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CASE REPORT

An Unusual Case of *Corynebacterium simulans* causes Infective Endocarditis with Embolic Events

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ABSTRACT

Corynebacterium species are often treated as contaminants. However, there were several recent outbreaks involving *Corynebacterium* species reported across the globe. We report a rare case of *Corynebacterium simulans* causes infective endocarditis which led to debilitating embolic events. A 39-year-old lady presented with a prolonged fever for three weeks. She was in septic shock and had dense right hemiplegia, a pansystolic murmur at the mitral area and hepatosplenomegaly. There were no peripheral stigmata of infective endocarditis. An urgent computed tomography (CT) of the brain showed an infarct at the left corona radiata extending to the left parietal, left basal ganglia and left temporal lobe. She deteriorated and required mechanical ventilation and intensive care. Echocardiogram showed vegetation at both her anterior and posterior mitral valve leaflets leading to severe mitral regurgitation. Splenic infarction was seen in her contrasted computed tomography (CECT) of her abdomen. Her three samples of blood culture were positive for *Corynebacterium simulans*. She deteriorated rapidly and went into multi-organ failure and succumbed. *Corynebacterium* species should be taken seriously and should not be neglected as a contaminant as it can cause potentially fatal complications as described in this case report.

INTRODUCTION

Invasive diseases caused by *Corynebacterium* have been increasingly described (Ogasawara et al., 2021). *Corynebacterium* species is only found in 0.4% of all infective endocarditis (Liesman et al., 2017). Ogasawara et al. (2020), Zheng et al. (2019) and Seng et al. (2015) published several case reports regarding infective endocarditis, pyogenic spondylitis, atopic dermatitis and breast implant infections due to *Corynebacterium simulans* (*C. simulans*) over the past decade. The rest includes *Corynebacterium striatum*, *Corynebacterium jeikeium*, *Corynebacterium amycolatum*, *Corynebacterium propinquum*, *Corynebacterium simulans* and others. For *Corynebacterium simulans*, its specific epidemiological data is not available and reports were saying that many laboratories misidentified *Corynebacterium simulans* as *Corynebacterium striatum* (McMullen et al., 2017). McMullen et al. (2017) reported that *Corynebacterium striatum* is most commonly found in wound and respiratory specimens from patients aged 50 to 69 years. *C. simulans* was first reported in 2000 in which was mainly detected in the skin and infrequently in specimens associated with mucous membranes (Liesman et al., 2017). Ogasawara et al. (2021) stated that the frequencies of isolation of *C. simulans* and *C. striatum* were 3.9% and 96%, respectively. *C. simulans* is prone to infections that require long-term treatment, such as pyogenic spondylitis, infections of prosthetic joints, and infective endocarditis (Ogasawara et al., 2021). However, there were only a few cases of pyogenic spondylitis and skin infections reported ever since the discovery of *C. simulans* in 2000 (Liesman et al., 2017). Here we report a rare case of *C. simulans* infective endocarditis.

CASE REPORT

A 39-year-old lady with underlying iron deficiency anaemia presented to the emergency department with sudden onset of right-sided body weakness with a background history of prolonged fever for three weeks associated with dyspnoea, lethargy, arthralgia and headache. Otherwise, there were no fitting episodes. On arrival at the emergency department, she was lethargic, febrile and septic looking. Physical examination revealed a dense right hemiparesis with MRC grade 1 power over the right upper and lower limbs. A Grade 3 pansystolic murmur at the mitral area radiating to the left axilla was noticed on cardiovascular examination while abdominal examination showed hepatosplenomegaly. There were no peripheral stigmata of infective endocarditis. Chest radiograph showed no consolidation while electrocardiogram revealed sinus tachycardia. An urgent computed tomography (CT) brain (Figure 1A) showed a recent infarct at the left corona radiata extending to the left parietal, left basal ganglia and left temporal lobe which was consistent with her neurological findings.

