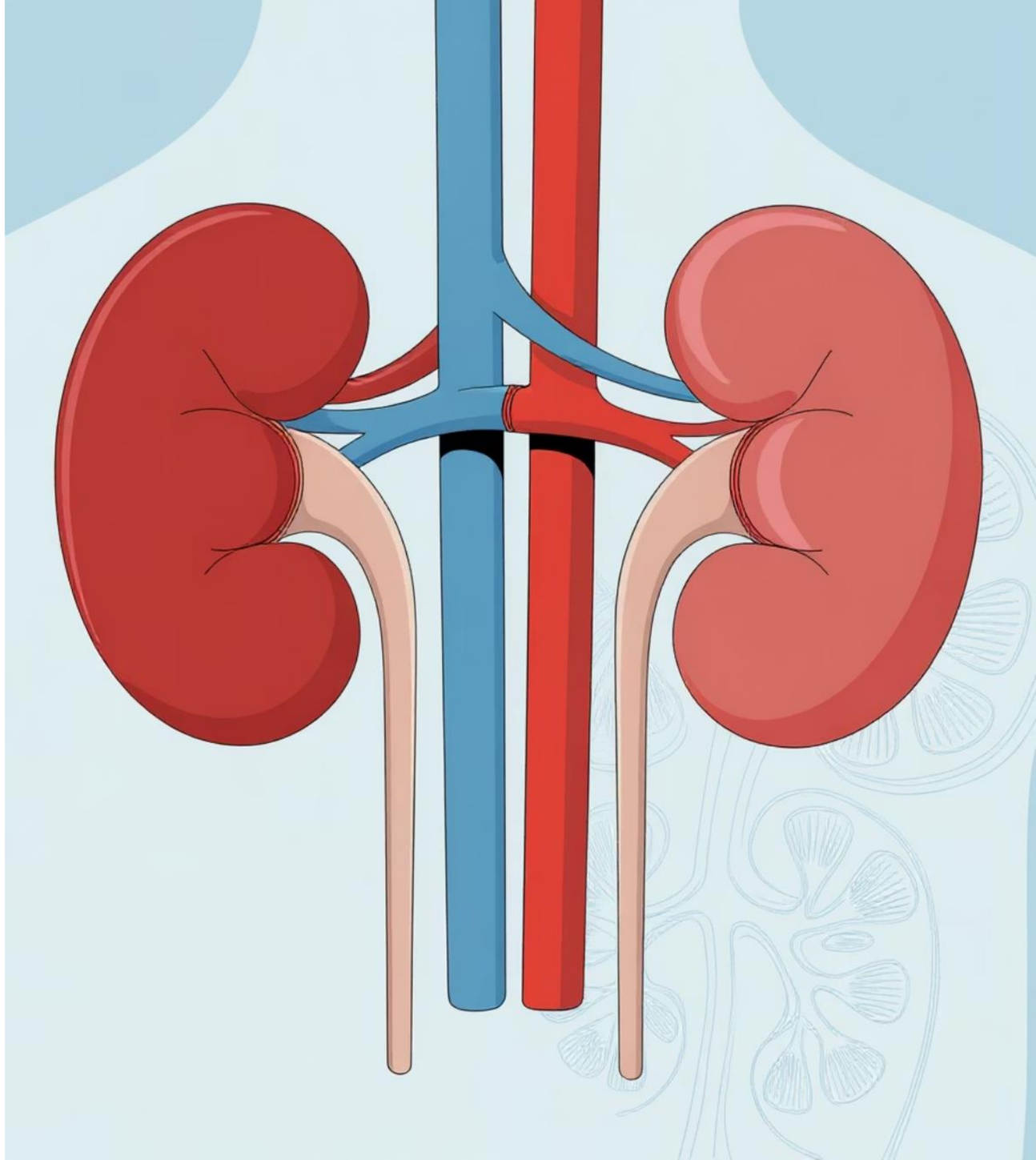


UCI Health

The Case

Case

A [redacted]-year-old [redacted] with ESRD due to diabetes mellitus type 1 on PD, subtotal gastrectomy with Roux-en-Y, HTN, HL, GERD, underwent simultaneous kidney and pancreas transplant.

Patient Background & Surgical Complexity

Medical History

[redacted]-year-old [redacted] with ESRD due to DM1 on peritoneal dialysis since [redacted] 2022, history of Roux-en-Y gastric bypass.

Surgical Challenge

Procedure took [redacted] hours (3 hours longer than standard) due to severe adhesions and scar tissue from previous gastric surgery.

