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Case Report

# Toxic shock and mortality in a dialysis patient

**Akbar Mahmood[1], Muhammad Imran[2] & Abdullah Balkhair[1]**

[1]Sultan Qaboos University Hospital, Oman

[2]Dow Institute of Medical Technology, Dow University of Health Sciences (DUHS).

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Corresponding Author Email:
imrmaan@gmail.com

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## Abstract

**Background:** Staphylococcus and Streptococcal infections are a matter of serious concern in the dialysis population especially those having tunnel catheter access. Importance of these organisms is their virulent nature, higher incidence and prevalence in tunnel catheters resulting in significant morbidity and mortality. Staphylococcal toxic shock syndrome (STSS) is an uncommon but potentially fatal disease with multisystem involvement. This is a case of toxin-producing methicillin sensitive staph aureus (MSSA) which is known to have high mortality. A high degree of clinical suspicion and prompt management is necessary to avoid fatality. The aim of the study was to get the idea for the management of the toxic shock in terms of reducing the morbidity and mortality rate.

**Case presentation:** This case progressed to state of shock within few hours of presentation to emergency room and admission, attributed to be toxic shock with multi-organ failure.

**Management and Results:** In the management of the patient at the very beginning the infected catheter was removed further aggressive resuscitation and empirical antibiotics were administered but this case resulted into a fatality.

**Conclusion:** The early action for source removal of the infection, appropriate antibiotic therapy and adjuvant therapy including clindamycin and immunoglobulin can effectively treat the toxic shock and its related complications.

## Keywords

Staph Aureus, Toxic Shock, Adjuvant Therapy, Mortality, Staphylococcus.

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## Introduction

Streptococcus and Staph Aureus infections are known to be associated with the production of toxin1 which can lead to grave consequence including shock known as toxic shock syndrome (TSS), resulting in multi-organ failure and death[1&2]. Staph Aureus produces exotoxins which stimulate T cells directly and produces cytokines[3]. These toxins are known as superantigens which has a unique mode of action in the activation of T cells[3].

Normally antigens are taken up by antigen presenting cells, this combination attaches with major histocompatibility complex type 2 MHC II and this complex attaches with T cell receptors resulting in the activation and cytokine release[4]. Activated T cells release interleukin (IL) 1 and 2, tumor necrosis factor (TNF) and interferon (INF) gamma resulting into the signs and symptoms of TSS. IL1 is pyrogenic and proteolytic to skeletal muscle membrane manifest as fever and high creatine phosphokinase (CPK)[5]. TNF inhibits chemotactic migration of neutrophils and staph exoprotein synthesis is halted by this staph toxin[6].

Neutrophil chemotaxis and production of exoprotein are the mechanisms involved in pus formation. This is the reason purulent discharge is not formed in TSS[7]. The infected individual usually develops an antibody against this toxin which is a protective mechanism but INF surge due to enormous activation of superantigen-mediated T cells inhibits immunoglobulin production. These inflammatory cytokines propagate TSS[8&9].

## Case Presentation

A 52 years old male was brought to the Emergency Room in a drowsy state with a history of weakness and poor respiratory effort noticed by the family about six hours earlier. On arrival he was poorly responsive to verbal commands, transcutaneous saturations recorded 87% on room air and lowish systolic blood pressure (SBP) 95mmHg. The family was unable to tell detailed history. Other clinical observations included the right jugular perm catheter, without any obvious sign of local infection and crackles on the right lung base. Rehydration and inotropes commenced, intubated immediately and baseline blood works collected along with the septic screen. Ten minutes after intubation he developed cardiac arrest due to pulseless electric activity (PEA). He revived after two minutes of cardiopulmonary resuscitation. After successful resuscitation, he was shifted to intensive care unit (ICU).

## Medical History

His medical history comprised of long-standing complicated diabetes, hypertension and maintenance hemodialysis of five years duration through perm catheter. After the failure of the first fistula two years ago he never proceeded for another one. He was hospitalized four months earlier for Cath related Methicillin-resistant staph aureus bacteremia (MRSA) which was complicated with discitis and infective endocarditis which, led to cardiac tamponade. He was treated with Vancomycin, catheter removal, reinsertion of another tunnel line after obtaining sterile blood culture and pericardiocentesis.

## Management & Results

In the ICU baseline laboratory, results showed: Hemoglobin 12.7g/dl. Hematocrit (HCT) 0.47L/L, White Blood Cells (WBC's) 10.5, Neutros 8.5, Platelets <45000, international normalized ratio (INR) 12.6, active partial thromboplastin time (APTT)>180 seconds, aspartate aminotransferase (AST)>6000 international units (IU), alkaline phosphatase 300U/L, Creatinine Kinase (CK ) 6936 U/L, hyperbilirubinemia, C reactive proteins (CRP) 385mg/L 385, serum albumin 18g/L, total

proteins 69g/L, Potassium K 5.3mmol/L, Sodium (Na) 125mmol/L, urea 8.3mmol/L, Creatinine 278ummol/L, corrected calcium 2.25mmol/L, Phosphate 1.9mmol/L and Troponin-t 299ng/L (ref.<14ng/L). Bedside echo revealed global hypokinesia, no evidence of intracardiac vegetation or pericardial effusion. Vancomycin & Amikacine were administered empirically by consulting infectious disease team on call. Preliminary blood culture was reported with MSSA. Based on the clinical presentation and rapid deterioration of the events diagnosis of STSS was unanimously agreed by the multidisciplinary teams, including acute medicine, infectious disease (ID), intensive care specialist intensives, microbiologist and nephrologist. Based on the high mortality risk of the condition Intra Venous Cloxacillin, Clindamycin and IV immunoglobulin was administered according to 1g/Kg Wt; along with inotropes and fluids. Permcath was removed within 24 hours of admission considering it sepsis source and a mandatory step towards source removal. Despite all this aggressive management approach, the patient didn't survive and died within 24 hours.

