Streptococcus gallolyticus bacteremia requiring 12-step desensitisation for penicillin

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Abstract
A 65-year-old Tongan man with significant comorbidities and anaphylaxis to penicillin developed infective endocarditis and spinal osteomyelitis as a consequence of recurrent Streptococcus galloccyticus bacteremia. He was commenced on 12-step drug desensitization for penicillin. This case report discusses the process of 12-step drug desensitization and the background of Streptococcus galloccyticus (previously known as Streptococcus bovis) bacteremia.

Background
This case offers unique insight into the role of antibiotic desensitisation and its potential value in circumstances where patients have an allergy to first-line treatment options, or when alternatives have been unsuccessful.

Case Presentation
Mr VF was a 65-year-old Tongan man with significant comorbidities and anaphylaxis to penicillin. He developed infective endocarditis and spinal osteomyelitis secondary to recurrent Streptococcus galloccyticus bacteremia.

Treatment
Due to his penicillin allergy, Mr VF was initially treated with intravenous vancomycin, before being changed to benzylpenicillin after undergoing a successful desensitisation procedure. He was discharged with a peripherally inserted central catheter in situ, and treated with a six-week course of IV benzylpenicillin 1.8 g Q4H via the outpatient intravenous antibiotic (OPIVA) service.

Discussion
Infective endocarditis (IE) describes an infection of the endothelial lining of the heart, typically involving one or several cardiac valves. Mr VF’s risk factors included his age (>60 years), male sex, and diabetes. Staphylococcus aureus is the most common pathogenic cause of IE, accounting for 31% of presentations in a large study evaluating a cohort of 2781 patients with IE, whereas Streptococcus bovis was responsible for 7% of cases. Streptococcus gallolyticus biotype I is a subspecies of the Group D streptococci; Streptococcus bovis. Group D streptococci are catalase-negative, Gram positive cocci. Streptococcus gallolyticus is the causative organism for the majority of Streptococcus bovis IE, and also has a strong association with CRC. In addition, there are documented cases of Streptococcus galloccyticus bacteremia causing infections of the bones and joints, as well as the meninges, peritoneum, and urinary tract. This is likely to have been the cause of Mr VF’s new diagnosis of spinal osteomyelitis.

One meta-analysis analysed seven case series, stratifying the number of IE cases among proven cases of Streptococcus galloccyticus bacteremia. Of these, 43%–100% of patients were found to have concurrent or subsequent IE. This indicates a reasonable probability that...
Mr VF may have had IE at the time of his initial admission in January 2020. The image quality of his transthoracic echocardiogram was hindered as a result of his BMI. The “trivial” finding of mitral regurgitation during his initial admission is not insignificant. We can only speculate that this may have been the first sign of IE-related sequelae in Mr VF. The specificity of transthoracic echocardiography only reaches 75% for diagnosing IE, thus, it is plausible for a small vegetation to be missed. While fever is by and large the most common symptom of IE (up to 90%), cardiac murmurs are present in 85% of cases, and while this was not documented on admission, adequate auscultation was also appreciably difficult. Nonetheless, the presence of any such valvular defect placed him at a greater risk of developing IE. Interestingly, patients with Streptococcus gallolyticus IE are less likely to have the typical risk factors for IE. The presence of chronic liver disease however, or in Mr VF’s case, diabetes, does increase one’s risk. 

Unfortunately, Streptococcus gallolyticus bacteraemia is also strongly associated with CRC. One meta-analysis analysed 6 studies and found that patients with Streptococcus gallolyticus bacteraemia had a statistically significant higher prevalence of CRC (prevalence range 33%–71%) compared to the normal population (10%–25%). Concomitant IE further elevates this risk. The reason for this association is not fully understood, but explains the importance of regular surveillance with colonoscopy for Mr VF. Due to the strong epidemiologic association, he warrants a further colonoscopy in 4–6 months.

Penicillin allergy is the most widely documented medication allergy in the modern world, yet, for a large proportion, further investigation will reveal that many do not exhibit true allergy, and are able to safely receive the drug. That being said, drug-induced anaphylaxis from penicillin is still a significant cause of morbidity and mortality. Caution should be taken before challenging a penicillin allergy. While vancomycin is an effective penicillin alternative in Mr VF’s case, the drug’s added cost, and associated risks surrounding drug-resistance from overuse, made penicillin desensitisation a worthy option.

Mr VF was unwell with active infection and extensive comorbidities; thus, a decision was made to bypass skin prick testing and to refer him early for desensitisation to minimise treatment delays. While penicillin allergies are commonly misdiagnosed, Mr VF’s documented tryptase elevations from prior reactions sufficiently warranted desensitisation.

Desensitisation involves administering a drug in extremely small doses, making gradual increases in a stepwise manner. Provided that it is performed by trained and experienced specialists, the success rate is notably high. Desensitisation can be performed safely on patients of any age. No documented deaths have occurred as a result of the procedure. Desensitisation alters a patient’s immune response, facilitating a “temporary tolerance,” thus allowing patients with hypersensitivity to safely receive an uninterrupted dose of the required medication. The mechanism by which this occurs is not yet fully understood. What is known is that it induces a temporary tolerance of the patient’s basophils and mast cells to the drug. Contraindications include any background of reactions relating to drug-related eosinophilia and systemic syndrome, acute generalised exanthematous pustulosis, or skin desquamation such as toxic epidermal necrolysis or Stevens-Johnson syndrome. About 20% of patients experience mild breakthrough reactions. Provided that the treating clinician is experienced at identifying and managing such symptoms, the risk of these becoming life-threatening is low. Management of symptoms involves temporary cessation of the infusion whilst administering relevant treatment for the symptoms. The infusion is then restarted at the same step as where the symptoms developed.

It was important to review the patient’s medical background and medications prior to commencing the procedure. Due to its added hypotensive effect, Mr VF’s cilazapril was withheld for 24 hours prior to desensitisation, in the event that anaphylaxis was to develop. Ideally, his metoprolol would also have been withheld in case a reaction necessitated adrenaline. However, due to the risk of arrhythmia secondary to his AF, the cessation of metoprolol was deemed to be unwise.

The procedure takes approximately six hours. The protocol commences with an initial intravenous dose that is a 1/10000\textsuperscript{th} dilution of the intended therapeutic dose. This infusion dose is then doubled every 15 minutes (with each increase signifying the next step in the 12-step protocol). This is done until the full therapeutic dose is achieved.

Upon completion, Mr VF was able to receive the indicated four-hourly 1.8 g dose of penicillin via a peripherally inserted central catheter for the required 42-day course. It is important to note that maintaining desensitisation relies on the continued presence of the drug. If doses are missed, the desensitisation will dissipate. The speed at which this occurs depends on the drug’s half-life, Mr VF’s renal function, and various other factors. The desensitisation is also dose-dependent, as any significant dose increase has the potential to trigger allergy.

It was important to inform Mr VF that the desensitisation had not permanently cured him of his allergy, and that once the drug left his system, his sensitivity would return.

References


Written consent was obtained from the patient for this publication.

About the author

Oliver Lyons is a PGY1 House Officer at Auckland City Hospital. He is interested in Anaesthesia, Emergency Medicine and Psychiatry. He is also passionate about music and musician’s health.

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