ESBL and "SPICE" Organisms

BACKGROUND

- Some Gram-negative bacilli produce "broad-spectrum" β-lactamases that can hydrolyze penicillins and cephalosporins
- The common classes of broad-spectrum β-lactamases are ESBLs (extended spectrum β-lactamases) and ampC beta-lactamases (those produced by "SPICE" organisms)
- While more challenging to treat (due to resistance issues), there is little evidence that these organisms are more virulent than susceptible Gram-negative bacteria

ESBL

- Genes that encode for ESBLs are primarily found on plasmids in some strains of *E. coli, K. pneumoniae*, and occasionally in *Proteus* species
- Although ESBLs may be inhibited by β-lactamase inhibitors (e.g. tazobactam) in vitro, there is concern of higher treatment failure when these agents are used in vivo

"SPICE"

- Colloquial acronym for gram-negative bacteria that have inducible, chromosomal β-lactamase genes known as AmpC
- Resistance may not be detectable initially but appears after a period of exposure to β-lactam antibiotics
- Organisms in this group include: **S**erratia, **P**rovidencia, "**I**ndole-positive" *Proteus* species, **C**itrobacter, and **E**nterobacter species
- Other organisms in this class include: *Acinetobacter*, *Cronobacter*, *Edwardsiella, Hafnia, Morganella*, and rarely *Pseudomonas*

EMPIRIC CHOICES

- Penicillins (with or without β-lactamase inhibitors) and cephalosporins should generally be avoided
- Options for therapy (pending susceptibilities) include: nitrofurantoin (for cystitis only), trimethoprim-sulfamethoxazole, carbapenems, aminoglycosides and fluoroquinolones
- For severe or life threatening illness: meropenem 1g IV q8h (2g IV q8h for CNS infections) OR ertapenem 1g IV q24h (if not treating *Pseudomonas, Acinetobacter* or CNS infection)
- Oral options (e.g. TMP-SMX or fluoroquinolones) may be considered in stable or improving patients

ALTERNATIVES FOR ALLERGIES

- Cross-reactivity for penicillin allergies with carbapenems is ~ 1% (see Clinical Summary on β–lactam allergy)
- Carbapenems may, therefore, be used safely in most patients, unless documented anaphylaxis to penicillin

RISK FACTORS AND OTHER TREATMENT CONSIDERATIONS

- Consider coverage for these organisms in empiric treatment regimens for patients with risk factors and severe, life-threatening infections; however, if no ESBL/"SPICE" organism isolated, switch to less broad-spectrum coverage
- Risk factors for infections caused by ESBL and "SPICE" organisms include:
  - Previous and/or prolonged hospital stay
  - Hemodialysis
  - Prior and/or prolonged antibiotic use
  - Prior infection or colonization with these organisms within past 3 months
  - Travel to areas with high rates of resistance

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