## Discussion

Considering relatively higher incidence of infection in a dialysis population especially among those with catheters and its serious consequences any trivial complaint and unexplained feature merits careful attention to the search for typical or atypical signs of infection systemic malfunction any obvious or hidden source of infection especially related to the catheter and its tunnel be searched meticulously[6]. In this case study, the uniqueness is based on the source of infection due to biofilm on the urinary catheterization, the toxic shock syndrome was developed and the dialysis patient died within 24 hours. In the case occasionally no obvious source was detected but catheter-associated biofilm should not be overlooked which is always a potential source which usually manifests without an obvious clue of Cath site or any other infective focus[4&10]. Leligdowicz (2014) retrospective multicenter big study data supported our views that the patients those received appropriate antibiotic therapy after hypotension, the source of infection was strongly associated with mortality after adjustment of both predisposing and downstream factors[11].

Wilkins (2017) studied that antibiotic use alone is not sufficient as it doesn`t alter the mortality outcome. This fact has been highlighted in Australian study where no mortality was reported due to the use of immunoglobulin in comparison to UK trial. Desirable is to start antibiotics within three hours of presentation to the hospital, which is considered as a golden window of opportunity[12]. Sganga (2016) also suggest considering treatment of exposed contacts of MSSA infected cases with prophylactic antibiotics whether they exhibit any sign or symptom of infection as exposed contacts are at particular risk for themselves and to the community[13]. Prompt initiation of treatment with fluids, inotropes and the first dose of antibiotic can make difference in terms of morbidity outcome. Delay in management, unnoticed or untreated infection leads to death. Mortality risk has been reported as high as up to 40% identified all infective sources merits immediate source removal with the appropriate use of antibiotics[14&15].

This is considered a lifesaving step. Early involvement of the infectious disease team helps faster and safe recovery with lesser events of relapse and hospitalization[16&17]. If the subject is hemodynamically stable, catheter site is clean and there is no clinical evidence of distant infection then initiate empirical broader spectrum antibiotics covering both gram-negative and positive organisms after obtaining septic screen including cultures from the central line. If the

Cath site depicts signs of infection or pus discharge then it is mandatory to remove it immediately as a measure of source control[17].

Studies have proven a clear benefit to cover both Methicillin-sensitive and resistant staph and streptococci which can be adjusted later based on the final culture and sensitivity results[18&19]. The yield of staphylococcus is very low as compare to streptococcus 5% and 60-70% retrospectively[20]. Methicillin-sensitive staph Aureus (MSSA) is sensitive to penicillin but this drug is not considered antibiotic of choice due to a higher incidence of resistance[21]. Cefazoline is the treatment of the first choice to treat MSSA because of less resistance, better tolerability and ease of use among dialysis patient as dose can be modified and administered post-hemodialysis[22].

A most important intervention in the management of TSS besides treatment mentioned so far is the administration of two agents one is clindamycin and intravenous immunoglobulin which is called adjuvant therapy[23]. Clindamycin has the advantage of halting the process of toxic antigen production thus inhibiting the perpetuation of shock state, tissue penetration and synergistic effect when used along with conventional antibiotic[24]. Clindamycin is bacteriostatic, recommended to be used only as an adjuvant agent with either penicillin or Cefazoline to avoid resistance[25]. Adjuvant use of immunoglobulin along with penicillin and clindamycin in this critical situation is considered lifesaving although evidence of widespread immunoglobulin use is weak, it is based on small observational studies only, no randomized control trial support its use but results are promising[26&27].

Most studies focusing on TSS are conducted on the pediatric population. Immunoglobulin acts as an immunomodulatory and anti-inflammatory agent, produces antibodies which neutralize toxin producing streptococcal and staphylococcal antigens thus aborting inflammatory cascade preventing shock. Two retrospective studies are worth mentioning in support of the use of adjunctive therapies in TSS. One is from United Kingdom (UK) and other from Australia British Pediatric Surveillance Unit reported 77% cases required intensive care and mortality incidence of 16% in streptococcal TSS due to the observation that only 20% received immunoglobulin[28]. An Australian study showed a higher incidence of staph-related TSS but 100% survival which is attributed to the use of clindamycin or immunoglobulin. Recommendation for treatment is two weeks with intravenous antibiotics, not oral therapy[29].

## Conclusion

Based on this case it can be concluded that TSS is a rare but not uncommon condition in the dialysis population particularly in those having indwelling tunnel catheters. The early detection of the infection and removal of the source of infection can reduce the morbidity and mortality rate among the patients of the dialysis.

## Conflicts of Interest

None.

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