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Case Report

First Reported Australian case of Fatal Streptococcal Group B Pneumonia (serotype 21) Necrotising fasciitis complicated by Toxic Shock Like Syndrome – A Case report and review

Nouran Gaber[a], Shalini Kandasamy[a], Alasdair Thomas[b], Timothy Chimunda[a,c,d,e,*]

[a] Critical Care Department, Goulburn Valley Health, Graham Street Campus, Shepparton, Victoria, Australia
[b] Surgical Department, Goulburn Valley Health, Graham Street Campus, Shepparton, Victoria, Australia
[c] University of Melbourne, School of Medicine, Victoria, Australia
[d] University of Queensland, School of Medicine, Queensland, Australia
[e] University of Toronto, Toronto, Canada

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ABSTRACT

Introduction: NF is a life-threatening infection and progressive disease resulting in widespread fulminant tissue destruction. It is rarely caused by Group B Streptococcus pneumonia. Early management with surgical removal of devitalized tissue and urgent antibiotic administration are key therapies.

Aim: The aim of this report is to highlight the importance of atypical microorganisms seen in NF.

Method: A case presentation and cohort summary of reported NF cases secondary to SPN from the year 2011 to 2020.

Results: We report the case of a 67-year-old male, not on immune-suppressive medications, admitted to our intensive care unit with septic shock and multiorgan failure secondary to left leg NF following a 3-week history of cactus prick with an SPN bacteraemia and LRINEC score of 5 on admission. He required multiple surgical debridements and was commenced on appropriate antibiotics. Despite continuous vasopressor supportive therapy, high flux CRRT, and IVIG, our patient died after an 8-day inpatient stay. A 10-year review showed only 5 reported GBSPn NF cases with an associated mortality rate of 40%.

Conclusion: A high clinical suspicion of SPN infections in NF is required to avoid high mortality with early diagnosis and targeted anti-microbial therapy. Severity scores may not align with clinical severity.

Introduction

Necrotizing fasciitis is a life-threatening clinical syndrome secondary to a serious bacterial infection leading to rapidly progressive involvement of multiple skin layers and culminating in fulminant tissue destruction (Puvanendran, Huey, and Pasupathy 2009). Presentations often vary and may resemble cellulitis initially, the sequelae of which are dependent upon the anatomical involvement, organisms identified, the necessity of debridement, degree of necrotizing soft tissue infection, and extent of surgical debridement warranted. NF is classified into four main types with different pathogens exhibiting anatomical predilection according to the NF subtype involved. The most affected sites are the limbs, trunk, and perineum. Fournier's gangrene is a polymicrobial NF of the perineal and the perianal areas and case series have shown a mortality rate of 20% to 40% with an incidence as high as 88% in some reports (Benjelloun el et al. 2013; Misiakos et al. 2014).

Type I, comprising mainly a polymicrobial infection (Staphylococcus aureus, Haemophilus, Vibrio, Escherichia coli, Bacteroides Fragilis), is commonly seen in elderly or diabetic patients. Type II, also referred to as flesh-eating disease, affects all healthy age groups and can include (Haemolytic Group A Streptococcus, Staphylococci including MRSA). Type III, which is caused by Clostridium Perfringes, is seen post injuries or surgeries, and clinically can only present with crepitus initially. It is commonly seen in intravenous drug users injecting heroin subcutaneously. Lastly, Type IV is due to marine organisms or fungal infections. Additional risk factors for NF are skin/mucosal breach, immunosuppression, major penetrating trauma, recent surgery, obesity, alcoholism, and malignancy (Khamnuan et al. 2015).

* CORRESPONDING AND PRIMARY CO-AUTHOR. Dr Timothy Chimunda. Clinical Director GV Health ICU, Director of Clinical Research GVH ICU, Senior Lecturer University of Melbourne and Queensland.

E-mail addresses: nouran.gaber@gmail.com (N. Gaber), shal_linnie@yahoo.co.uk (S. Kandasamy), alasdair.Thomas@gvhealth.org.au (A. Thomas), drchimunda@gmail.com (T. Chimunda).

