Insights for Nosocomial Infection of *Stenotrophamonas maltophilia* in a Diabetic Patient Following Long Term Antibiotic Usage: A Case Study

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PURPOSE

Long term antibiotic therapy may cause the development of multi-drug resistant nosocomial infections in patient with significant co-morbidities . Recognizing opportunistic infection development in the diabetic foot is essential for the foot and ankle surgeon to appropriately manage and treat these cases. This case study demonstrates the ability for rare nosocomial infections to occur in immunocompromised patients with diabetic foot infections.

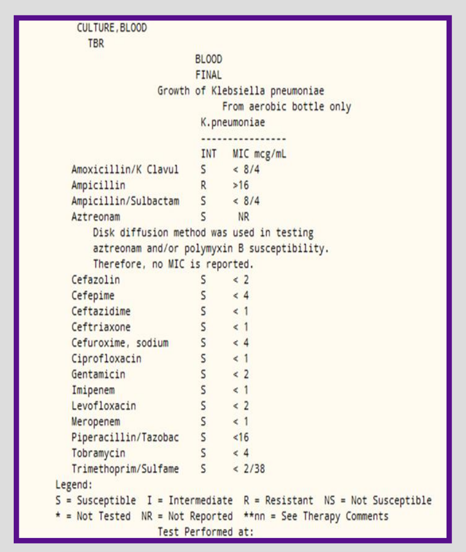
INTRODUCTION

- The genus *Stenotrophomonas* is prevalent across a number of microbiological environments in the clinical setting[1]. The genus is composed of 12 separate species isolated from a variety of diverse habitats[1, 2].
- *Stenotrophomonas maltophilia* is an opportunistic bacterium often seen in at risk populations such as immunocompromised hosts, hospitalized patients and dialyzed patients as well as patient who have undergone extending treatment with broad spectrum antibiotics[1].
- Dialyzed patients are at high risk for S. maltophilia colonization as they are often immunocompromised and utilize catheters[3].
- In a recent report from WHO *S. maltophilia* is a major drug resistant pathogen worldwide in hospital settings[1, 4]. Alavi et al suggest that *S. maltophilia* has a high affinity for acquiring adaptive traits from the surrounding environment, allowing for colonization of a variety of surfaces despite antibiotic or antiseptic treatment.
- *S. maltophilia* is not a common organism causing infection in the general healthy population. Statistical surveillance of the pathogen determines that incidence worldwide ranges from 1.3 to 1.68%[4].

Methodology

- The patient was admitted to NYU Langone Brooklyn Hospital Center for the duration of treatment. All wound cultures and sensitivities were resulted by the NYU Hospitals Center Department of Microbiology.
- The department of Podiatry performed all operative management of the diabetic wound infection. Antibiotic regimens were determined by the department of Infectious Disease in collaboration with the department of Podiatry.
- Following discharge a review of literature was conducted to determine the prevalence of *S. maltophilia* in diabetic wound infections
- Following literature review data and consent for publication were obtained and analyzed in accordance with NYU Langone Health and Hospitals research policy

Tables

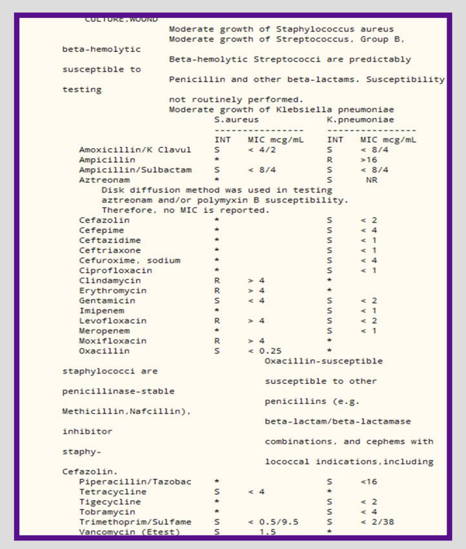


CULTURE,BLOOD
TBR
BLOOD
FINAL
Growth of Klebsiella pneumoniae
From aerobic bottle only
K.pneumoniae