Extended Cold Ischemia Times

Pancreas: [redacted] hours, Kidney: [redacted] hours - both exceeding optimal timeframes and increasing thrombosis risk.

Early Post-transplant Course

PTD #1

Intermittent hypotension (SBP 90s), fluid responsive, then hypertensive to 170s due to significant pain

PTD #2

Hypotension to 70s/50s and tachycardic to 120s at 11pm without fever. No blood cultures obtained.

PTD #3

CT scan showed postsurgical changes, anasarca, bilateral pleural effusions, and nonspecific enterocolitis

Clinical Progression

PTD #3: Pancreatic Graft Thrombosis

Concerns for pancreatic graft thrombosis led to exploratory laparotomy. The procedure revealed an ischemic pancreatic allograft requiring explantation.

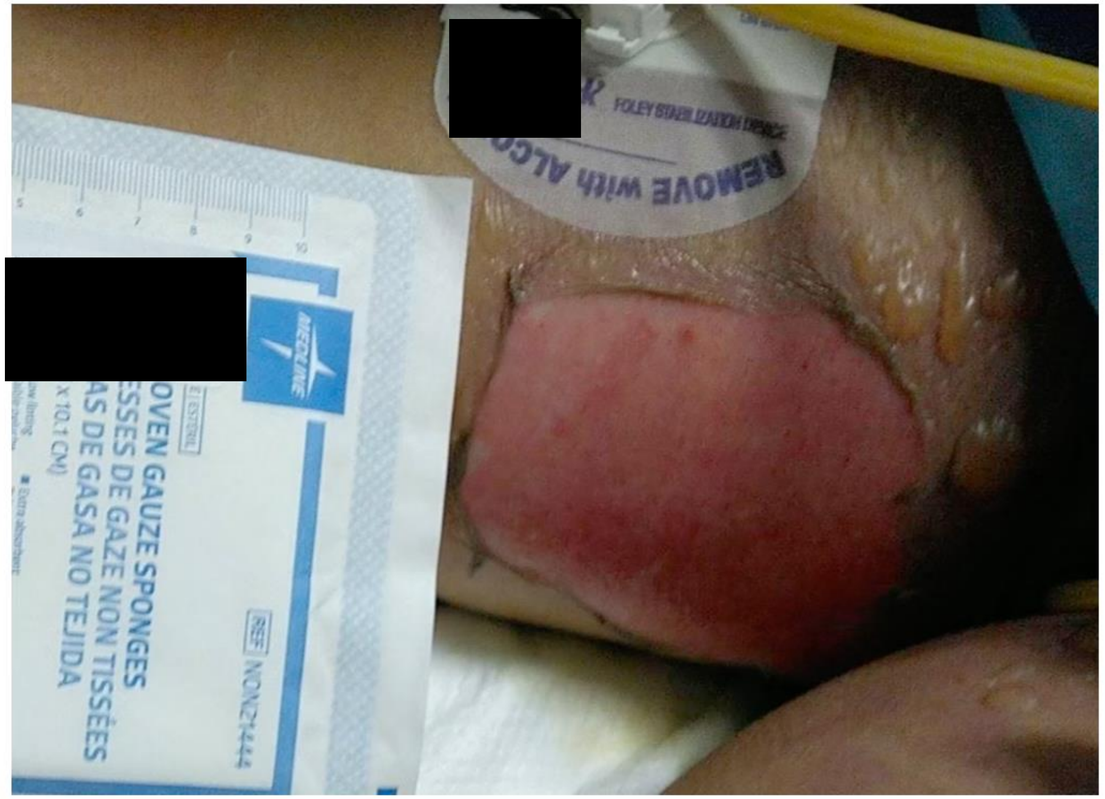
PTD #4-5: Rapid Deterioration

Rapid clinical deterioration with SICU transfer, volume overload, and septic shock requiring vasopressors.

Placed on empiric therapy with Vancomycin, Cefepime and blood cultures sent.

