CASE REPORT

Native valve endocarditis caused by *Lactococcus garvieae*: an emerging human pathogen

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SUMMARY

A 57-year-old man presented with native mitral valve endocarditis caused by *Lactococcus garvieae*, a known animal pathogen that is increasingly being reported as a cause of human infections. The organism was cultured in four sets of blood cultures and identification was initially made by matrix-assisted laser desorption/ionisation—time of flight mass spectrometry and confirmed by 16S rDNA PCR of the blood culture isolate. He was successfully treated with 6 weeks of both amoxicillin and gentamicin and underwent valve replacement surgery after 4 weeks of antimicrobial treatment. The removed valve was sterile but *L. garvieae* DNA was detected on the valve using 16S rDNA PCR. The cause of the *L. garvieae* infection could not be ascertained but flexible sigmoidoscopy demonstrated colonic polyps, which have been linked to infection with this organism.

BACKGROUND

Lactococcus garvieae is a known pathogen of marine and terrestrial animals^{1 2} that has been associated increasingly with human infections in recent years.^{3 4}

We present a case of native valve endocarditis caused by *L. garvieae*. Diagnosis of this infection was made possible by recent developments in microbiological methods increasingly employed in diagnostic laboratories, namely matrix-assisted laser desorption—time of flight mass spectrometry (MALDI-TOF MS) and bacterial 16S ribosomal (r) DNA PCR.

CASE PRESENTATION

A 57-year-old man presented with a 2-month history of weight loss, fever and anaemia. On examination, he had a pansystolic cardiac murmur. He had a background history of gallstones, Bell's palsy, bilateral renal stones and pneumothorax secondary to traumatic rib fractures. There was a travel history to Spain, the Netherlands and Germany in the preceding year, and he had consumed cooked seafood during his travels. There was no history of contact with raw seafood or marine animals at any point.

INVESTIGATIONS

Transthoracic echocardiography on admission showed vegetations on the posterior mitral valve leaflet with severe mitral regurgitation and moderate to severe aortic valve regurgitation.

There was good left ventricular systolic function.

Four sets of blood cultures taken on admission grew Gram-positive cocci identified as *L. garvieae* by MALDI-TOF MS (confidence value 99.9%, Vitek MS bioMérieux) and 16S rDNA PCR. The explanted mitral valve was culture negative, but 16S rDNA PCR of the valve material was positive for *L. garvieae* DNA (99.9% match to *L. garvieae* ATCC 49156, GenBank accession number AP009332). The organism had a penicillin minimum inhibitory concentration (MIC) of 1 mg/L (Etest, bioMérieux) and was sensitive to high-level gentamicin (gentamicin 200 µg, Oxoid) by disc diffusion testing.

The patient also underwent flexible sigmoidoscopy for an in-hospital episode of rectal bleeding, and two colonic polyps were detected and excised. Histology revealed them to be tubulovillous adenomas with low-grade dysplasia.

TREATMENT

The patient was treated with intravenous amoxicillin 2 g every 4 hours and gentamicin 1 mg/kg twice daily for 6 weeks. Gentamicin dosage was titrated according to therapeutic drug monitoring with target predose levels of <1 mg/L and post-dose levels of 3–5 mg/L.

Mechanical mitral and aortic valve replacement took place after 4 weeks of intravenous antibiotic treatment. Valve replacement surgery was performed due to the development of severe mitral and aortic valve regurgitation. Mechanical valves were chosen over tissue valves because of the patient's younger age and the greater longevity of mechanical valves over tissue valves. The requirement for anticoagulant therapy as a consequence of selecting a mechanical valve was assessed a reasonable risk despite the single episode of rectal bleeding, considered to be due to discrete polyps which had since been excised.

OUTCOME AND FOLLOW-UP

The patient made good clinical progress and was discharged 6 weeks after admission. He was reviewed at 6 weeks postdischarge due to an isolated episode of night sweat without an accompanying fever and was found to be clinically well. Three sets of blood cultures taken 6 weeks after cessation of antibiotic therapy were negative and his C reactive protein at the time was 12. Further follow-up has been arranged.

