Multi drug resistant pseudomonas infection in open fractures post definitive fixation leading to limb loss: A report of three cases

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ABSTRACT

Introduction: Infection is a common complication in multiply traumatized patients with the majority being nosocomial in origin. We report a series of three patients with open fractures of lower limb which were initially debrided and stabilized with external fixation. Subsequent conversion to definitive internal fixation was performed. All three patients subsequently suffered limb loss as a result of multiple drug resistant pseudomonas aeruginosa infection. Case report: We report three cases. Case 1 is a 48-year-old alcoholic male who sustained a Gustilo grade 3 (a) open fracture of the right tibia and Gustilo grade 1 open fracture on the contralateral tibia. He underwent definitive fixation but subsequently developed a multiple drug resistant pseudomonas aeruginosa infection of the wound. Failure to eradicate the infection and deteriorating soft tissue conditions with infected non-union lead to a final outcome of below knee amputation and secondary stump closure. Case 2 is a 62-year-old male with no significant medical history who sustained a right grade 3 (a) supracondylar femur fracture and a left grade 3 (c) supracondylar femur fracture. He underwent definitive fixation after negative culture results but later developed multiple drug resistant pseudomonas aeruginosa wound infection. Failure to eradicate the infection, bony destruction and deteriorating soft tissue conditions led to a final outcome of removal of implant and above knee amputation post trauma. Case 3 is a 32-year-old female with no significant medical history who sustained a right gustilo 3 (a) supracondylar femur fracture. She later underwent definitive fixation after negative cultures. She subsequently had a multiple drug resistant pseudomonas aeruginosa wound infection. Failure to eradicate the infection and deteriorating soft tissue conditions with progressive destruction of bone led to a final outcome of above knee amputation. Conclusion: Multiple drug resistant pseudomonas wound infection is a very serious complication for patients with high energy open fractures; with a high likelihood of limb loss. Hospital measures to prevent the spread of nosocomial infection is critical for such patients.

Keywords: Open fracture, Internal fixation, Drug resistant pseudomonas, Amputation

INTRODUCTION

Infectious complications of open fractures continue to pose a challenge to orthopedic surgeons and patients. This is an increasing concern with multi-drug resistant nosocomial pathogens. Aggressive and timely repeated surgical debridement, negative pressure dressing and antibiotics (local and systemic) have led to a favorable outcome in many cases. However, the impact of emerging multi-drug resistant Pseudomonas aeruginosa (MDRPA) in musculo-skeletal injuries has not been described in surgical literature. We report a series of three open fractures, which were managed appropriately with wound debridement and external fixation followed by definitive internal fixation when wounds were sterile. Subsequent infection by MDRPA resulted in soft tissue loss and bony destruction leading to amputation in all three cases.

CASE SERIES

Case 1: A 48-year-old, chronic alcoholic male was involved in a road traffic accident and presented with a Gustilo grade 3 (a) open fracture of the right tibia and Gustilo grade 1 open fracture on the contralateral tibia. The left tibia was fixed definitively with an intramedullary nail. Meanwhile, the right tibia required extensive wound debridement and an application of external fixator. Initial wound culture was positive for Enterobacter cloacae sensitive to imipenam and treated accordingly. Extensive skin loss over the fracture site required a local soleus muscle flap and skin grafting on day 21 post-trauma which healed satisfactorily though the wound remained colonized. The patient was discharged well with oral antibiotics, but unfortunately defaulted follow-up and presented five months later with dislodged Shanz pins from the tibia and non-union of fracture.