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Table 1
Clinical and Biochemical Summary of Events.

Day	Events	Investigations	Management
0	Presentation to ED via ambulance for worsening left leg swelling from a recent cactus plant prick **(see supplementary fig 1A)**. Blood Pressure (BP): 71/41mmHg, Mean Arterial Pressure (MAP): 48mmHg, Respiratory Rate: 36 breaths per minute, Heart Rate (HR): 125 beats per minute, sinus tachycardia, Temperature: 39°C, Oxygen Saturation: 86% with 0.21 FiO2. Admitted to the intensive care unit (ICU).	pH 7.15 (7.35-7.45), PO2 84 (83-108 mmHg), HCO3 15 (21-27 mmol/L), Lactate 7.6 (0.5-1.6 mmol/L), Sodium (Na) 134 (135-145 mmol/L), Urea 7.6 (3.3-7.6 mmol/L), Creatinine (sCr) 173 (44-80 μmol/L), eGFR 27 (>60 ml/min/1.73m^2), White Cell Count (WCC) 13.8 (3.6-9.2 x10^9/L), C-reactive protein (CRP) 22, Hemoglobin (Hb) 114 (120-152 g/L), Platelet (Plt) 81 (140-380 x10^9/L), Liver Function Test (LFT)- Total Bilirubin (Bili) 99 (<17 μmol/L), Alanine transaminase (ALT) 61 (4-31 U/L), Aspartate aminotransferase (AST) 83 (4-31 U/L), Alkaline Phosphatase (ALP) 96 (30-110) U/L)	Triple vasopressor support initiated: Noradrenaline 20mcg/min, Adrenaline 20mcg/min , Vasopressin 0.04units/min. Antibiotics: Piperacillin-Tazobactam IV 4.5g stat and then ceased. Meropenem IV 2g, Lincomycin IV 600mg, Vancomycin IV 2g. Source control: Emergency left lower limb fasciotomy, debridement and below knee amputation for high suspicion of necrotizing fasciitis with an LRINEC Score of 5. Intraoperatively, he had an extensive left foot and below knee tissue necrosis **(see supplementary fig.1B)** with "dishwasher fluid" in appearance along with liquefied fat. There were large areas of unviable skin and muscle. Histopathology was undertaken to confirm diagnosis **(see supplementary fig.1C)**
1	Post operatively, patient was transferred to ICU intubated for possible re-exploration in 24-48hrs. Patient developed oliguria 10-14ml/hour and his blood gas showed severe acidosis requiring left internal jugular vascath insertion in preparation for continuous renal replacement therapy (CRRT).	pH 7.28, Lactate 4.7, Na 130, sCr 206, Hb 89, Plt 105, WCC 17, CRP 78, International normalized ratio (INR) 2.2 (0.8-1.2), Activated Partial Thromboplastin Time (APTT) 150 (26 - 36 secs), Initial blood cultures (BCs) isolated Group B Streptococcus pneumoniae (GBSPn)	Ventilation sedation: Propofol 170mg/hr, Fentanyl 40mcg/hr. CRRT (Day 1) on heparin circuit commenced. Renal dose - 30ml/kg/hr. Triple vasopressor support continued: Noradrenaline 23mcg/min, Adrenaline 18mcg/min, Vasopressin 0.04units/min. Antibiotics (MLV): Meropenem IV 2g TDS, Lincomycin IV 600mg TDS, Vancomycin IV 2g BD. Intravenous Immunoglobin G (IVIgG) therapy 100g was initiated. He was taken back to theatre to confirm source control and the viability of the left stump noting no evidence of necrotic tissue.
2	Remained intubated but developed new onset of Rapid Atrial Fibrillation (RAF) with HR 110bpm. Patient remained oliguric 7-25ml/hour despite ongoing hemofiltration.	pH 7.40, Lactate 3.9, Na 131, sCr 116, WCC 26, CRP 105, Procalcitonin (PCT) 21.18 μg/L, Hb 83, Plt 63, INR 3.1, Fibrinogen 2.4 (2.0-4.0 g/L). Echocardiography: Moderate segmental left ventricular dysfunction, Ejection Fraction 40-45%, Dilated atria bilaterally, Raised Right Atrial Pressure.	Amiodarone loading dose 300mg over 1 hour followed by maintenance dose 900mg over 24 hours. Antibiotics remained unchanged (MLV). CRRT (Day 2) – AN69 anti-inflammatory heparin laden adsorbing filter applied (Oxiris Filter) to dampen the inflammatory surge. Citrate based anticoagulation circuit applied.
3	Patient developed features consistent with Sepsis Induced Coagulopathy (ISTH -SIC criteria). Bedside surgical debridement was performed by surgical team.	pH 7.31, Lactate 2.4, Na 135, sCr 79, WCC 27, CRP 127, Hb 78, Plt 50, INR 2.0. Histopathology consistent with NF. Wound culture for microscopy culture and sensitivity (MCS) had medium growth of GBSPn. Tissue culture (intraoperatively) had medium growth of GBSPn.	Vasopressor support - weaning: Noradrenaline 20mcg/min, Adrenaline weaned off , Vasopressin 2.4units/min. Antibiotics remained unchanged (MLV). CRRT (Day 3) - ongoing.
4	Patient remained oliguric (6-20ml/hr) despite being challenged with a single dose Furosemide IV 250mg stat to assess renal response to which he did not respond. Citrated based CRRT was continued. New onset purpura over the right forearm along with multiple weeping skin tears on right upper thigh. Ongoing RAF HR 130.	pH 7.36, Lactate 1.5, Na 130, sCr 116, WCC 33, CRP 103, PCT 15.37, Hb 91, Plt 53, INR 1.7, LFT - Bili 131, AST 127, ALP 121	Double inotropic support: Noradrenaline 20mcg/min, Vasopressin 2.4units/min. Antibiotics remained unchanged (MLV). CRRT (Day 4). Amiodarone infusion.
5	Patient developed fulminant hepatic failure/ encephalopathy. Refractory oliguria 0-5ml/hr was noted.	pH 7.39, Lactate 1.2, Na 134, sCr 124, WCC 39.5, CRP 74, Hb 116, Plt 49, INR 1.5, LFT- Bili 139, AST 69, ALT 97, ALP 140	Dual inotropic support: Noradrenaline 20mcg/min, Vasopressin weaned off. Antibiotics remained unchanged (MLV). CRRT (Day 5).