Skin Findings

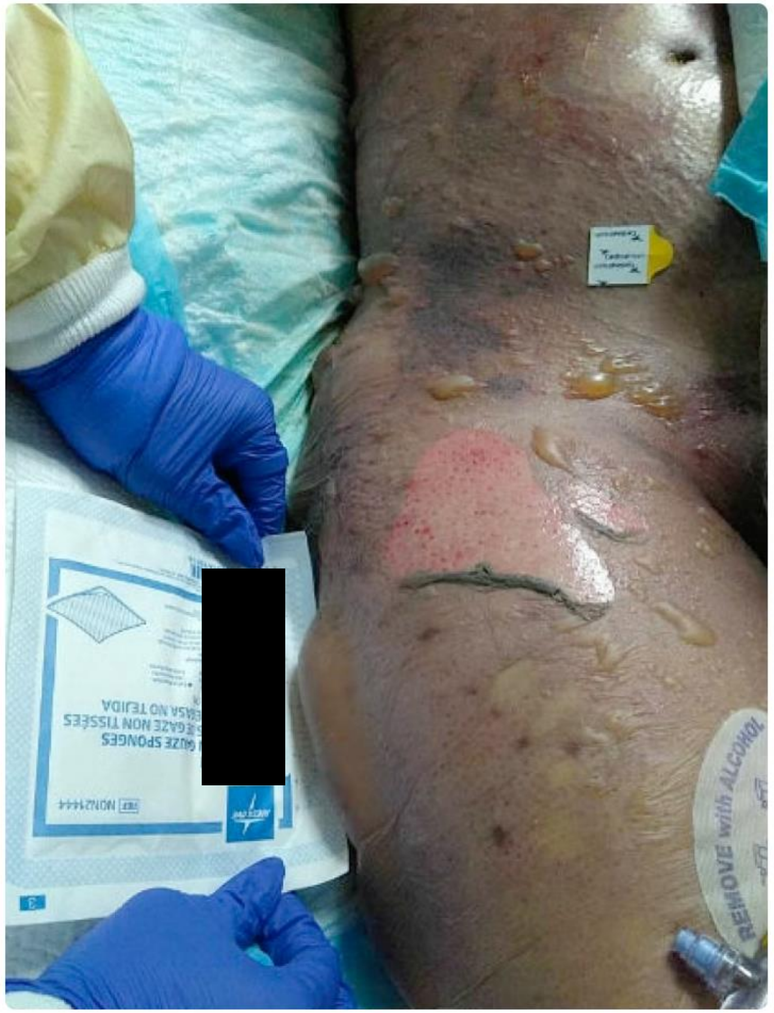
PTD #5, Patient started developing skin findings.



⚠ Tense bullae with erosions of the torso, upper legs, vulva (BSA 15-20% detached skin)

Dusky discoloration of skin (BSA 20-25% impending detachment)