	INT	MIC mcg/mL
Amoxicillin/K Clavul	S	< 8/4
Ampicillin	R	>16
Ampicillin/Sulbactam	S	< 8/4
Aztreonam	S	NR
Disk diffusion method was used in testing aztreonam and/or polymyxin B susceptibility. Therefore, no MIC is reported.		
Cefazolin	S	< 2
Cefepime	S	< 4
Ceftazidime	S	< 1
Ceftriaxone	S	< 1
Cefuroxime, sodium	S	< 4
Ciprofloxacin	S	< 1
Gentamicin	S	< 2
Imipenem	S	< 1
Levofloxacin	S	< 2
Meropenem	S	< 1
Piperacillin/Tazobac	S	<16
Tobramycin	S	< 4
Trimethoprim/Sulfame	S	< 2/38

Legend:
S = Susceptible I = Intermediate R = Resistant NS = Not Susceptible
* = Not Tested NR = Not Reported **nn = See Therapy Comments
Test Performed at:

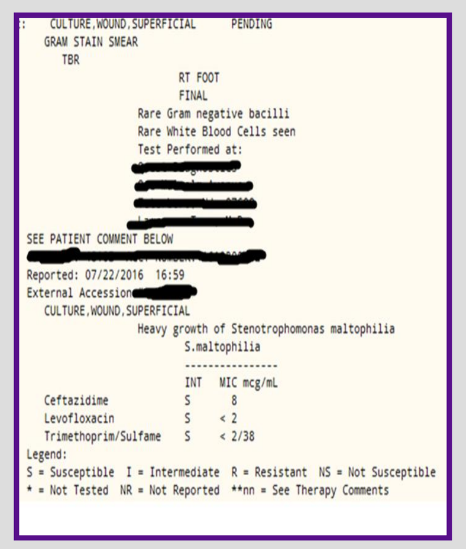
Table 1: Blood culture from hospital day #1 demonstrating growth of *K. pneumoniae*. Sequential blood cultures demonstrated no growth after 5 days of incubation.



CULTURE,WOUND
Moderate growth of Staphylococcus aureus
Moderate growth of Streptococcus, Group B,
beta-hemolytic Beta-hemolytic Streptococci are predictably
susceptible to Penicillin and other beta-lactams. Susceptibility
testing not routinely performed.
Moderate growth of Klebsiella pneumoniae

	S.aureus INT	S.aureus MIC mcg/mL	K.pneumoniae INT	K.pneumoniae MIC mcg/mL
Amoxicillin/K Clavul	S	< 4/2	S	< 8/4
Ampicillin	*		R	>16
Ampicillin/Sulbactam	S	< 8/4	S	< 8/4
Aztreonam	*		S	NR
Disk diffusion method was used in testing aztreonam and/or polymyxin B susceptibility. Therefore, no MIC is reported.				
Cefazolin	*		S	< 2
Cefepime	*		S	< 4
Ceftazidime	*		S	< 1
Ceftriaxone	*		S	< 1
Cefuroxime, sodium	*		S	< 4
Ciprofloxacin	*		S	< 1
Clindamycin	R	> 4	*	
Erythromycin	R	> 4	*	
Gentamicin	S	< 4	S	< 2
Imipenem	*		S	< 1
Levofloxacin	R	> 4	S	< 2
Meropenem	*		S	< 1
Moxifloxacin	R	> 4	*	
Oxacillin	S	< 0.25	*	
Oxacillin-susceptible staphylococci are susceptible to other penicillinase-stable penicillins (e.g. Methicillin,Nafcillin), beta-lactam/beta-lactamase inhibitor combinations, and cephems with staphy- lococcal indications,including Cefazolin.				
Piperacillin/Tazobac	*		S	<16
Tetracycline	S	< 4	*	
Tigecycline	*		S	< 2
Tobramycin	*		S	< 4
Trimethoprim/Sulfame	S	< 0.5/9.5	S	< 2/38
Vancomycin (Etest)	S	1.5	*	

Table 2: Preliminary wound cultures from initial debridement demonstrating growth of *Staphylococcus aureus*, group B *Streptococcus* and *Klebsiella pneumoniae* with antibiotic sensitivities.



