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CASE REPORT

An Uncommon Aetiology of Native Valve Infective Endocarditis: Corynebacterium glutamicum Infective Endocarditis

Carwen Siaw[1]*, Nor Izzah Binti Mazan[2], Seng Wee Cheo[3], Qin Jian Low[1]

[1] Department of Internal Medicine, Hospital Sultanah Nora Ismail, Jalan Korma, Taman Soga, 83000 Batu Pahat, Johor, Malaysia.
[2] Department of Microbiology, Hospital Sultanah Nora Ismail, Jalan Korma, Taman Soga, 83000 Batu Pahat, Johor, Malaysia.
[3] Department of Internal Medicine, Hospital Lahad Datu, 91100 Lahad Datu, Sabah, Malaysia.

*Corresponding author's email: carwen1312@gmail.com

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ABSTRACT

Corynebacterium glutamicum is a rare cause of infective endocarditis increasingly identified as a pathogen causing significant morbidity and mortality. We report a middle-age female with underlying end-stage renal failure who developed *Corynebacterium glutamicum* catheter-related bloodstream infection and eventually succumbed. This case highlights the importance of recognizing *Corynebacterium* as an emerging nosocomial pathogen and early management to improve clinical outcome.

INTRODUCTION

Corynebacterium are gram-positive, catalase-positive, aerobic or facultatively anaerobic organisms. They are generally non-motile rods. The genus can be subdivided into the*Corynebacterium diphtheriae* and the non-diphtherial *Corynebacteria* species. Non-diptherial *Corynebacteria* is generally considered as part of the normal human skin and mucus membranes. Thus, when isolated from clinical specimens, they are frequently dismissed as contaminants. Nonetheless, they have been increasingly identified as pathogenic over the past two decades, especially in patients with immunodeficiency state such as malignancy or chronic diseases (Coyle et al., 1990; Chen et al., 2012).

CASE PRESENTATION

A 37-year-old woman with underlying end stage renal failure (ESRF) on regular haemodialysis was admitted due to bleeding from her arteriovenous fistula (AVF) post dialysis at her haemodialysis centre. Her bleeding from the AVF had stopped upon arrival at the hospital and she was transfused with packed red blood cells due to severe anaemia (haemoglobin of 5.2 g/dL) (*Table 1*). A temporary femoral dialysis catheter was inserted while her AVF was put on rest. Unfortunately, she developed fever on day 3 of admission with pus discharge noted from her arteriovenous fistula. Ultrasound of the AVF demonstrated collection with possible partial thrombosis of the AVF. She was started on empirical intravenous ampicillin-sulbactam 1.5g twice a day. Due to her fever, her femoral dialysis catheter was removed on day 3 of admission with blood cultures obtained from both lumens prior removal.

Her blood cultures grew Corynebacterium species. Microbiology assessment of biochemical set and comparison with Vitek 2 Automated System were performed to identify the species of *Corynebacterium*. From the biochemical set, the organisms were catalase and urease positive. They were able to ferment glucose and maltose. All the isolates were reverse Camp test positive with *Staphylococcus aureus*. *Corynebacterium glutamicum* was identified with a probability of 96%. Possibility of the organism being contaminant was lowered as the repeated blood cultures three days apart from periphery and both lumens of the femoral dialysis catheter grew the same organism. Unfortunately, drug sensitivity test was not done. Due to her persistent spiking fever, a transthoracic echocardiogram was ordered and showed a vegetation over her posterior mitral valve leaflet with presence of moderate mitral regurgitation (*Figure 1a & 1b*). The size of vegetation was ± 0.8 cm^2. She had no physical stigmata of infective endocarditis. She was switched to intravenous benzylpenicillin 4 mega unit twice a day for her *Corynebacterium glutamicum* catheter related blood stream infection and infective endocarditis (*Figure 2a*). On day 12 of admission, she developed sudden onset multiple generalized tonic-clonic seizures. Computed tomography (CT) scan of the brain showed multiple acute subarachnoid haemorrhage (*Figure 2b*). She succumbed later that day due to sepsis from *Corynebacterium glutamicum* catheter related blood stream infection and infective endocarditis complicated with subarachnoid bleeding.