Purpura of abdomen and upper legs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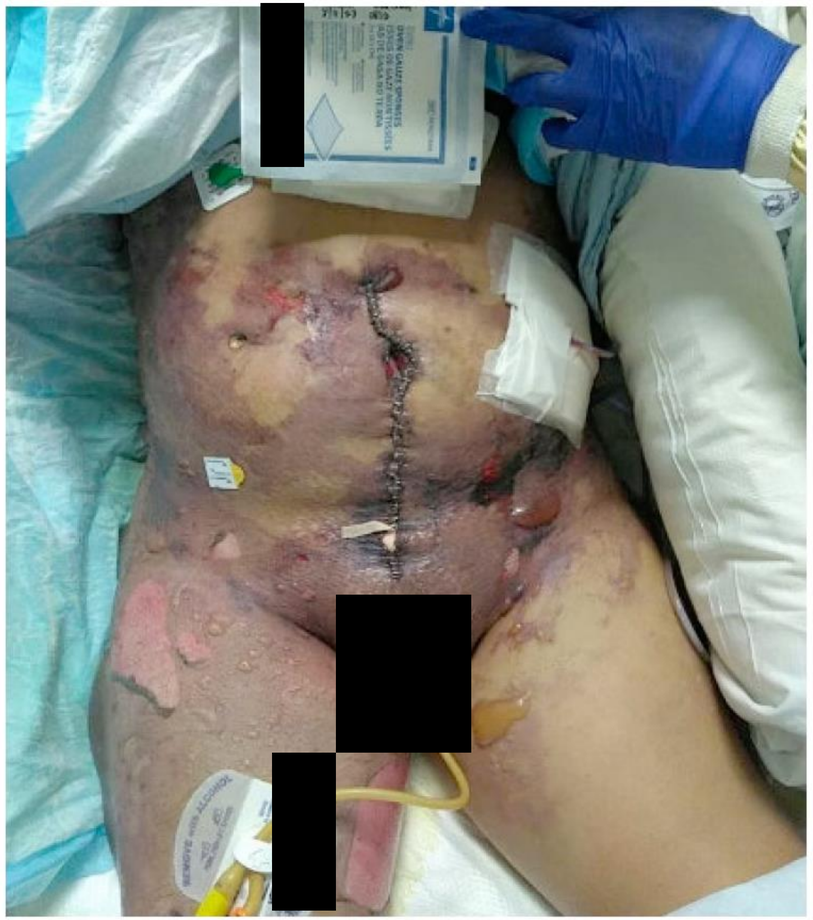
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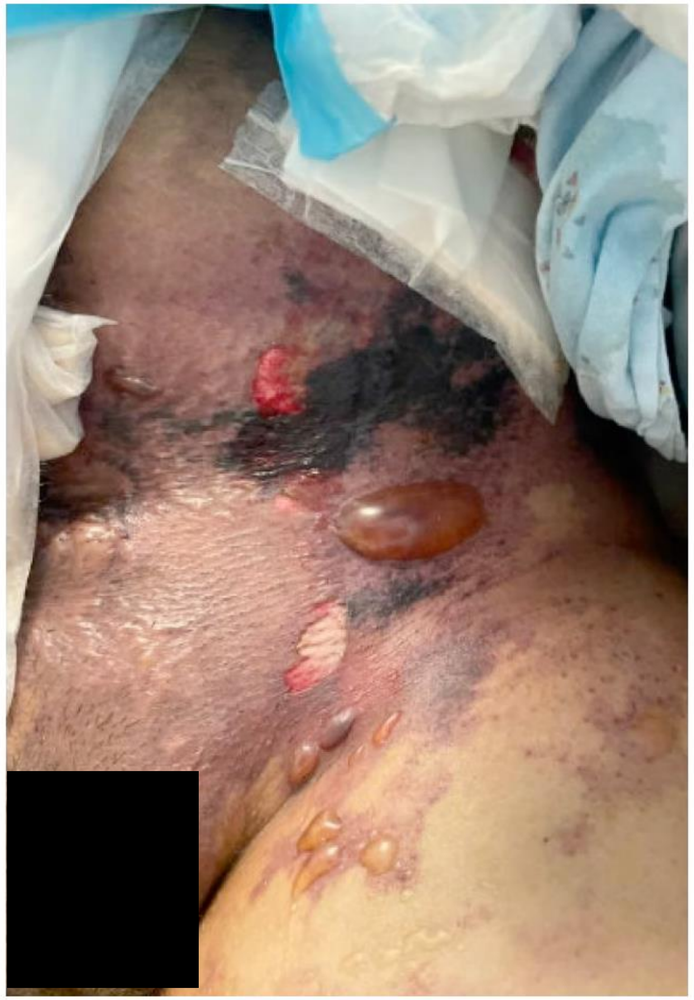
Poll Question 1.



Based on the skin findings, what is your leading diagnosis?

A. Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN)
B. Linear IgA Bullous Disorder (Vancomycin-associated)
C. Purpura Fulminans
D. Necrotizing Fasciitis
E. Bullous Pemphigoid

Biopsies were taken.

PTD #5-6

Blood Culture Blood Culture Set [redacted] (Abnormal)
Specimen: Blood

Description	BLOOD L ARM
Special Info	NONE
Nucleic Acid Detection	ESCHERICHIA COLI !
Nucleic Acid Detection	CTX-M gene detected !
Nucleic Acid Detection	Likely extended spectrum beta lactamase producer (ESBL) !
Nucleic Acid Detection	Preferred therapy is meropenem (extended infusion). Consider antimicrobial stewardship or infectious disease consult.
Nucleic Acid Detection	Molecular results to be confirmed. The ePlex Gram-negative panel includes the following organisms and resistance gene targets: Acinetobacter baumannii, Bacteroides fragilis, Citrobacter spp., Cronobacter sakazakii, Enterobacter cloacae complex,
Nucleic Acid Detection	-- Enterobacter spp. (non-cloacae complex), Escherichia coli, Fusobacterium necrophorum, Fusobacterium nucleatum, Haemophilus influenzae, Klebsiella oxytoca, Klebsiella pneumoniae, Morganella morganii, Proteus spp., Proteus mirabilis, Pseudomonas aeruginosa, Salmonella spp., Serratia spp., Serratia marcescens, Stenotrophomonas maltophilia, CTX-M, IMP, KPC, NDM, OXA and VIM.
Culture Result	ESCHERICHIA COLI: Extended spectrum beta lactamase producer (ESBL). (isolated from both blood culture bottles) !