Removal of external fixator and debridement of pin sites was performed and the non-united tibia was stabilized with a cast. Initial superficial pin track cultures were positive for Methicillin-resistant Staphylococcus aureus (MRSA) sensitive only to vancomycin and fusidic acid, and were treated with topical mupirocin (Bactroban R) to the pin tracks with readmission plans one month later. The patient defaulted follow-up again and presented three months later with healed pin track wounds but with non-union of the tibia. Since inflammatory markers were normal and soft tissue condition was favorable, the patient was subjected to plating of the tibia with autologous bone grafting though persistent colonization with MRSA was not ruled out at that point in time. Intra-operative cultures taken from the fracture at the time of surgery grew MRSA however it was not treated systemically as the patient was asymptomatic and as advised by the infectious disease team. The patient was discharged well at day 14, however subsequent early wound breakdown at day 30 required multiple debridements and vacuum assisted closure (VAC) dressings with intravenous vancomycin. Though the wound was granulating well initially, subsequent progressive wound breakdown resulted in exposure of implant and non-union of the fracture was evident (Figure 1). At this point in time cultures obtained aseptically were repeatedly positive for MDRPA susceptible only to polymyxin with no traces of MRSA. Failure to eradicate the infection and deteriorating soft tissue conditions with infected non-union lead to a final outcome of below knee amputation and secondary stump closure. The stump healed well with no evidence of infection (Figure 2). There were no complications for the left tibia and patient was ambulating full weight bearing on the left limb three months after the surgery.

Figure 1: Intra-operative picture of fracture non-union of Case 1.

Figure 2: Picture of amputation stump wound of Case 1.
Case 2: A 62-year-old male machine operator with unremarkable past medical history was run over by tractor. He sustained a right grade 3 (a) supracondylar femur fracture and a left grade 3 (c) supracondylar femur fracture. Both legs were debrided and stabilized with a bridging external fixator. The left lower limb had an associated vascular injury which required revascularization. After wound debridement was carried out and upon a negative culture result from the surgical site at debridement, both limbs were stabilised definitively with titanium locked plates.

The left leg developed acute ischemic trauma post fixation due to graft thrombosis which was management urgently with a thrombectomy. The wounds healed well in the left leg however there was wound breakdown in the right limb which required multiple debridement and VAC dressings. A subsequent operative culture was positive for MDRPA and was started on polymyxin based on culture sensitivity. However, the patient went into acute renal failure and the polymyxin had to be withdrawn. The acute renal failure resolved thereafter. The patient underwent multiple debridement and VAC dressing with instillation of 2 % acetic acid. However the wound continued deteriorating (Figure 3) and finally developed positive cultures for MDRPA. Failure to eradicate the infection, bony destruction and deteriorating soft tissue conditions led to a final outcome of removal of implant and above knee amputation post trauma. The stump was closed secondarily and healed well with no evidence of infection (Figure 4). Meanwhile the left femur had radiological evidence of healing with no soft tissue issues and good vascularity after six months of follow-up.

Case 3: A 32 year old female (motorcycle pilon rider) with unremarkable past medical history was involved in a road traffic accident. She sustained a right gustilo 3 (a) supracondylar femur fracture with a soil contamination of the wound. Extensive wound debridement with a bridging external fixation was applied. The large open wound was treated with multiple wound debridements and VAC dressings. A definitive fixation with a titanium locked plate was performed with adequate soft tissue cover after negative culture results.

Subsequent wound breakdown was associated with Enterobacter cloacae infection requiring multiple wound debridement and VAC dressings together with systemic ceftriaxone. Cultures were subsequently positive for Pseudomonas and intravenous piperacillin was commenced based on sensitivity. The patient underwent multiple wound debridements with VAC dressings. However, the local wound never improved and the inflammatory markers remained persistently elevated. Therefore, a more radical approach was attempted. The titanium plate was removed and fracture ends excised to healthy bone level. Reconversion to external fixation was performed at the same setting with gentamicin impregnated cement spacer (Figure 5). Subsequent cultures grew MDRPA sensitive only to polymyxin, however the patient developed a serious cutaneous drug allergy and polymyxin was stopped. The patient underwent repeated debridement of soft tissue and aggressive debridement of unhealthy bone followed by VAC dressings. Failure to eradicate the infection and deteriorating soft tissue conditions with progressive destruction of bone led to a final outcome of above knee amputation. The stump was closed secondarily and healed well with no evidence of infection after 4 months of follow-up (Figure 6).

