Characterization of Ceftriaxone-Resistant Viridans Streptococci Bacteremia Among Patients at a Comprehensive Cancer Center

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Poster ID: 909307

Modified Abstract

Background: Viridans streptococci (VS) are opportunistic oral commensals and a common cause of bacteremia, particularly in neutropenic patients. We sought to investigate the prevalence of ceftriaxone (CTX) resistance in VS blood isolates at our medical center among patients with cancer or treated with hematopoietic cell transplant (HCT), and to describe treatment and clinical course. **Methods:** In this retrospective single center cohort study, we identified CTX-resistant (CTX-R) VS isolates among patients between January 2005 – June 2020. VS in blood cultures were identified using a combination of biochemicals and mass spectrometry. Susceptibility testing was performed by Kirby Bauer and E-Test. Demographic data, clinical outcomes, and antimicrobial use, including prophylactic, empiric treatment and definitive therapy choices were assessed through electronic medical record review. **Results:** Of unique VS with sensitivities (n=647), 27 (4.2%) patients had confirmed CTX-R VS bacteremia over the 15-year period; the majority were *S. mitis* (23/27 [85%]). 17 (63%) were cancer center patients, of whom 15/17 (88%) had a known hematologic malignancy, 11 (65%) had undergone HCT, and 15 (88%) were neutropenic (absolute neutrophil count ≤500 cells/microliter). Of CTX-R strains, 15/17 (88%) had concomitant resistance to penicillin, erythromycin (12 [71%]), and levofloxacin (12 [71%]); all were sensitive to vancomycin. Most were on levofloxacin prophylaxis (11/17 [65%]) at the time of diagnosis. Initial empiric antibiotic choices primarily included cefepime, ceftazidime, or meropenem, with 16/17 (94%) receiving concomitant empiric vancomycin; 14/17 (82%) were de-escalated to vancomycin once sensitivities were obtained. 2/17 (12%) patients died within 30 days of CTX-R VS bacteremia. Despite increasing susceptibility testing among VS isolates, there did not appear to be an increase in the percentage of CTX-R over time. **Conclusions:** VS is a common pathogen in neutropenic cancer patients treated with chemo and/or BMT, and multi-drug resistant CTX-R strains are of concern. In the modern era of ambulatory cancer care, prescribers must be cautious using ceftriaxone monotherapy in the absence of susceptibility information, particularly among patients with hematologic malignancies.

Introduction

- Viridans streptococci (VS) are opportunistic oral and gut commensals and a common cause of bacteremia in neutropenic patients
- Antibiotic resistance among VS are increasingly reported among cancer patients

Study objectives

- Determine the prevalence of ceftriaxone resistant (CTX-R) VS isolated from blood culture from patients at a large comprehensive cancer center (SCCA)
- Describe antimicrobial resistance, treatment and clinical course

Methods

- VS identification from blood culture: biochemical tests and MALDI-TOF mass spectrometry
- Antimicrobial susceptibilities: Kirby Bauer and E-test
- Patient demographics, hospital course, and treatment regimens assessed via electronic medical record review

Results

Figure 1. Patient selection flow chart

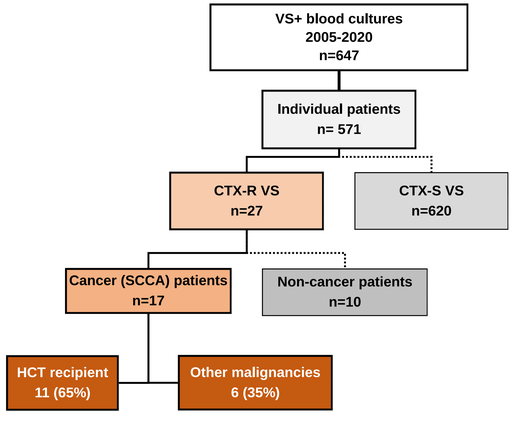

Table 1: CTX-R VS positive patient demographics

Patient demographics	
Age	Average 41.4 (IQR 29.4, 54.4)
Sex	Female 7/17 (42%) Male 10/17 (59%)
SCCA patient	17/27 (63%)
SCCA patients	N=17
Average days inpatient when culture positive	9 (IQR 1, 11.3)
Underlying diagnosis	N (%)
Acute lymphoblastic leukemia	4 (23.5)
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Diffuse large B cell lymphoma	4 (23.5)
Follicular lymphoma	1 (5.9)
Hodgkin lymphoma	1 (5.9)
Myelodysplastic syndrome	1 (5.9)
Multiple sclerosis	1 (5.9)
Sickle cell disease	1 (5.9)
Hematopoietic cell transplant	11 (64.7)
Average time (days) since transplant	8.4 (IQR 5.3, 8)
Neutropenic at time of culture positive	15 (88.2)

