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Reminder of important clinical lesson

Diphtheroids as a cause of endocarditis in a haemodialysis patient

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Summary

The authors report a fatal case of *Corynebacterium* sp. endocarditis. *Corynebacterium* spp. are non-sporulating, pleomorphic Gram-positive bacilli. In particular the authors have identified a species of *Corynebacterium* very closely related to *C striatum*. This is *C simulans.* The authors were able to identify the genus and species using various phenotypic tests. Highlighted here is the importance of identifying diphtheroids as a significant pathogen in the appropriate setting and the need to start antibiotic therapy if this is suspected.

BACKGROUND

Diphtheroids are commonly isolated in laboratory cultures but are often regarded as contaminants. However evidence has been available to suggest that these organisms can cause a wide range of infections.[1] These aerobic, non-sporulating, pleomorphic Gram-positive bacilli are usually commensals of the skin and mucous membranes.[1 2]In fact, infective endocarditis caused by *Corynebacterium* spp. was recognised as early as 1932, but diphtheroids are still disregarded when isolated.[2–5] Here, we present a fatal case of infective endocarditis due to *C simulans* in a haemodialysis patient from Jamaica.

CASE PRESENTATION

A middle aged male patient was first seen at the emergency department of a hospital in the West Indies. The patient had been transferred from another urban hospital for evaluation of his dialysis catheter. He was on regular haemodialysis treatment for 1 year via a right tunnelled, internal jugular catheter.

He was admitted to the hospital with a history of fever for 1 day, cough for 1 week productive of white sputum and diarrhoea for 2 weeks. He had watery diarrhoea three to four times daily with no blood in the stools. He complained of shortness of breath at rest but no history of chest pain. His past medical history included hypertension.

His family history was unknown and he could not remember the names of his medication. He lived with his wife and did not smoke or drink alcohol.

On examination he was in no obvious cardiopulmonary distress. The patient was afebrile and examination of his respiratory, abdominal and central nervous systems revealed no significant abnormality. However cardiovascular examination revealed a pansystolic murmur at the apex which did not radiate.

Blood from the catheter and peripheral veins were sent to the microbiology laboratory for culture and sensitivity testing. Four sets of peripheral blood cultures from different sites and at different times were taken. The two sets of catheter blood cultures were also taken at different times. Stool was cultured and examined for ova, cysts and parasites.

The patient was diagnosed with end stage renal disease chest x-ray confirmed cardiomegaly. Gram-positive bacilli with catheter sepsis and started empirically on co-amoxiclav 1.2 grams intravenously every (q) 24 h (four times a day) and ceftazidime 1 g intravenously once daily. The dosages were renally adjusted. Other medications included hydralazine 25 mg orally (po) three times a day, ferrous sulphate two tablets po twice daily, folic acid 5 mg po once daily and calcium carbonate two tablets po three times a day and he was kept on a renal diet and fluid restriction. These medications were started based on his presenting symptoms and treatment at the previous hospital.

ECG showed left ventricular hypertrophy and bacteria was isolated from both peripheral and catheter blood samples. The bacteria was identified as diphtheroids and as a result regarded as contaminants so the patient was discharged from hospital 3 days after admission with a plan for medical review in one week. No further identification was done on these specimens, especially since they were considered insignificant. He was not considered for cardiology evaluation of possible infective endocarditis as the differential diagnosis did not include infective endocarditis at this time. He was also not considered for echocardiogram evaluation.

On routine review of this patient 1 week later, he complained of fever, cough, exertional dyspnoea, chills and rigors. He had orthopnoea, paroxysmal nocturnal dyspnoea and occasional bilateral leg swelling. On examination he was febrile and in moderate cardiopulmonary distress. His jugular venous pressure was elevated and the apex beat was displaced. He had a grade 4/5 pansystolic murmur at the apex which radiated to the axilla and a grade 3/5 late diastolic murmur over the aortic area. In addition, patient

had hepatomegaly and examination of his respiratory system revealed bilateral basal crepitations.

He was diagnosed with unresolved dialysis catheter sepsis and acute left ventricular failure. The patient was started on ceftriaxone 1 g intravenously once daily. A chest x-ray showed right mid and lower zone opacities indicating a lower respiratory tract infection and the patient's antibiotic treatment was changed to ceftazidime 1 g intravenously once daily and ciprofloxacin 500 mg po twice daily.

The patient showed no improvement and his antibiotics were changed empirically to co-amoxiclav 1.2 g intravenously four times a day and levofloxacin 750 mg intravenously four times a day. He was referred to cardiology services for further management of infective endocarditis.

INVESTIGATIONS

The echocardiogram report showed that the posterior mitral leaflet had on its inflow surface a large mass 2.16 mm by 1.36 mm. This could have been vegetation. There was severe mitral regurgitation into a moderately dilated left atrium. There was also severe tricuspid regurgitation into a severely dilated right atrium and the estimated pulmonary systolic pressure was 73 mm Hg. The left ventricular systolic function was moderately reduced at 37% ejection fraction. The right ventricular systolic function was also moderately reduced. The semilunar valves functioned normally. The septa were intact and great vessels were normal. The patient showed marked deterioration from the previous admission. A chest x-ray showed right mid and lower zone opacities.

