Challenging Cases in Infectious Diseases
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Disclosures
• Speaker’s Bureau
• Cubist Pharmaceuticals

Objectives
• Become familiar with treatment challenges of invasive MRSA infections
• Understand changing epidemiology of community-acquired urinary tract infections and current options for multi-drug resistant pathogens
• Differentiate potential treatment options for invasive Candida infections
• Become proficient in treatment recommendations for Clostridium difficile

Survey Question

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Strain of 1997
You are the next class of drug-resistant bacteria. As humans continue to abuse and overdose antibiotics, your ranks will swell. So go out there and mutate! And remember: that which does not kill us makes us stronger!
Case 1

60 yo BM with non-Hodgkin’s lymphoma requiring chemotherapy presents with fever (temperature in ED of 103.3), rigors, chills, and overall poor appetite. Upon examination of his groshong catheter, notable fluctuance is present and erythema around the catheter site. Paired blood cultures are drawn both centrally and peripherally. Twelve hours after admission, all four cultures grow gram positive cocci in clusters. After removing the catheter, the team asks for your recommendation regarding antimicrobial therapy.

Case Question 1

S. aureus Bacteremia

- S. aureus bacteremia is deadly!!
- Mortality
- Morbidity
  - Complications
  - Relapse
- Treatment of SAB and IE depends on:
  - Extent of disease
  - Source control
  - Appropriate therapy
- S. aureus bacteremia is increasing
  - Driven by MRSA

S. aureus bacteremia/endocarditis-
Initial treatment options

- Antistaphylococcal penicillins (i.e. nafcillin/cefaZolin)
- Superior to vancomycin for MSSA
- Vancomycin 15-20mg/kg/dose q8-12h
- Doses based on normal renal function
- Gentamicin/rifampin no longer recommended for native valve endocarditis
- Daptomycin 6mg/kg once daily
- Higher doses (8 or 10mg/kg) sometimes utilized

Case 1 Continued

Blood cultures reveal methicillin-resistant S. aureus (MRSA). You initially chose vancomycin 15mg/kg IV q12h. The groshong catheter is removed and a temporary catheter is placed. During his first seven days of therapy, he continues to be febrile (Tmax 102 on day 7 of therapy) with a WBC of 14.2 and continues to have positive blood cultures for MRSA. His latest vancomycin trough was 17 two days ago.
Case Question 2

Case Question 3

Vancomycin in 2011

- Over 50 years since introduction
- Approved based on open label data by FDA in 1958 on 15 patients
- "Drug of Choice" for serious MRSA infections for many years
- "Slowly" bactericidal aka "Dial-up internet killing"
- Increased failure rates in MRSA isolates within the susceptible range (MIC ≤ 2mg/L)

Management of Persistent Bacteremia/Vanc Tx Failures

- Search/removal of other foci of infection
- Daptomycin 10mg/kg plus one of the following:
  - Gentamicin img/kg IV q8h
  - Rifampin 600mg PO/IV daily or 300mg/450mg PO/IV BID
  - Linezolid 600mg PO/IV BID
  - TMP/SMX 5mg/kg IV BID
  - ...or a beta-lactam antibiotic

Case 2

- CR, a 37 year old white female reports to her PCM with symptoms of dysuria and increased urinary frequency. Her vital signs are normal and patient is not experiencing any flank pain. Dipstick urinalysis shows 2+ leukocyte esterase, 55 WBC, and nitrite negative. Urine culture is drawn as well. Her last UTI was several years ago. She has NKDA.

Case Question 1
Uncomplicated Cystitis-Options

- Assess the following
  - Allergies
  - Availability
  - Previous use
  - Local resistance rates
  - Fluoroquinolones reserved for patients who are not candidates for other first-line agents

Uncomplicated Cystitis-Options

- Nitrofurantoin macrocrystals (e.g. Macrobid)
  - Good data for 5-day regimens
  - Avoid in pyelonephritis
- Trimethoprim/Sulfamethoxazole
  - 3-day regimens
  - Avoid if recent UTI or local E.coli resistance ≥ 20%
- Fosfomycin
  - Avoid in pyelonephritis
  - Single dose but slight decrease in efficacy
- Beta-lactams
  - Decreased efficacy compared to other agents

Case Question 2 continued

- CR reports back 2 months later with similar symptoms of her previous UTI. Her urinalysis again shows 3+ leukocyte esterase with many WBC and nitrite positive. She has a temperature of 101.0 F, HR of 130, and rigors in the clinic and has some mild intermittent back pain that started yesterday and is worsened today. You examine her last urine culture and it revealed a pan susceptible E. coli isolate. She is admitted to the hospital for escalated care.