CULTURE,WOUND,SUPERFICIAL PENDING
GRAM STAIN SMEAR
TBR
RT FOOT
FINAL
Rare Gram negative bacilli
Rare White Blood Cells seen
Test Performed at:
[redacted]
SEE PATIENT COMMENT BELOW
[redacted]
Reported: 07/22/2016 16:59
External Accession [redacted]
CULTURE,WOUND,SUPERFICIAL
Heavy growth of Stenotrophomonas maltophilia
S.maltophilia

	INT	MIC mcg/mL
Ceftazidime	S	8
Levofloxacin	S	< 2
Trimethoprim/Sulfame	S	< 2/38

Legend:
S = Susceptible I = Intermediate R = Resistant NS = Not Susceptible
* = Not Tested NR = Not Reported **nn = See Therapy Comments

Table 3: Wound culture from second operative debridement demonstrating heavy growth of *S. maltophilia* with sensitivities.

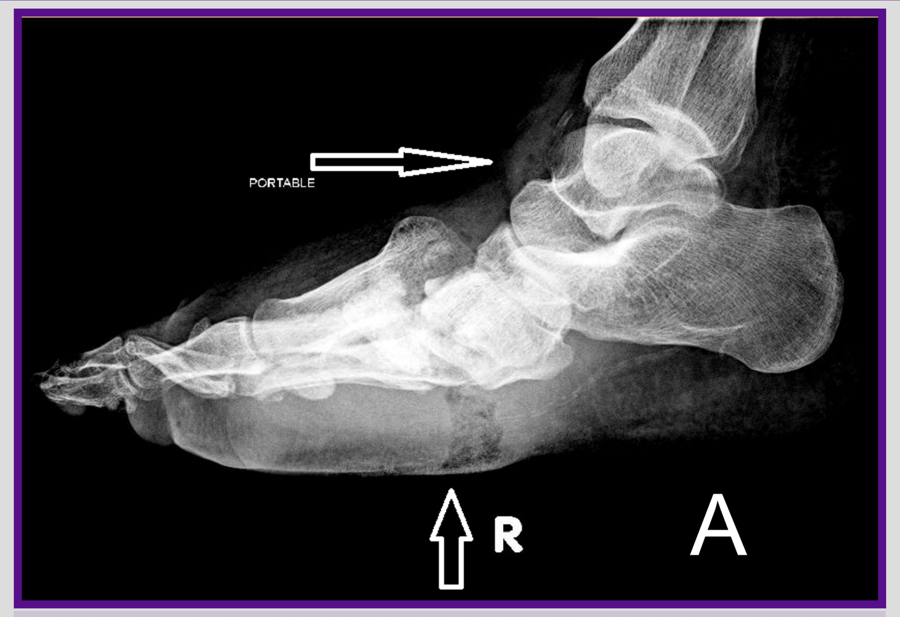
Case Description

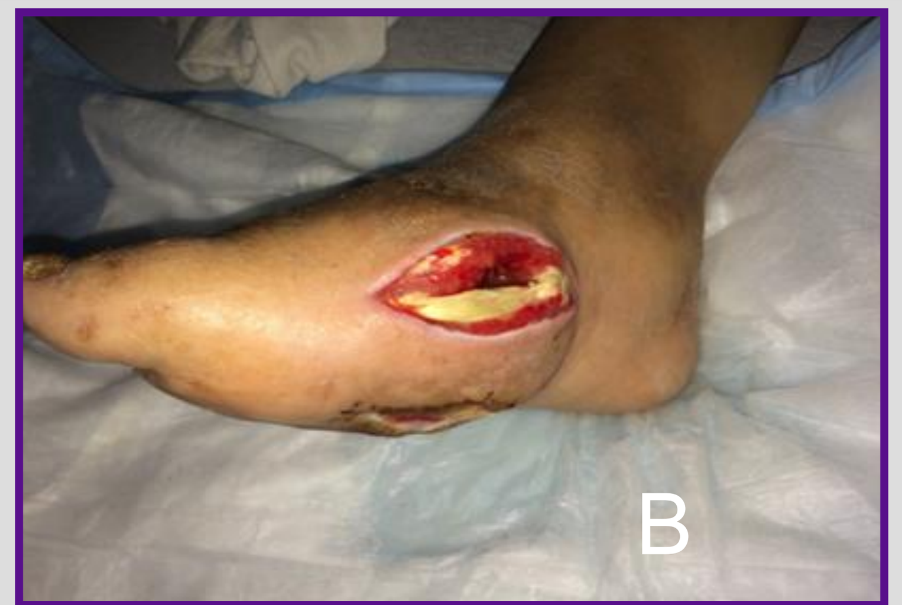
42 year old female with past medical history of HTN, HLD, uncontrolled NIDDM (HbA1C >12%), and ESRD presented to the NYU Langone Brooklyn Hospital Center complaining of lethargy, fever, chills, and a chronically infected diabetic foot ulceration. The patient had history of diabetic ulcerations to both feet with multiple digital amputations and a chronic charcot arthropathy deformity to the right foot as well as a history of long term antibiotic therapy secondary to history of MRSA. An allergy to iodine contrast was noted. Upon presentation patient was transferred to hemodialysis emergently with a creatinine level of 14.5 mg/dL. Department of Podiatry was consulted for a right foot ulceration which had been present prior to hospital admission.

The patient appeared diaphoretic with distinctive facial pallor. There was a Wagner grade 3 ulceration to the plantar medial aspect of the right foot. The right lower extremity was markedly edematous and erythematous. The right foot ulceration actively expressed gray purulent drainage upon compression and was grossly malodorous with crepitus extending proximally to the talonavicular joint. **Lab studies demonstrated a white blood cell count of 32.9 K/µL with an oral temperature of 99.4 degrees Fahrenheit.