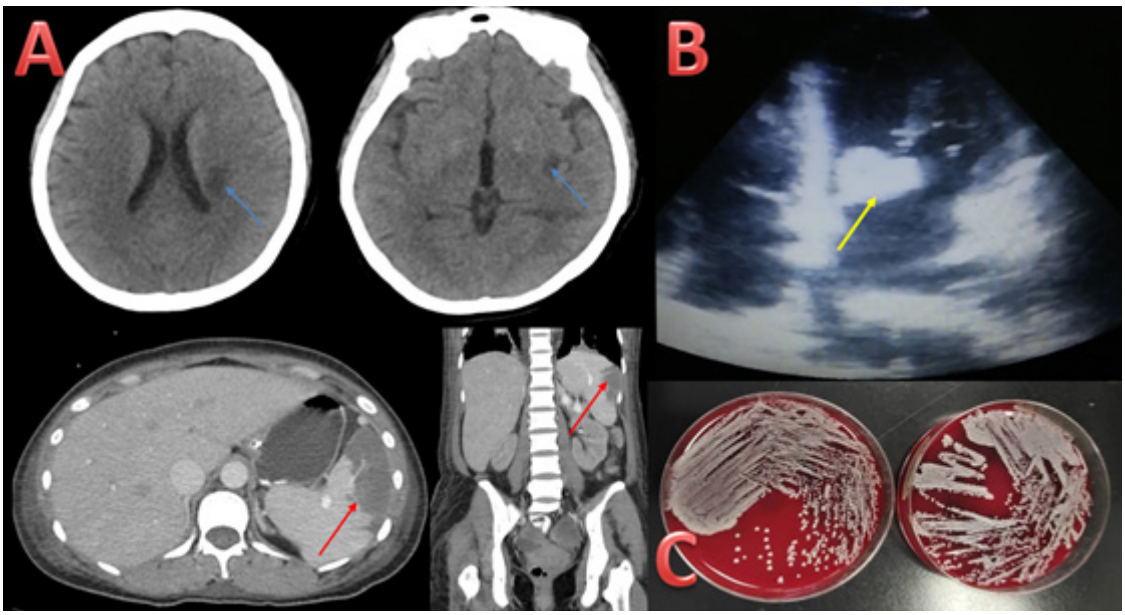

Figure 1 (A) CT brain shows ill-defined hypodensities (blue arrows) at the left corona radiata and left external capsule (blue arrow) in keeping recent infarcts. Differential diagnosis includes septic emboli to the brain. CT abdomen shows well-defined wedge shape hypodensity (red arrows) at the peripheral aspect of the mid-pole spleen (blue arrow) in keeping with splenic infarct. (B) Transthoracic echocardiogram shows large vegetation on the mitral valve (red arrow). (C) Greyish-white non-haemolytic colonies of *Corynebacterium simulans* on blood agar (using Vitek 2 Automated System)

Her condition deteriorated on the first day of admission with impending respiratory collapse and severe arterial hypotension requiring orotracheal intubation, mechanical ventilation, inotropes and intensive care unit admission. The clinical suspicion of acute infective endocarditis was confirmed by an urgent transthoracic echocardiogram (Figure 1B) which revealed 1.4 cm^2 and 4.7 cm^2 vegetations at anterior and posterior mitral valve leaflets respectively causing severe mitral regurgitation with preserved left ventricular ejection fraction (55%). Contrast-enhanced CT abdomen and pelvis (Figure 1A) noted splenic infarct. *C. simulans* were identified on all 3 sets of blood cultures using Vitek 2 Automated System (Figure 1C). She was treated aggressively with IV Vancomycin based on blood culture sensitivity. Therapeutic drug monitoring (TDM) showed vancomycin level was within the therapeutic range. However, her condition further deteriorated with acute renal impairment and coagulopathy. She was subjected to continuous renal replacement therapy (CRRT) due to oliguric acute kidney injury with metabolic acidosis. Since she had a severe septic shock with sustained fever, the cardiothoracic and anaesthetic team feels she was unstable for operation for a valve surgery at that junction. Other broad-spectrum antibiotics such as IV C-penicillin, IV ceftriaxone and IV meropenem were added in an escalating manner to treat the invasive organisms. Despite aggressive antibiotics treatment and haemodialysis, her condition continued to worsen with persistently raised inflammatory markers and leukocytosis (Table 1) despite repeated blood cultures yielding no growth. Since then, she requires increasing ventilation settings and inotropic support. Eventually, she succumbed to death from severe *Corynebacterium* infective endocarditis with embolic events and multiorgan failure after two weeks of intensive therapy.

Table 1 Laboratory investigations

Blood parameters	Reference range	On arrival	2 weeks after treatment
Haemoglobin	12 – 18g/dL	7.1	10.1
Platelets	$150 \times 10^3 – 450 \times 10^3$/microlitre	154	111
White Cell Counts	$4 \times 10^3 – 9 \times 10^3$/microlitre	27	30
Sodium	135 – 145 mmol/L	122	145
Potassium	3.5 – 5.1mmol/L	4	4.3
Urea	2.8 – 7.2 mmol/L	16	23
Creatinine	59 – 104 micromol/L	148	106
Total protein	66 – 83 g/L	60	57
Albumin	35 – 52 g/L	23	21
Globulin	28 – 36 g/L	37	37
Total Bilirubin	5 – 21 micromol/L	15	13
Alanine Transferase	0 – 50 U/L	22	11
Alkaline Phosphatase	30 – 120 U/L	325	159
Erythrocyte Sedimentation Rate	0 – 20 mm/hour	69	63
Prothrombin time	9.9 – 11.9 seconds	38.8	12.4
International normalized ratio (INR)	0.9 – 1.10	4.26	1.18
Activated Partial Thromboplastin Time (aPTT)	25.4 – 35.2 seconds	71.8	33
C-Reactive protein	Less than 5	263	260
pH	7.35 – 7.45	7.25	7.28
HCO3	22 – 26 mmol/L	14	16
Peripheral Blood cultures (MIC, mcg)	Left arm, right arm, right femoral: Sensitive to:	C. simulans Clindamycin (2) Gentamicin (10) Penicillin (10) Rifampicin (5) Vancomycin (3)	No growth
TDM Vancomycin	Pre-dose: 15 – 25 mcg/ml Post dose: 25 – 40 mcg/ml	20 30	22 35