DISCUSSION

Infection is a common complication in multiply traumatized patients with the majority being nosocomial in origin which is related to various...
procedures performed especially for the critically ill [1]. However, in musculoskeletal injuries, especially open fractures, the early bacterial contamination is of greatest concern. This is particularly so for the cases being discussed as all were Gustilo grade 3 open fractures which are known to have a high rate of infection. Therefore, timely and thorough wound debridement is of paramount importance. Besides surgical debridement, local dressings are important for wound coverage. Though conventional antibiotic dressings are commonly used for open wounds, VAC dressings have a promising outcome in large and deep wounds. It is a viable adjunct for the treatment of open high-energy injuries [2] and has been shown to result in earlier and more reliable primary closure [3]. All 3 cases were thoroughly debrided with an application of an external fixation and VAC dressing. They were given initial systemic broad spectrum antibiotics (cephalosporins and gentamicin). Subsequent modifications based on culture and sensitivity of microorganisms from specimens obtained at surgical debridement was co-managed by the infectious disease team as per protocol.

The goal in managing open fractures is to achieve a sterile wound early to accommodate a stable internal fixation as a definitive treatment. Clinical judgment is necessary with particular attention to soft tissue conditions and ensuring a sterile base with repeated debridement. Due to the nature of injury requiring prolonged hospital stay, there is a significant risk of developing secondary nosocomial infection or colonization that can alter the final outcome. Based on previously published reports [4], the initial organisms may be polymicrobial (both gram positive and negative), however the gram negative isolates from initial wound culture are not recovered again at the time of second operation in contrast to persistence of gram positive isolates. In our patients, isolates from initial cultures were successfully eradicated but subsequent positive cultures were nosocomial in origin being highly drug resistant. Administration of broad spectrum antibiotics and multiple wound debridements with VAC dressing did create a sterile wound initially for internal fixation for two cases, but unfortunately this did not remain so perhaps due to cross contamination.

Definitive fixation was performed using a titanium plate with a healthy soft tissue cover. Though the use of titanium implants reduces the risk of infection as compared to conventional stainless steel plate [5], multiplication of bacteria on the surface of implants in a biofilm poses a risk of infection when considering definitive treatment. In vitro studies have shown that a synergistic combination of antibiotics reduces the occurrence of resistant strains [6] though this has not been shown in orthopaedic clinical practice. There were no major intra-operative complications; however, there was wound breakdown in all the three cases within two weeks post-fixation. Cultures taken from all three patients after wound breakdown demonstrated the presence of MDRPA infection. Interestingly, apart from the first patient who was a constant defaulter, none of the other patients had gram-positive organisms isolated from late operative cultures post implantation.

The emergence of multi-drug resistance is multifactorial. Wound culture studies in open musculo-skeletal injuries has reported gram negative isolates to be as high as 40% with pseudomonas aeruginosa being close to 11% [7]. Although 80% of
pseudomonas isolates are sensitive to gentamicin [8], the emergence of multi resistance poses a significant problem of eradication. This is particularly so in East Asia including Singapore [9]. The interplay of persistence, transfer of resistance elements, and cell – cell interaction contribute to difficulty in treating multidrug – resistant strains [10]. All three patients had deteriorating soft tissue infection failing repeated debridement and VAC dressings. Non -union of the fracture site also suggest sub-clinical osteomyelitis as there were radiological features of osteomyelitis. Nevertheless, X-ray might be less sensitive for detection of osteomyelitis due to Pseudomonas infection, hence leading to delayed detection radiologically. This is consistent with an experimental model of osteomyelitis which showed decreased severity of infection as demonstrated by X ray, and less evidence of sequestrum formation with P. aeruginosa when compared with Staphylococcus [11]. Though there was no clinical evidence of systemic sepsis, with negative blood cultures and the downward trend of inflammatory markers, all three patients eventually had to have amputations due to the local effects of infection. This is consistent with a similar case series of pseudomonas infection of sternum and costal cartilage which eventually required extensive excision for complete healing [12].