Figure 2. VS positive blood cultures from 2005-June 2020

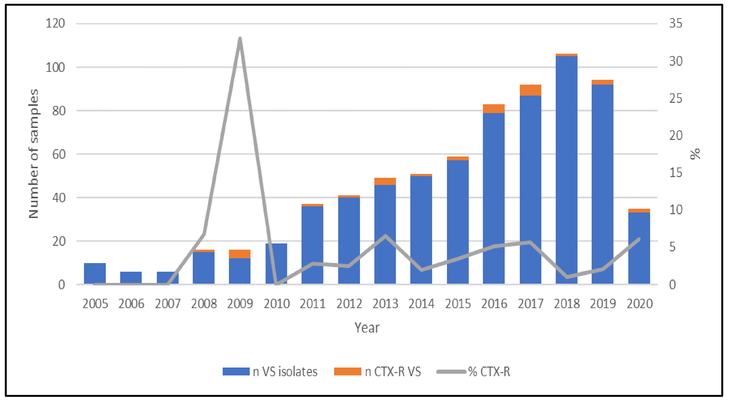


Figure 3. Percent antibiotic resistance in CTX-R VS isolates 2005-June 2020.

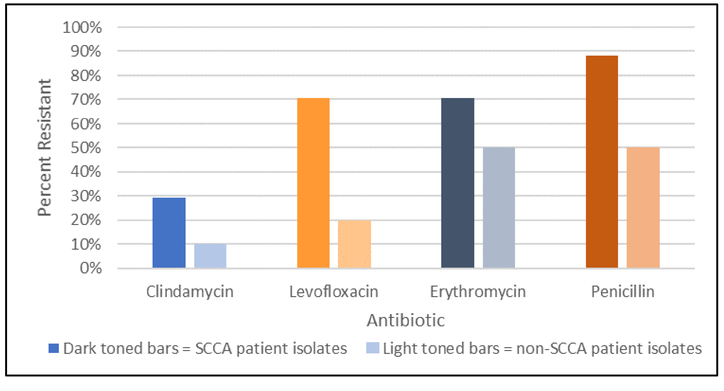


Figure 4A. Prophylactic antibiotics in use at the time of culture positivity (SCCA patients only)

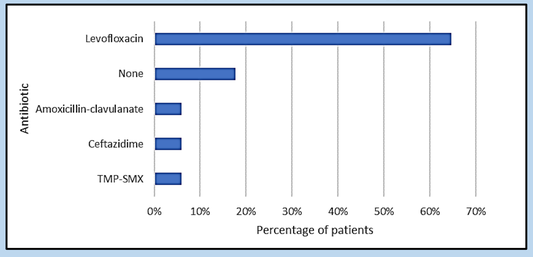
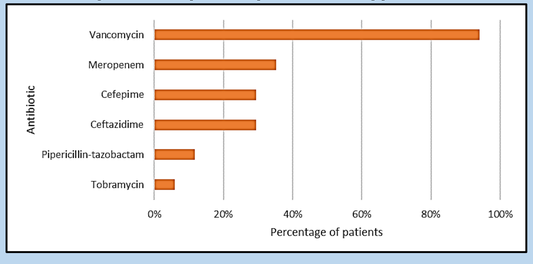


Figure 4B. Empiric antibiotic choices prior to sensitivity results (SCCA patients only)



Conclusions

- CTX-R VS were infrequently found in cancer patients but most were multidrug resistant (MDR) pathogens
- There was no evidence of clustering or increasing prevalence of CTX-R VS over the 15 year study period
- Despite finding MDR VS, available empiric antibiotic choices for neutropenic fever provide coverage for these resistant strains

Summary

- Providers need to be aware of the dangers of antibiotic resistant VS in the neutropenic population, and should be cautious of prescribing ceftriaxone monotherapy prior to susceptibility results