DISCUSSION

Non-diphtherial *Corynebacteria*, with the example of species including *Corynebacterium ulcerans*, *Cpseudotuberculosis*, *Corynebacterium pyogenes*, commonly colonize human skin and mucus membranes. Only lately is the pathogenicity of these organisms evident in human or even livestock infections[1]. Patients at a high risk of infection include those who are immunocompromised or have co-morbidities such as HIV infection (Roig-Rico et al., 2011; Gutiérrez-Rodero et al., 1999; Roig et al., 1993), malignancies, chemotherapy (Waters, 1989; Kebbe et al., 2015) and conditions that affect their poly-morphonuclear cells function, for instance diabetes mellitus, alcoholism (Martinez-Martinez, L. et al., 1994) or end stage renal failure, as seen in our case. *Corynebacterium* spp. causes approximately 0.2 to 0.4% of native valve endocarditis and 9% of early and 4% of late prosthetic valve endocarditis (Knox et al., 2002; Riegel et al., 1996). *Corynebacterium glutamicum* is an industrial microorganism conventionally utilized for amino acids production (Gopinath et al., 2014). Although other *Corynebacterium* spp. especially *Corynebacterium striatum* has been reported to cause infection such as infective endocarditis (Bläckberg et al., 2021), we would like to highlight the possibility of *Corynebacterium glutamicum* being an important pathogen in immunosuppressed patients. There have been insufficient reports on infection caused by *Corynebacterium* species and more knowledge is required.

Traditionally, diphtheroid species are identified using cultures. They mostly require special media such as sheep's blood agar, Loeffler or tellurite plates, to grow. Communication with the microbiology laboratory is essential for appropriate processing of the cultures, as the colony types have a variety of biochemical characteristics. Lately 16S ribosomal ribonucleic acid (rRNA) probes have been invented for identification of corynebacterial genus and species. The new anaerobe and *Corynebacterium* (ANC) identification card for Vitek 2 met all performance criteria within a 95% confidence interval when compared with 16S rRNA gene sequencing reference method (Rennie et al., 2008). A multiplex PCR system can also be utilized for identification and determination of toxigenicity of corynebacterial species with zoonotic potential (Bernard, 2016; De Fátima Costa Torres et al., 2013; Sekar et al., 2017).

To date, there are still no guideline on the management of *Corynebacterium* CRBSI and infective endocarditis. Fortunately, most of the *Corynebacterium* species are sensitive to various antibiotics including penicillin and vancomycin. We think that that vancomycin would have been a better choice of antibiotic for her as she was septic. Corynebacterial species had been reported to be susceptible to vancomycin in most circumstances. There were some reported vancomycin-resistant species in the literatures (Williams et al., 1993). Among the true *Corynebacterium* species reported to have multiple antibiotic resistances are *C. xerosis*, *C. urealyticum*, *C. jeikeium*, and *C.* minutissimum (Soriano et al., 1995). Nevertheless, vancomycin is still considered the drug of choice for the treatment of corynebacterial infection until susceptibility testing has been determined (Wood, 1993). Duration of vancomycin therapy in native valve infective endocarditis is 6 weeks (Marrie et al., 1984). Numerous studies have proven that *Corynebacterium* species can produce biofilm on the surface of catheters (Baddour et al., 2015; Olson et al., 2002), which can be less effectively eradicated by vancomycin (Darouiche et al., 1994), thus necessitate longer hospitalization for resolution of fever when removal of indwelling catheter is not performed. A study completed by S. Ghide et al. (Ghide et al., 2009) has suggested that removal of central venous catheter may not be necessary in patients with *Corynebacterial* CRBSI, especially when a non-glycopeptide antibiotic is administered.

CONCLUSION

It is crucial to recognize *Corynebacterium* as an emerging nosocomial pathogen. Although *Corynebacterium* could be isolated from a blood culture as a common contaminant, in some cases it could conceal a serious underlying infection, especially in critically unwell patients with medical devices such as central venous catheter or implanted indwelling device. Due to the patient's poor general condition and comorbidity, our patient succumbed from catheter-related bloodstream infection caused by *Corynebacerium glutamicum*.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in the publication of this paper. The authors receive no financial support for research, authorship and publication of this article.

CONSENTS

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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FIGURE LEGENDS