In case 1, both legs were injured however the right limb with grade 3(a) injury succumbed compared to the grade 1 injury on the contralateral limb. In case 2, the right limb with grade 3(a) injury succumbed however the contralateral limb with greater severity and initial vascular compromise healed satisfactorily. The patient in case 1 is a Cierny type C host who defaulted follow-up, however, the final outcome showed only local compromise requiring amputation with no systemic complications. Meanwhile, when compared with the management of case 2, the more radical approach in case 3 with timely removal of implant and excision of bone led to similar outcomes although they were both at a lower risk of infection as Cierny type A host. These findings suggest that local host factors after severe trauma and the presence of an implant may be less important factors for wound breakdown. Instead, the prolonged hospital stay due to the nature of injury might predispose to colonization with multi-resistant organisms. However, all the three patients in our series presented at different occasions with no particular cluster of MDRPA present in the wards during the time of treatment respectively. Though this reduces the possibility of cross infections in all three cases, a larger comparative study would be required to show this definitively.

We conclude that MDRPA infection can cause significant patient morbidity in otherwise healthy young individuals in association with high energy injuries. Though, the host may not be immuno-compromised systemically or locally, the local soft tissue and bony milieu in grade 3 injuries favour rapid colonization of these resistant opportunistic organisms. After colonization, these organisms cause progressive soft tissue loss and sub-clinical infected non-union eventually requiring limb amputation for complete eradication. It must be emphasized that the extreme difficulty to eradicate the infection despite multiple soft tissue and bony debridements demonstrates the unique ‘surgical resistance’ of drug resistant pseudomonas.

Measures to prevent the spread of nosocomial infection should be taken in all patients, but especially so in patients with high energy fractures undergoing definitive fixation. This includes meticulous training of all health care staff to comply with judicious hand washing between individual patient contact as well as avoiding formites. Patients should be warded in relative isolation from infected cases, given the limits of the hospital resources. In fact, post-operative patients may benefit from being discharged to a dedicated rehabilitation hospital where there may be less risk of infection. VAC dressings can provide an impermeable barrier between the wound and the external environment to limit the spread of infection. It is an advantage to have a dedicated orthopedic trauma surgeon, who has experience managing complicated open fractures. Vigilance post operatively for subsequent infection, as well as awareness that P. aeruginosa osteomyelitis may not be so evident radiologically is important.

In the presence of infection, timely and adequate surgical debridement with removal of bone graft and implants should be done. Regular, objective assessment should be done to determine if the infection is improving. Finally however, if all measures have failed to eradicate the infection; an amputation in the presence of infection should be taken in all patients, but especially so in patients with high energy fractures undergoing definitive fixation. This includes meticulous training of all health care staff to comply with judicious hand washing between individual patient contact as well as avoiding formites. Patients should be warded in relative isolation from infected cases, given the limits of the hospital resources. In fact, post-operative patients may benefit from being discharged to a dedicated rehabilitation hospital where there may be less risk of infection. VAC dressings can provide an impermeable barrier between the wound and the external environment to limit the spread of infection. It is an advantage to have a dedicated orthopedic trauma surgeon, who has experience managing complicated open fractures. Vigilance post operatively for subsequent infection, as well as awareness that P. aeruginosa osteomyelitis may not be so evident radiologically is important.

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CONCLUSION

Multi-resistant pseudomonas infected open fractures have a poor prognosis. It is very difficult to eradicate the infection once it has been established. Definite measures should be taken in patients with high impact open fractures to prevent the spread of nosocomial infections. Timely amputation may be the only way to save these patients’ lives if the infection fails to improve.

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Author Contributions
Hitendra Doshi - Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, final approval of the version to be published
Kenon Chua - Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Fareed Kagda - Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Paul Ananth Thambyah - Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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REFERENCES