** The patient could not be optimized for surgery at the time and instead underwent incision and drainage with blunt dissection of fascial planes to during emergent dialysis. Initial wound cultures were taken and broad spectrum antibiotic therapy was initiated to include **vancomycin, flagyl and cefepime**. Following bedside debridement, the next blood draw measured a **white blood cell count of 23.3 K/µL**. Blood cultures resulted in growth of ***K. pneumoniae*** with accompanying wound cultures growing **Beta-hemolytic *Streptococcus* and *K. pneumoniae***. After medical optimization the patient underwent a surgical incision and drainage, debridement of devitalized and necrotic tissue and pulse lavage the following day. Pre and postoperative x rays are seen in figure (1) along with the first postoperative clinical photo.

The patient demonstrated increased awareness and subjective constitutional status with **decreased white blood cell count, down to 9.0 K/µL**, and no growth in blood cultures. Pathology from bone demonstrated acute inflammation associated with acute osteomyelitis. However, the surgical site showed little to no improvement and continued to express purulent drainage. In the days following the **white blood cell count increased to 19.0 K/µL**, accompanied by fever and emesis peaking on post op day #4. A magnetic resonance image (MRI) of the right foot was performed on hospital day #6 in order to determine if a drainable collection of fluid was present (figure 2). No collection was demonstrated. Broad spectrum antibiotic therapy was continued as the patient required temporary shiley catheter access for daily hemodialysis. Serial cultures were taken to plan for delayed primary closure. On hospital day #7 bedside cultures demonstrated growth of *S. maltophilia*. An angioplasty of the right lower extremity was performed to increase blood flow proximally to increase limb viability. A second surgical debridement was performed on hospital day #10 with cultures obtained. A singular organism, *Stenotrophomonas maltophilia*, was isolated from perioperative cultures. The second debridement did not resolve clinical signs of infection nor improve abnormal laboratory markers of infection. Antibiotic therapy was adjusted for new sensitivities and colonization by the opportunistic organism. The patient stabilized and was able to be discharged and managed in an outpatient setting. The progression of leukocytosis and temperature is shown in Graphs 1, 2. Cultures and sensitivities are shown in table 1, 2, 3 from blood and wound sites respectively.