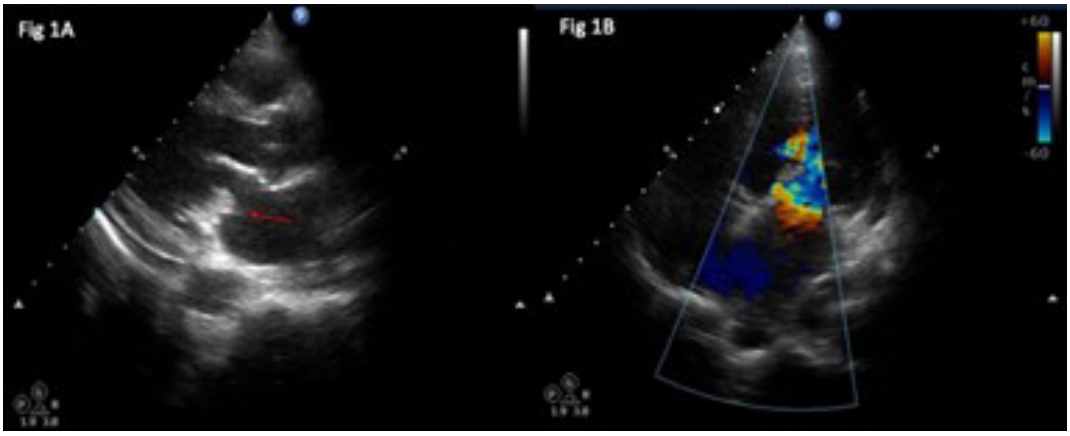

Figure 1: (A) Transthoracic echocardiogram shows a vegetation (arrow) on the posterior mitral valve leaflet (Parasternal long axis view). **(B)** Transthoracic echocardiogram shows moderate mitral regurgitation with colour doppler imaging in the apical 4 chamber view.

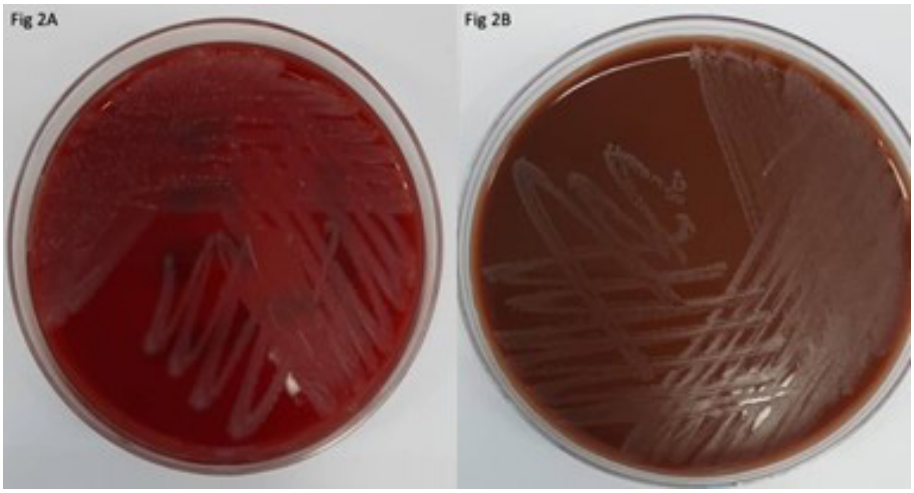

Figure 2: (A) On blood agar, Corynebacterium colonies form small white to cream colour non-haemolytic colonies with dry granular appearances, mostly translucent but with opaque centres, convex with continuous borders. **(B)** On chocolate media, Corynebacterium form tiny, creamy-white colonies.

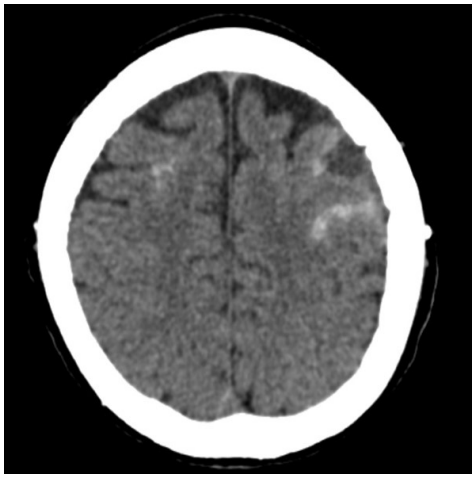

Figure 3: Plain Computed tomography (CT) scan of the brain showed multiple acute subarachnoid haemorrhages.

Table 1: Investigations

	Units	Reference range	Day 1 Admission	Day 6 Admission
Haemoglobin	g/L	135 – 176	52	98
White cell count	10^12/L	4.5 – 11	6.06	8.4
Platelet count	10^9/L	150 – 410	50	113
International normalized ratio (INR)			1.29	
Urea	mmol/l	2.8 – 7.2	25.9	26.8
Sodium	mmol/l	136 – 146	129	135
Potassium	mmol/l	3.5 – 5.1	3.5	3.7
Creatinine	µmol/l	59 – 104	719	791
Total bilirubin	µmol/l	5 – 21	10.6	
Alanine transaminase	U/l	0 – 50	11	
Alkaline phosphatase	U/l	30 – 120	164	
C-reactive protein	mg/l	0 – 5	166.6	
Blood culture from periphery Day 3 of admission			*Corynebacterium glutamicum*	
Blood culture from both femoral dialysis catheter lumens			*Corynebacterium glutamicum*	
Blood culture from periphery Day 6 of admission			*Corynebacterium glutamicum*	