(*continued on next page*)

Table 1 (*continued*)

Day	Events	Investigations	Management
6	Patient was severely deconditioned and developed ICU acquired weakness. He was unarousable and had no response to noxious stimuli. Remained intubated and ventilated on Pressure Support Ventilation. Refractory oliguria at 5ml/hr.	PH 7.44, Lactate 1.1, WCC 43.5, CRP 109, Hb 90, Plt 57, INR 1.5, LFT - Bili 150, AST 95, ALP 154	Sedation weaned off. Off vasopressor, Noradrenaline weaned off. Antibiotic de-escalation: Lincomycin and Vancomycin ceased, Meropenem IV 2g TDS continued. CRRT (Day 6). Hyper-Ammonium Therapy initiated -Rifaximin NGT 550mg BD, Lactulose NGT 20ml TDS. 2 units of PRBCs transfusion.
7	Patient developed jaundice. Hypoactive delirium, remained deeply sedated despite being off sedation with a RASS -5. New onset lateralizing signs to the left upon painful stimuli compared to the right side. Refractory oliguria.	CT Brain: No acute intracranial pathology. Ultrasound abdomen: Acute Calculous Cholecystitis noted. pH 7.44, Lactate 1.1, WCC 44.3, CRP 109, Hb 129, Plt 66, INR 1.3, LFT - Bili 235, AST 75, ALP 175, Conjugated Bilirubin 142 (<5.1 μmol/L)	Meropenem IV 2g TDS. CRRT (Day 7) on a Heparin circuit.
8	Anuria was established by this stage. Hypotensive BP 71/33, MAP 51mmHg, Febrile 39°C, RAF HR 160. Significant deterioration despite ongoing medical therapy. Patient was commenced on palliative care pathway, deceased shortly post treatment withdrawal. Family was involved in this decision and consent for critical care supportive therapy was withdrawn. The patient was not deemed to be a coroner's case.	Troponin 616, Ammonia 158 (11-32 umol/L), LFT - Bili 352, AST 100, ALP 299	CRRT (Day 8) Renal recovery assessment -challenged with combination of Furosemide IV 250mg and Acetazolamide IV 500mg. Recommenced Vasopressor support; Noradrenaline 2.5mcg/min. Antibiotic regimen: Lincomycin IV 600mg TDS – recommenced as antitoxin. Meropenem IV 2g TDS – continued. Digoxin IV 500mcg, Metoprolol IV 15mg.