FIGURES





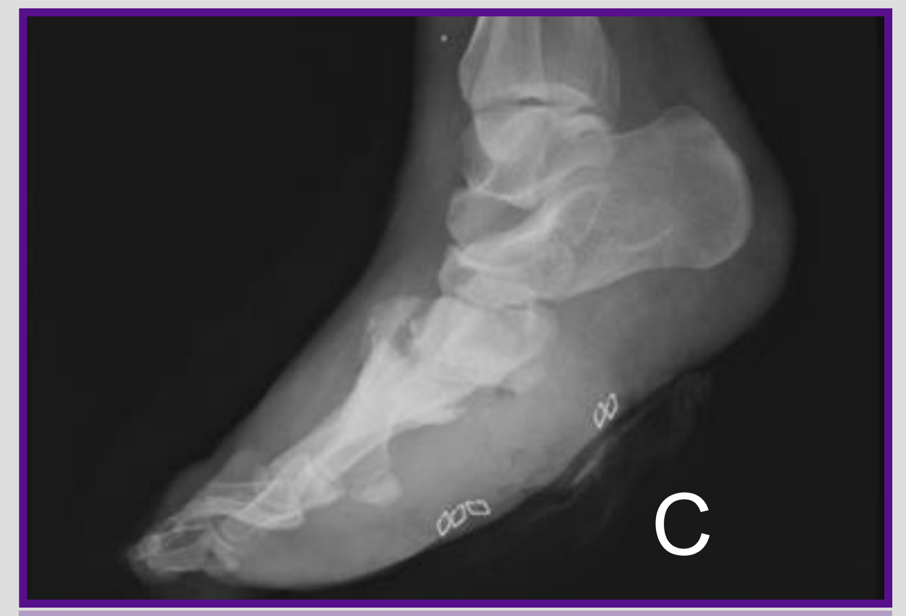


Figure 1: Preoperative radiograph (A) demonstrating soft tissue emphysema, previous amputation and significant, neuroarthropathy to the midfoot. Postoperative clinical photo (B) and postoperative radiograph following incision and drainage (C)