Historical Review

Culture, Urine

Specimen: Urine - Urine specimen obtained via indwelling urinary catheter (specimen)

Component	5 yr ago
Culture	>100,000 CFU/ml Escherichia coli, ESBL !
Culture	1,000 CFU/ml Gram Positive Flora
Resulting Agency	[redacted]

Susceptibility

Organism	Antibiotic	Susceptibility
Escherichia coli, ESBL	Ampicillin + Sulbactam	16: Intermediate
Escherichia coli, ESBL	Cefepime	<=1: Sensitive
Escherichia coli, ESBL	Ertapenem	<=0.5: Sensitive
Escherichia coli, ESBL	Gentamicin	<=1: Sensitive
Escherichia coli, ESBL	Meropenem	<=0.25: Sensitive
Escherichia coli, ESBL	Nitrofurantoin	32: Sensitive
Escherichia coli, ESBL	Trimethoprim + Sulfamethoxazole	<=20: Sensitive
Escherichia coli, ESBL	Fosfomycin	0.50 ug/mL: Sensitive

Narrative [redacted]

View Encounter

Patient had a history of ESBL E coli urinary tract infection from an OSH 5 years prior; none after.

Poll Question 2.

With a known history of prior ESBL colonization, consideration for carbapenem with early septic shock should have been potentially been made sooner.

Would this history also change your standard perioperative antibiotic prophylaxis for this kidney-pancreas transplant?

> A. Yes, I would provide prophylaxis with a carbapenem.
> B. Yes, but I would use a carbapenem-sparing agent like piperacillin-tazobactam.
> C. No, the history is too remote to influence my choice.
> D. No, I do not alter prophylaxis for ESBL colonization history.

Perioperative Prophylaxis

The Dilemma

Our case had a remote history of ESBL *E. coli*. Should this guide prophylaxis?

Pro Evidence

A study in liver transplant showed that targeted prophylaxis active against a colonizing ESBL-E strain significantly reduced post-op infections (29.8% vs 63.6%).

Con Evidence

Guidelines are cautious due to carbapenem overuse concerns. One study showed patients receiving targeted CRE prophylaxis had *worse* outcomes, likely due to confounding (sicker patients received it).

AST Guidelines on Perioperative Prophylaxis

The 2019 American Society of Transplantation guidelines highlight key gaps in current practice:

Limited Evidence

No randomized trials evaluating duration of perioperative antibiotic prophylaxis in solid organ transplant recipients

Individualized Approach

Prophylaxis should be optimized for each organ type and each patient's unique circumstances

MDRO Consideration

Need to address recipient colonization with multidrug-resistant organisms pre-transplantation

Current guidelines rely primarily on general surgical prophylaxis recommendations from IDSA, which may be inadequate for transplant patients with known MDRO history.

Back to the case… PTD #6

Ex lap to rule out concerns for bowel perforation. Her midline laparotomy incision was reopened with no evidence of necrotizing fasciitis. Cultures were taken. The bowel appeared well perfused and there was no frank contamination.

OR Cultures:

Anaerobic Culture [redacted]

Description	ABDOMINAL FLUID INTRA NO.2
Special Info	NONE
Gram Stain	-- 2+ RED BLOOD CELLS
Gram Stain	-- 2+ WBC'S SEEN
Gram Stain	-- ! 2+ GRAM NEGATIVE RODS !
Culture Result	2+ ESCHERICHIA COLI: Extended spectrum beta lactamase producer (ESBL). ! NO ANAEROBES ISOLATED

Susceptibility

	Escherichia coli: extended spectrum beta lactamase producer (esbl). VITEK MIC (MCG/ML)	
Amikacin	4	Susceptible
Ampicillin	>=32	Resistant
Ampicillin/Sulbactam	>=32	Resistant
Cefazolin		Resistant [1]
Cefepime	>=32	Resistant
Ceftriaxone		Resistant [2]
Cefuroxime	>=64	Resistant
Ciprofloxacin	>=4	Resistant
Ertapenem		Susceptible [3]
Gentamicin	>=16	Resistant
Imipenem	<=0.25	Susceptible
Levofloxacin	>=8	Resistant
Meropenem	<=0.25	Susceptible
Piperacillin/Tazobactam	64	Resistant
Tobramycin	>=16	Resistant
Trimethoprim/Sulfamethoxazole	<=20	Susceptible

Poll Question 3.

Do you screen or send cultures for MDRO assessment around the time of renal transplantation (**multiple choice**)?