Description: Table outlining daily case summary
CRRT, Continuous Renal Replacement Therapy; ED, Emergency Department; ISTH-SIC, International Society on Thrombosis and Hemostasis – Sepsis Induced Coagulopathy; GBSPn, Group B Streptococcus pneumonia; LRINEC, Laboratory Risk Indicator for Necrotising Fasciitis scoring system; MLV, Meropenem Lincomicin Vancomycin; PRBCs, Packed Red Blood Cells; RAF, Rapid Atrial Fibrillation

The systemic involvement of sepsis, single or multi-organ failure along with the locally spreading erythema, pain area disproportionate to clinical exam, crepitus, skin bullae, necrosis, and or ecchymosis are the main clinical manifestations of NF. The Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) is a scoring system that aids to risk-stratify patients presenting with signs of cellulitis for likelihood of necrotizing fasciitis based on six parameters (**see supplementary Table 1**). A score of ≤5 = <50% risk (low); 6–7 = risk (intermediate); ≥8 = >75% risk (high) (Wong et al. 2004). Radiological imaging including X-ray of the affected area, CT scan, and MRI can identify areas of fluid collection, inflammation, and gas loculations within affected soft tissues.

Group B infections have started to become more prominent compared to Group A Streptococcal infections, as noted in case studies and series. We describe a case of Group B Streptococcus Pneumonia Necrotising Fasciitis (GBSPn NF) with refractory Streptococcal Toxic Shock Like Syndrome (TSLS) within the ICU and revisit the literature surrounding the emergence of GBSPn NF.

Case description

Mr X, a 67-year-old male, presented to our Emergency Department at a university teaching Regional Hospital via ambulance with worsening left leg swelling from a recent cactus plant injury. A week prior to presentation he had sustained a minor penetrating injury to his left lower leg from a cactus plant. He reported progressive left leg swelling, worsening of erythema along with pain for 2 days and felt generally unwell, requiring paramedic assistance.

He had a background history of Primary Sclerosing Cholangitis and mild Ulcerative Colitis. He was not on any immunosuppressants. He had long-standing deranged liver function tests and was being followed up by a gastroenterologist. Table 1 reflects a complete case description.

Discussion

GBSPn remains an extremely uncommon pathogenic agent of NF. Whilst the precipitating event was a cactus spine injury, the resultant inflammation often leads to granulomas and if infections do occur, they are associated with Mycobacterium Marinum, Staphylococcus Aureus, Clostridium Tetani, Enterobacter, and Nocardia infections as causative organisms as noted by Deiter et al and Snyder et al (Dieter, Whitehouse, and Gulliver 2017; Snyder and Schwartz 1983). Despite a background of Primary Sclerosing Cholangitis and Cactus spine prick, no association could be found in the literature with development of GBSPn NF by these conditions. The case had risk factors associated with increased mortality in NF as noted by P. Khamnuan et al (Khamnuan et al. 2015).