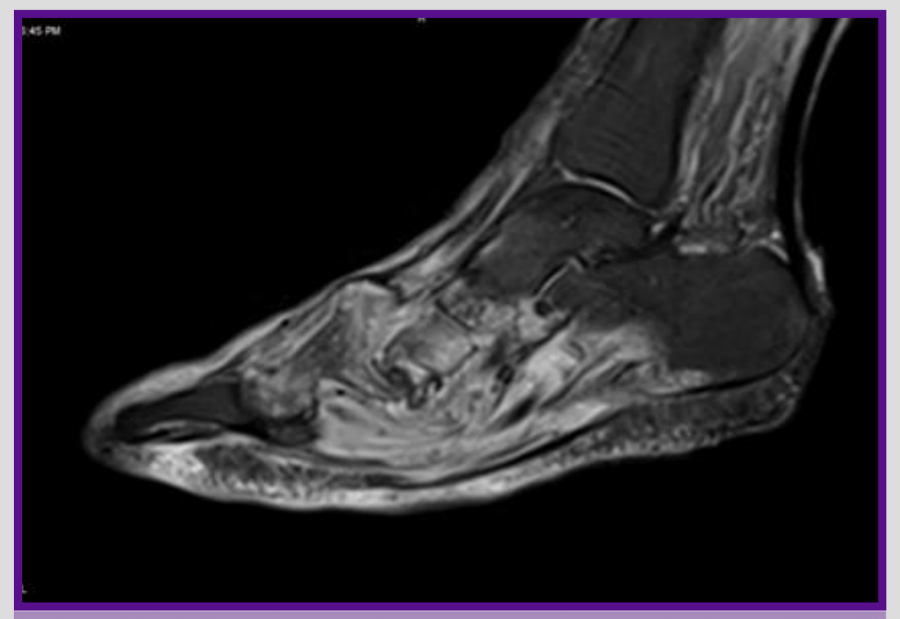
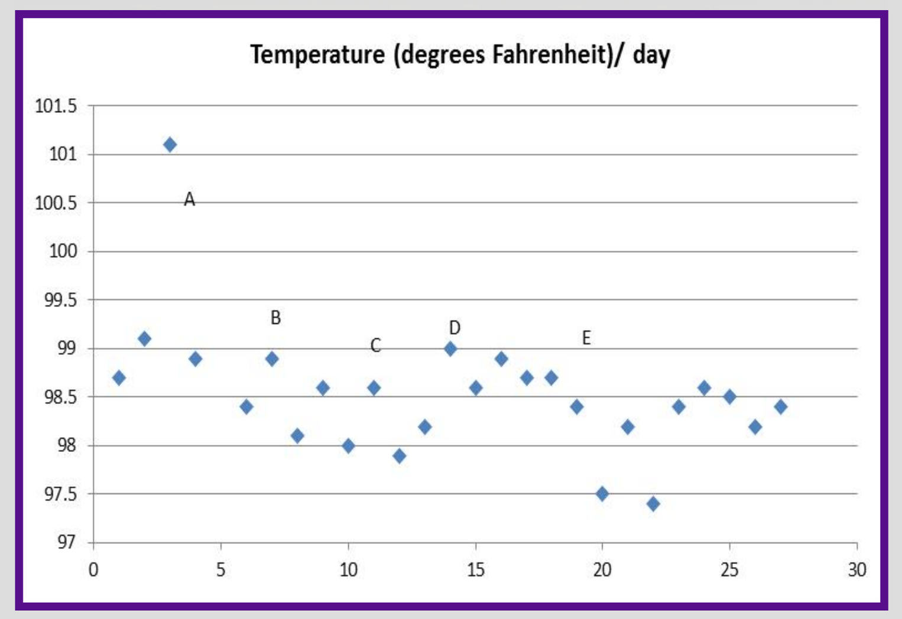
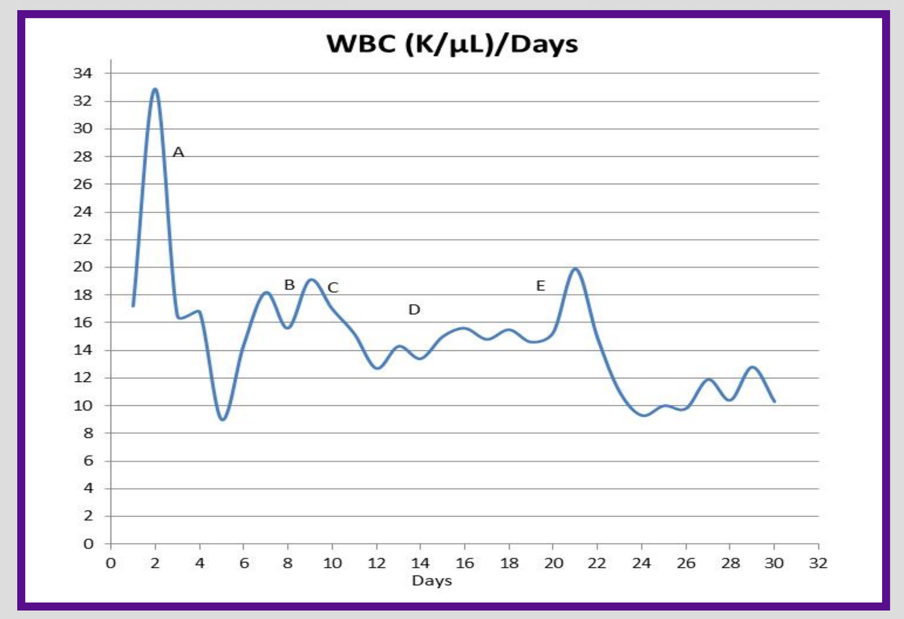


Figure 2: T2 Magnetic resonance imaging sagittal cross section at level surgical incision with no drainable collection noted. Significant signal uptake is noted to the midfoot.