Treatment options-pyelonephritis (hospitalized)

- Intravenous therapy recommended
- Fluoroquinolones (except moxifloxacin)
- Aminoglycosides +/- ampicillin
- Extended spectrum ceph/pcn +/- aminoglycoside
- Carbapenem
Case 2 continued

- CR responds to treatment. Several months later she represents with recurrent symptoms of a UTI with fever, back pain, and tachycardia for which she is readmitted. She recently received a 2-week course of amoxicillin/clavulanate for acute sinusitis. Her urine culture comes back today revealing an E. coli isolate with the following susceptibilities: Ampicillin(R); Amox/Clav(R); Ceftriaxone (R); Ertapenem (S); Gentamicin(S); Levofoxacin (R); Meropenem (S); TMP/SMX (R); Tobramycin (S). The family medicine physician would like a recommendation for an oral antibiotic for transition.

ESBL-producing bacteria

- Extended-spectrum beta-lactamase
- Generally E. coli or K. pneumoniae
- Becoming more common in community settings including cystitis/pyelonephritis
- Often resistant to all beta-lactams as well as fluoroquinolones and aminoglycosides
- Carbapenems first-line for serious infections
- Ertapenem or aminoglycosides suitable for UTI due to once daily dosing

Case Question 3

- An 80 year old white male (BD) represents to the ED with fever(100.7°F), severe nausea, vomiting, mental confusion, and abdominal pain. PMH significant for hypertension, DM, and ESRD requiring hemodialysis. He is placed on piperacillin/tazobactam for possible cholecystitis per ultrasound of gall bladder. Patient was recently hospitalized and discharged a couple of days ago for similar symptoms. A urinalysis is performed showing many WBC, leukocyte esterase, and many yeast. Urine culture is pending.

Case Question 1

- BD's nausea/vomiting worsens as well as his abdominal pain. WBC 35K with 15% bands. T 102.3. On HD 3 his original CT scan was reviewed again. Free air was visualized and BD is taken emergently to the OR and severe diverticulitis complicated by perforation is visualized. Patient receives a hemicolectomy with colostomy placement and is placed in the SICU where he is clinically improves. On POD 7 after clinically improving, BD has a fever of 100.0 which prompts blood cultures. On POD 9, blood cultures reveal yeast that are germ tube negative.

Case 3

- An 80 year old white male (BD) represents to the ED with fever(100.7°F), severe nausea, vomiting, mental confusion, and abdominal pain. PMH significant for hypertension, DM, and ESRD requiring hemodialysis. He is placed on piperacillin/tazobactam for possible cholecystitis per ultrasound of gall bladder. Patient was recently hospitalized and discharged a couple of days ago for similar symptoms. A urinalysis is performed showing many WBC, leukocyte esterase, and many yeast. Urine culture is pending.
Invasive Candidiasis
- Nonneutropenic patients
- Fluconazole
  - 800mg x 1 dose, then 400mg daily
  - Caution in treatment of C. glabrata
- Echinocandins
  - Preferred in C. glabrata infections
  - Preferred empirically in patients with recent azole exposure, hemodynamic instability, or areas with high endemicity of C. glabrata
- Voriconazole
  - Little advantage over fluconazole except for C. krusei or possibly C. glabrata (rare)
- Amphotericin
  - Only used if allergies/intolerances/lack of availability


Case 4
- CF is a 75 year old male who presents with 3-5 loose, nonbloody, watery bowel movements daily, fever of 100.4, and abdominal pain. Other vitals are normal and appears euvoletic. CBC and Chem-7 notable only for a WBC of 13.2. He completed a 10-day course of clindamycin for an uncomplicated skin abscess that grew methicillin-resistant S. aureus after I & D approximately one week ago. Stool cultures are sent off as well as clostridium difficile toxin assays. He reports no change in eating habits, diet or travel history. He has NKDA.
C. difficile treatment options

- Metronidazole
  - Preferred in mild-moderate disease
  - Obtains relatively low fecal concentrations
  - 500mg PO/IV TID for 10-14 days
- Vancomycin
  - Preferred in moderate-severe disease
  - Intravenous therapy ineffective
  - Initial dose of 125mg PO/G—tube q6h


Case 4 Continued

- CF completes his 10 day course of metronidazole therapy with resolution of symptoms after his C. difficile toxin assay was positive. Approximately two weeks after completion, he presents to the ED with a 3 day history of 8-10 watery, nonbloody bowel movements. His temperature is 103.3, and is exhibiting mental status confusion. BP is 80/50, pulse of 115, and respiratory rate of 18. WBC is 38K with 20% bands. Aggressive volume resuscitation is begun and the patient is transferred to the MICU for continued volume resuscitation and vasopressors.

Case 4 Continued

- CF continues to deteriorate requiring higher doses of vasopressors and increased lactic acid levels (latest 3.0). WBC has now increased to 60K with a profound left shift.

Case Question 3

Case Question 4

Treatment of Severe-Complicated CDI

- Vancomycin 500mg PO/NG q6h + metronidazole 500mg IV q8h
  - May use rectal vancomycin in cases with ileus
- Passive immunotherapy (IVIG)
  - Usual dosage of 150mg/kg – 400mg/kg
  - Case reports/series only
- Colectomy
  - Lifesaving for megacolon, septic shock, acute abdomen, perforation