Repeat blood cultures were positive using the automated Bactec system with a total of six peripheral and catheter blood specimens growing Gram-positive bacilli after 24 h to 3 days. The presence of multiple positive cultures prompted the laboratory to do antibiotic susceptibility testing. The organism was found to be uniformly susceptible to gentamicin and vancomycin in the peripheral blood cultures. The catheter blood cultures showed susceptibility to gentamicin, vancomycin and co-amoxiclav.

Four peripheral blood culture samples were received, two were positive for Gram-positive bacilli after 24 h and the other two after 48 h. Two catheter blood samples were positive for Gram-positive bacilli within 24 h.

It is important to note that on first admission the patient also grew Gram-positive bacilli in the blood but this was thought to be insignificant.

Microbiological investigations

The Gram-positive bacilli isolated were characterised using the catalase reaction and fermentation of the sugars dextrose and sucrose as well as additional tests.[1] These results narrowed down identity of the organisms to *C striatum* or *C simulans*. Tests such as growth at 20°C and ethylene glycol acidification confirmed the identity of the organism as *C simulans*.[6–8] After reviewing the article by Wattiau *et al* it was found that the phenotypic tests performed were adequate.[6] Molecular identification was not done. This would have been a disadvantage as molecular identification is more reliable for confirmation of the organism. Hence we emphasise the importance of considering diphtheroids as pathogens and not just *C simulans*.

DIFFERENTIAL DIAGNOSIS

Unresolved dialysis catheter sepsis and acute left ventricular failure was entertained as a diagnosis as the patient presented previously with symptoms of infection and the catheter was thought to be the source. However after interspecialty consultation it was decided the patient had infective endocarditis, pulmonary hypertension, dilated cardiomyopathy and end stage renal disease.

TREATMENT

Microbiological treatment

The Kirby–Bauer disc diffusion method was used to test antibiotic susceptibility. The antibiogram for the isolates from peripheral blood culture were susceptibile to gentamicin and vancomycin. While the catheter blood samples showed sensitivity to gentamicin, vancomycin and co-amoxiclav.

Empiric treatment with co-amoxiclav 1.2 g intravenously once daily (adjusted for renal impairment) and levofloxacin 750 mg intravenously four times a day was commenced after the second admission and the patient deteriorated.

There was discussion between microbiology and the attending physicians concerning the need for this patient to be treated with renal doses of gentamicin 60 mg intravenously once daily and vancomycin 1 g intarvenously on alternate days, however the patient died before this could have been done.

Diuretics, nitrates and other medications for heart failure were not commenced.

OUTCOME AND FOLLOW-UP

The patient died before appropriate antibiotics could be started.

DISCUSSION

Diphtheroids are commonly isolated in laboratory cultures but are often regarded as contaminants. This case, along with other cases reported in the literature, highlights the fact that *Corynebacterium* spp. can be pathogenic. Where multiple peripheral blood cultures are positive for *Corynebacterium* spp., especially when cultures become positive within 24–48 h, then antibiotic susceptibility testing should be considered and clinical correlation advised with consideration of the modified Duke's criteria. This is important as antibiotic coverage for *Corynebacterium* spp. may not be provided by empiric antibiotic therapy. In this case, both catheter blood samples were positive within 24 h and of the four peripheral blood samples, two were positive after 24 h and the other two after 48 h.

Only a few other cases of infective endocarditis caused by *C simulans* have been previously reported.[9] *C simulans* was first recognised as a new species in 2000 by Wattiau *et al*.[6] It is genetically quite similar to *C striatum* with greater than 98% gene homology with 16S rRNA. It has been shown by Belmares *et al* that the average age of a patient with *C striatum* endocarditis is 61.3+/–16.5 years.[2] There is a greater predilection for the left side of the heart and there is a statistically significant association with nosocomial risk factors such as the presence of an intravascular access device, dialysis fistula, pacemaker or presence of a prosthetic device other than a valve.[2 10] This case shows this pattern. *C striatum* is mentioned because of its high

genetic homology with *C simulans*. It should also be noted that some of those organisms classified as *C striatum* may in fact have been *C simulans*.

The consistent isolation of *Corynebacterium* spp. should alert the clinician to a significant clinical finding.[11] It should be noted that this patient also had the additional complication of having end-stage renal disease, which affected appropriate choice and dosage of antibiotic therapy employed.

In one study 27% of patients had non-cardiac predisposing factors with chronic haemodialysis and haemodialysis being factors.[8] In another study, over a quarter of patients with *Corynebacterium* spp. endocarditis required valve replacement and the death rate was over 40%.[2] *C simulans* has previously been isolated from the blood.[12]

If *Corynebacterium* spp. endocarditis is suspected, empirical treatment with appropriate antibiotic treatment should be considered, and in cases of renal impairment appropriate renal doses should be started.[8 11]

This case showed that *C simulans* is a cause of disease and *Corynebacterium* spp. should be considered as a cause of bacterial endocarditis where there is persistent isolation of these bacteria, with no other bacteria being isolated.[2 8]

Learning points

- Gram-positive bacteria, especially diphtheroids, in certain patient populations, should be regarded as potential pathogens and cultures should not simply be disregarded as contaminants.
- Haemodialysis patients are susceptible to rare infections.
- Modified Duke's criteria and multiple peripheral blood cultures are important for a microbiological diagnosis of rare causes of endocarditis.
- Multi-disciplinary approach is important for proper patient management, particularly early involvement of cardiologists, infectious diseases specialist and medical microbiologist in suspected cases of infective endocarditis.

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Competing interests None.

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