Graph 1: Graph trending oral temperature over the course of hospital admission. Point A represents the first operative incision and drainage, B represents *S. maltophilia* first growing on wound cultures, point C represents a second debridement and tissue washout, point D represents adjustment of antibiotic therapy, and point E represents proximal angioplasty performed by vascular surgery. service.



Graph 2: Graph trending leukocytosis over the course of admission. Point A represents the first operative incision and drainage, B represents *S. maltophilia* first growing on wound cultures, point C represents a second debridement and tissue washout, point D represents adjustment of antibiotic therapy, and point E represents proximal angioplasty performed by vascular surgery.

Results

- The cultured secondary pathogen was sensitive to ceftazidime, levofloxacin and trimethoprim/ sulfamethoxazole.
- The treatment team chose to use ceftazidime as it also provided antibiotic coverage for the initial wound and blood cultures.
- Change in antibiotic therapy was initiated following multiple surgical debridements and proximal angioplasty of the lower limb.
- The patient was discharged with a peripheral intravenous central catheter for outpatient antibiotic therapy.

Discussion/ Literature Review

- The patient was subjected to multiple regimens of broad spectrum antibiotic therapy over the course of multiple digital amputations and hospital admissions. In combination with extensive comorbidities a less virulent pathogen was able to opportunistically cause reinfection of the foot.
- This bacterium in particular is notorious for broad spectrum antibiotic resistance and virulence factors that promote survival in the hospital setting[5]. This organism has the ability to adhere to plastics, glass, and thrive in liquids as well as remain unharmed by various sterilizing agents[6]
- *S. maltophilia* is an emerging nosocomial pathogen that may present problematic for individuals who undergo prolonged antibiotic therapy[1, 2, 3, 4].
- Long term antibiotic therapy may suppress more virulent organisms and allows normally non-pathogenic organisms to become the dominant colonizers of a wound[11].
- The first line treatment for *S. maltophilia* is typically trimethoprim sulfamethoxazole, and levaquin[5], which demonstrated increased sensitivity in our cultures, however due to previous history of methicillin resistance staphylococcus aureus infection, our treatment team felt that rapid resistance and superinfection were risk factors.
- Optimal treatment of nosocomial infections has been shown to decrease morbidity and mortality as well as length of stay in intensive care units[2].
- There are relatively few cases reported of *S. maltophilia* involved in skin and soft tissue infection[8]. Abdulhak et al. identified 16 reported cases of intact skin infections of *S. maltophilia*. Nag *et al.* describes one case of a primary community associated infection of an immunocompetent host who sustained a farming injury to the lower leg. This case was successfully treated with TMP-SMX.
- In a survey of bacterial diversity in chronic wounds using advanced sequencing techniques the United States Department of Agriculture determined that *S. maltophilia* was a wound colonizer in only 1.83% of the samples sequenced and none of the bacterial cultures[6].

Conclusions

It is important to recognize and treat nosocomial infections appropriately. In this case study, a highly resilient bacterium, S. maltophilia, was able to thrive in a host environment in which more pathogenic bacteria were subdued by extensive broad spectrum antibiotic therapy both during and previous to the course of one individual hospital stay. We have noted that skin and soft tissue infections with this organism are exceedingly rare. However, the emergence of nosocomial infections in individuals who have undergone extensive exposure to broad spectrum antibiotics must be managed accordingly. S. maltophilia may play an important role in the pathogenesis of diabetic foot infections and strategy for effective treatment of nosocomial infection.

References

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