DISCUSSION

Corynebacterium is a 'club-shaped' Gram-positive bacilli or coccobacili. It was historically nearly always dismissed as contaminants when isolated from patients but increasingly has been implicated as the cause of significant infections. The increasing number of opportunistic infections of elderly and immunocompromised patients caused by *Corynebacterium* indicates that effective treatment is crucial (Ogasawara et al., 2021).

Identification of *C. simulans* is often obscured as it is not included in the usual conventional tests database; therefore, it has been easily misclassified as *C. striatum* (Ogasawara et al., 2021). Several identification

systems based on biochemical tests have been developed to aid the laboratory diagnosis of *Corynebacterium* infections, such as API Coryne (BioMerieux, Lyon, France), RapID CB Plus (Remel/ThermoFisher Scientific, Waltham, MA, USA), BBL Crystal Gram Positive ID System (Becton Dickinson, Franklin Lakes, NJ, USA), MICRONAUT-RPO (Merlin Diagnostics, Bomheim, Germany) (Zasada & Mosiej, 2018). Our laboratory uses Vitek 2 Automated system to identify *C. simulans*. Rennie et al. (2008) conducted a multicentre evaluation of Vitek 2 for anaerobe and *Corynebacterium* identification which revealed a 95% confidence interval was met for quality control and reproducibility. In a more recent paper, Xu et al. (2021) published on the direct detection of *Corynebacterium striatum*, *Corynebacterium propinquum*, and *Corynebacterium simulans* in sputum samples by high-resolution melt curve analysis which can detect 22 additional positive specimens, reflecting a 23.9% relative increase in detection rate.

C. simulans is generally more susceptible to antibiotics such as anti-methicillin-resistant *Staphylococcus aureus* (MRSAs), β-lactams, and cephems, especially those that can be served via the oral route compared to *C. striatum* (Ogasawara et al., 2021). This is consistent with our patient's blood culture and sensitivity (shown in Table 1). *C. simulans* is sensitive to vancomycin (anti-MRSAs). However, our patient failed to respond to the appropriate antibiotics which may be attributed to the late presentations with massive septic emboli and hospital-acquired infections.

This is to the author's best knowledge the first case of *C. simulans* infective endocarditis, fulfilling the two major clinical criteria of the Modified Duke diagnostic scheme as evidenced by three sets of blood cultures from different sites and timing yielded *C. simulans* combining with findings of vegetation causing mitral regurgitation on echocardiogram. She presented with right hemiplegia as a late presentation of septic embolism from the infective endocarditis. The comprehensive clinical assessment successfully identified the cause of the hemiparesis and appropriate treatment was administered. The present case stands out for the clinical aggressiveness of the disease.

Arterial embolism of valvular vegetation is frequent and diverse which urges the need for immediate intervention. Arterial embolisms of the lower limbs are reported in 20 to 30% of cases (Pessinaba et al., 2012). The peak incidence of these phenomena is usually in the first 2 weeks of antimicrobial treatment and is influenced by the size and mobility of vegetation (Pessinaba et al., 2012). Our patient transthoracic echocardiography demonstrated large vegetations (1.4 cm^2 and 4.7 cm^2) and certainly a major risk factor for the multiple related embolic complications.

Even with appropriate antimicrobial therapy, our patient remained hemodynamically unstable with persistently elevated inflammatory markers, indicating a failure of medical treatment with the need for valve replacement surgery. The lack of standardized procedures for antibiotic testing is a limiting factor, although the community strains of *C. simulans* are usually susceptible to anti-MRSAs (Ogasawara et al., 2021).

CONCLUSIONS

This case highlights an uncommon cause of infective endocarditis. Clinicians should consider *C. simulans* as a possible pathogen based on the clinical context. Although *C. simulans* bacteremia is rare, it is fairly treatable with prompt initiation of antibiotics.

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