A. MRSA

B. ESBL

C. VRE

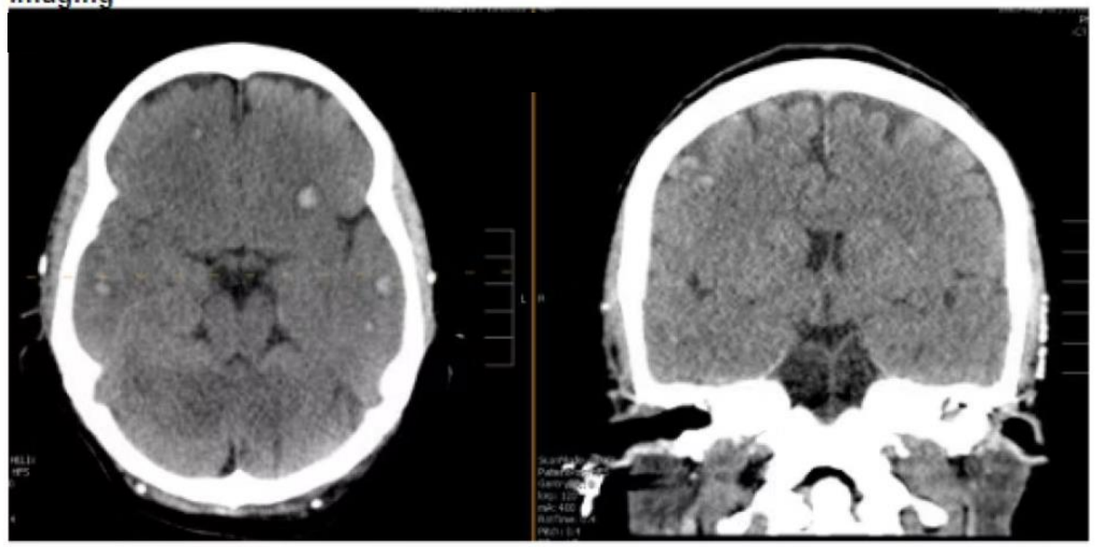
D. Bladder wash/urine cultures

E. Preservation fluid

Neurological Catastrophe

On PTD #7, the patient experienced sudden neurological deterioration with unreactive pupils and NIHSS score of 26.

Imaging



- **Septic Emboli**

  Multiple supratentorial hyperdensities at gray-white matter junctions

- **Hemorrhage**

  Intracranial bleeding in setting of severe thrombocytopenia

- **Cerebral Edema**

  Diffuse brain swelling with loss of gray-white differentiation

Final Outcome

Despite maximal medical intervention including broad-spectrum antimicrobials and multiple vasopressors, the patient's condition continued to deteriorate.

PTD #8

Intractable seizures, nonresponsive pupils, maximal vasopressor support

PTD #9

Neurosurgery declined intervention for worsening intracranial hemorrhage

End of Life

Patient transitioned to inpatient hospice care and passed away

Dermatology Diagnosis

Dermatology Final Diagnosis:

Bullous vasculopathy secondary to E. coli bacteremia-induced purpura fulminans

A. Leg, Upper Right, Blister roof (R. upper leg):

-SECTION OF EPIDERMIS WITH NO EVIDENCE OF EPIDERMAL NECROSIS

There is a clean subepidermal split. In context of the patient's other biopsy findings (D23-03465), this subepidermal blistering process is favored to be due to dermal necrosis secondary to a vasculopathy.

MDRO in SOT

MDRO Burden in ESRD/Hemodialysis Patients

6.2%

VRE Colonization

Risk factors: antibiotic use (especially vancomycin) and recent hospitalization.

6.2%

MRSA Colonization

Hemodialysis patients are more likely to be colonized than peritoneal dialysis patients.

18%

ESBL Colonization

Typically 10-40%.

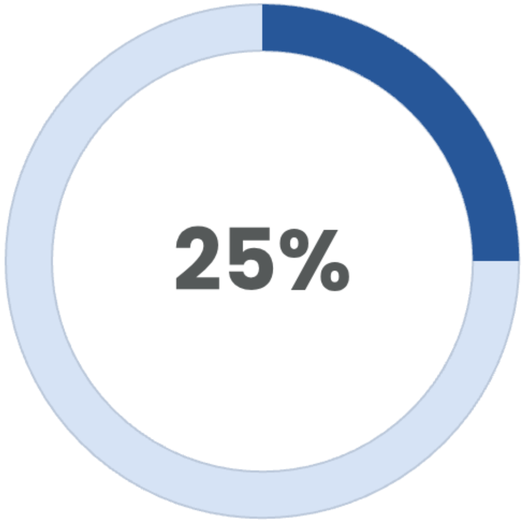
Risk factors: antibiotic use, prolonged hospital stays, and invasive procedures.