We conducted a cohort review from PubMed, EMBASE, and CINAHL of the literature describing NF caused by GBSPn which yielded 5 case reports published between 2011 and 2020 **(see supplementary Table 2)**. Serotyping was reported in only 3 cases, 9V, 23F and 9N, Park et al, Zhang et al and Hovmand et al respectively. Hovmand et al had reported 14 cases between the year 2001 and 2016 (Hovmand et al. 2019). This again supports the notion that GBSPn NF remains a rare finding underpinning the importance of this uncommon causative organism that leads to fatal NF.

Despite imploring source control, anti-inflammatory measures, an Oxiris filter, IVIG, and Lincomycin, our patient still succumbed to GBSPn induced TSLS. GBSPn from tissue showed intermediate minimum inhibitory concentration to penicillin. The LRINEC initially ascribed a low risk for NF in stark contrast to the clinical presentation. This is in keeping with literature that states that there is poor sensitivity and external validity issues and one should rely more on clinical suspicion (Bechar et al. 2017; Young et al. 2006; Broman et al. 2019). Whilst imaging can be useful in atypical presentations, it should not delay treatment,

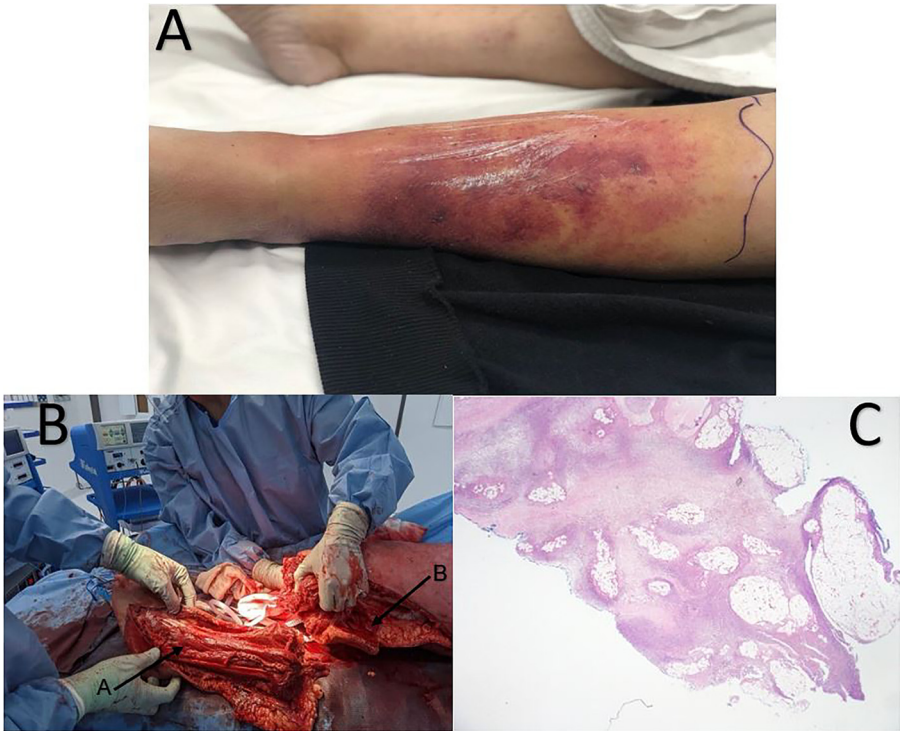

Figure 1.

as this can lead to high mortality rates, quoted as high as 60% in the literature (El-Qushayri et al. 2020).

Conclusion

GBSPn NF with TSLS remains a condition associated with high mortality, and reliance on scoring systems could have a deleterious outcome on patients. Clinical suspicion and empirical antibiotic coverage according to local therapeutic guidelines is an essential key element, while early debridement and critical care support remain the mainstay of therapy.

Declaration of Competing Interest

No potential conflicts of interest to disclose.

Ethical approval

Ethical approval was obtained and a written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2022.01.005.

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