7 years

Dialysis Duration with MDRO

Median dialysis duration for renal transplant recipients with MDRO detected within 30 days of transplant.

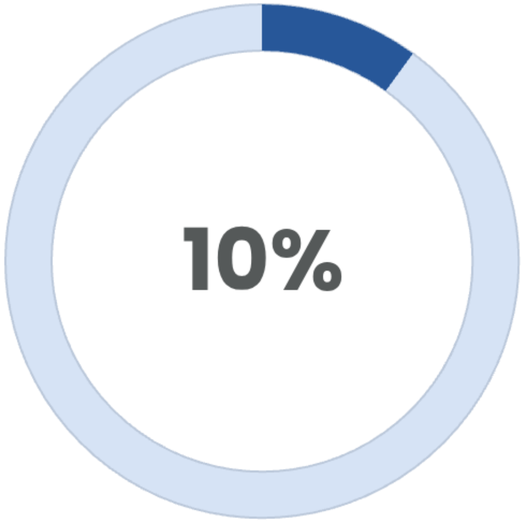
MDRO Burden in SOT



MDR-E Colonization

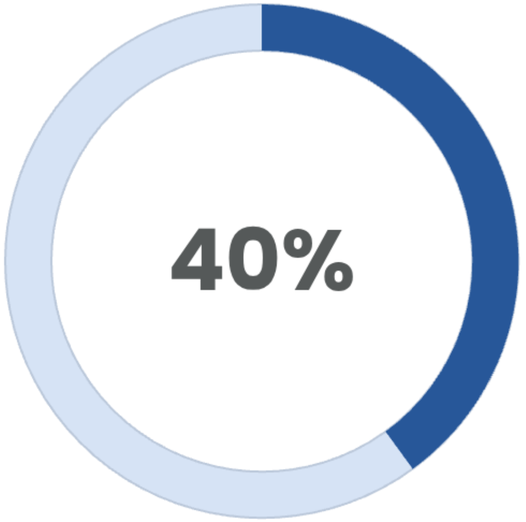
Lung, liver, and small bowel transplant recipients GI-colonized with MDR-E within 100 days post-transplant.

Kidney transplant: 26-45%



MDR-E Infection

of colonized patients develop MDR-E infection within 6 months.



ESBL-EB Bacteremia

In SOT recipients with *Enterobacterales* BSI, caused by ESBL-producing organisms.

- **CRE Infection Rates:** Estimated at 1-16% in liver, 1-11% in kidney, and 1-8.1% in lung transplant recipients.
- **Renal Transplant:** In a cohort of 3507 RTRs, MDRO detection prevalence within 30 days of transplant was 1.3%.

Key Risk Factors for MDRO Infection

Prior Colonization

Previous detection of ESBL-EB is the biggest risk for later ESBL-EB BSI (aOR **12.75**).

Immunosuppression

- Maintenance regimens with corticosteroids (aOR 1.30).
- Treatment for acute rejection with corticosteroids (aOR 1.18).

Antibiotic Use

- Prior use of 3rd-generation cephalosporins (aOR 1.95).
- Prior use of Trimethoprim-Sulfamethoxazole (TMP-SMX) (aOR 1.35). Important because it's used to prevent PJP.

Surgical Factors: Needing more surgery raises the risk of CRE infection (OR 10.2).

The Impact of MDRO on SOT Outcomes

Graft Loss and Mortality

In renal transplant, MDRO detection within 30 days is significantly associated with a composite of 1-year allograft loss or mortality (aHR **3.29**). This was driven primarily by a >7-fold increased hazard of death-censored allograft loss.

CRE survival

In patients with pre-transplant CRE, those who developed a post-transplant CRE infection had a **50% lower chance of 1-year survival** compared to those who remained uninfected (P=.0204).

Morbidity & Resource Utilization

- MDR-E infected patients have significantly longer hospitalizations (median 31 vs. 17 days).
- Recurrence is common: 44% of survivors of an MDR-E infection developed recurrent infections, sometimes years later.

Predicting ESBL-EB BSI: Clinical Tool (Wang et al.)

A 10-variable scoring system to predict the likelihood of an ESBL-Enterobacterales BSI at the time of initial blood culture identification in a solid organ transplant recipient.

Category / Clinical Variable

- Prior Colonization/Infection (in past 12 months)
  - ESBL-Enterobacterales organism isolated on any prior culture: **+5**
  - *E. coli* isolated on any prior culture: **-1**
  - Enterobacterales organism isolated from a prior urinary culture: **-2**
- Antimicrobial Exposure (in past 6 months)
  - Third-generation cephalosporin: **+3**
  - Trimethoprim-sulfamethoxazole: **+2**
  - Aminoglycoside: **+1**

Category / Clinical Variable (cont.)

- Severity of Illness (in past 48 hours)
  - Mechanical ventilation: **+2**
  - Hypotension: **+1**
- Immunosuppressive Regimen
  - Receipt of non-corticosteroid immunomodulator (in past 30 days): **+2**
  - Corticosteroid-containing chronic regimen: **+2**

A score of ⩾ 2 can be used to define a patient as high risk for an ESBL-Enterobacterales BSI (NPV of 89.9%).

Purpura Fulminans

Purpura Fulminans: Definition and Pathophysiology

Definition: A life-threatening emergency characterized by thrombotic DIC, leading to rapid skin necrosis and organ failure.

Pathophysiology: Severe deficiency of the protein C anticoagulant pathway causes uncontrolled microvascular clotting.

Neonatal

Congenital loss of protein C or S.

Idiopathic

Autoantibodies to protein S after a benign illness.

Acute Infectious (AIPF)

- *Neisseria meningitidis*
- *Streptococcus pneumoniae*
- *Staphylococcus aureus*
- *E. coli* is uncommon, rare case reports

Key Laboratory Findings: Severe DIC with profound protein C depletion (<40%), low protein S and antithrombin, thrombocytopenia, prolonged coagulation times, and elevated D-dimer.

Purpura Fulminans in the Post-Surgical Setting

- **Context**

  AIPF is a devastating, though uncommon, postoperative complication.

- **Onset**

  Can occur rapidly, with a mean onset of **3.9 days** following surgery.

- **High-Risk Procedures**

  A case series of 7 cases found a predominance of AIPF following vascular and abdominal surgeries (prolonged ties and tissue manipulation). One case report detailed PF developing four days after a heart transplant due to *E. coli* sepsis.

- **Causative Pathogens**

  Klebsiella pneumoniae and *Escherichia coli*, are the most prevalent pathogens in the postoperative setting, likely due to endotoxin release that fuels the hypercoagulable state.

Clinical Presentation: Typical vs. Our Case

Classic Skin Manifestations

- Begins with erythema or livedo racemosa (a reddish-blue mottling of the skin).
- Rapidly progresses to irregular, blue-black areas of hemorrhagic necrosis (retiform purpura) and full-thickness skin loss.
- Vesicles and bullae may form on the necrotic areas.

Typical Distribution

The rash classically begins on **acral surfaces** (distal extremities) such as the **nose, knees, hands, and feet**.

Atypical Presentation in Our Case

The patient's rash was most prominent centrally on the **abdomen, upper legs, groin, and vulva**.

Management of Purpura Fulminans

Treat the Infection

Prompt broad-spectrum antibiotics to combat infection.

Restore Anticoagulation

- **Protein C Concentrate:** Key repletion therapy (100-150 IU/kg).
- **Antithrombin Concentrate:** Supports heparin effectiveness.

Therapeutic Anticoagulation

IV unfractionated heparin to halt thrombosis, despite coagulopathy.

Aggressive Supportive Care

Resuscitation, mechanical ventilation, and clotting factor replacement (FFP, cryoprecipitate).

Surgical Approach

Favor conservative amputation. Delay debridement until clear demarcation, unless wet gangrene is present.

Despite best efforts... Mortality

57% and 60%.

Polling Question 4

Reflecting on this case, what do you believe was the most critical factor contributing to the fatal outcome?

> A. The complexity and duration of the initial surgery.
> B. The inherent virulence of the ESBL *E. coli* strain causing purpura fulminans.
> C. The delay in escalating from cefepime to a carbapenem while the patient was evolving septic shock.
> D. The patient's underlying immunosuppression and comorbidities.
> E. Other: free text

Summary: Key Takeaways

MDRO Risk

MDROs pose a significant threat in SOT recipients, increasing graft loss, mortality, and healthcare costs.

Prophylaxis Challenges

Balancing targeted prophylaxis with avoiding carbapenem overuse is a complex challenge.

Atypical Presentation

Purpura fulminans can manifest atypically, potentially delaying diagnosis.

Predictive Tools

Tools like the Wang et al. scoring system can identify high-risk transplant recipients.

Purpura Fulminans

Purpura fulminans is a rare, devastating complication requiring swift recognition and aggressive management.

Personalized Approach

A comprehensive approach to risk stratification and individualized decisions are necessary.

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