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DISCUSSION

Reports of human infections caused by *L. garvieae* have been rising in recent years, likely due to improved microbiological identification methods. The majority of reported infections have been endocarditis cases from Europe, USA and Asia. Other reported infections include biliary, musculoskeletal and urinary tract infections. Although some of these cases were associated with a history of contact with handling fish or seafood consumption, most of them did not have a discernible source.³ To date in the literature, there has only been a single case report of human infection caused by *L. garvieae* in the UK. The reported patient had osteomyelitis and a suspected prosthetic valve endocarditis.⁵

In our patient, *L. garvieae* native valve endocarditis was established by two independent methods, MALDI-TOF MS and 16S rDNA PCR. MALDI-TOF MS is an increasingly available method of rapid identification of bacterial cultures using MS. The mass spectrum generated is species specific and is compared with a database for organism identification.⁶

Identification of bacteria with PCR-based amplification and sequencing of bacterial 16S rDNA⁷ is an innovation so far only available in a limited number of medical microbiology laboratories. This methodology does not require the presence of conventionally culturable organisms; non-culturable and even dead bacteria can be detected if sufficient intact DNA is present. Consequently, 16S rDNA PCR of infected tissue is increasingly being used for the identification of bacteria where the likely pathogen is slow growing or fastidious or where the patient has already received antibiotic treatment.

The use of beta lactam and aminoglycoside combination treatment in our patient was based, by analogy, on published treatment regimens for streptococcal and enterococcal endocarditis⁸ and previous case reports of *L. garvieae* endocarditis.^{4,9} Although lack of synergism with aminoglycosides have been reported in some isolates of *L. garvieae*,¹⁰ the relatively high penicillin MIC of this isolate compared with other streptococci prompted the decision to use combination treatment in this patient.

The explanted mitral valve was culture negative, and subsequent blood cultures several weeks after the completion of antimicrobial therapy were also negative, indicating probably successful antimicrobial treatment. However, a longer follow-up period would provide more reassurance of treatment success. The detection of *L. garvieae* DNA from the valve material confirms that this organism was the causative agent of the endocarditis infection. To our knowledge, this is the first report of *L. garvieae* causing native valve endocarditis in the UK.

The patient had no established exposure history known to be relevant to this organism. However, colonic polyps were found on flexible sigmoidoscopy. Bowel pathology could be a potential risk factor for *L. garvieae* infection.⁹

Contributors FHL and DRJ contributed equally to the investigation and microbiological management of the case. FHL drafted and DRJ revised the manuscript. Both authors approved the final manuscript.

Competing interests None declared.

Patient consent Obtained.

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Patient's perspective

My patient's experience with infective endocarditis

Initial feelings of illness

During August 2016, I developed a mild but persistent irritating cough which failed to resolve itself, I eventually saw my general practitioner (GP) in mid-September who sent me for an X-ray.

The X-ray found that I had atelectasis in the left base of the lung and also cardiomegaly. I was given a course of antibiotics and advised to carry out some breathing exercises. The GP thought this had been caused following surgery on broken ribs on 25 December 2015.

During the period from mid-August to the end of September, I also experienced some episodes of sweating during the day and some feelings of general illness which present to me like 'a bit of a virus'; however by the end of the antibiotic courses, I did feel much better generally. I asked my GP if there was any reason I should not go on a Holiday to Gran Canaria; he advised I was OK to travel.

While on holiday

After the first 3 days on holiday, I began to get pain in my left side and kidneys I was also feeling rather lethargic and generally ill, it was getting to be a struggle to climb the many stairs in the hotel, I also noticed my appetite getting worse, I was eating but with little enthusiasm.

Return from holiday

On return from holiday still feeling ill, I attended the urgent care centre at the Leicester Royal Infirmary (LRI) on 23 October 2016, from where I was referred to the clinical decisions unit (CDU) at Glenfield, where I was examined and had blood tests. I was told my infection and inflammation markers were high but not dangerously so, I was given a further course of antibiotics and sent home.

Further contact with GP

Following antibiotics, I was not feeling any better, I still had the pain and was feeling unwell on a regular basis and was developing high temperatures and fever, I also started to have night sweats which felt as if my whole body was wet. I saw my GP again and he referred me for a CT scan on my thorax and also for a bladder examination as there was a trace of blood in my urine. I also had numerous blood tests during this period. The GP was not able to explain why I was getting fevers, sweats and was generally feeling unwell, I told him I felt like I had infection in my body.

Following the CT scan, it was found I had two kidney stones and that two of my ribs had not healed properly. It also found I had obstructive stones in my gall bladder.

The feelings of unwellness, lack of appetite, fevers and night sweats continued into December, the fevers usually came on in the late afternoon or early evening and I had to go to bed to sleep it off; my temperature sometimes reached 39°C but this usually went down after an hour or so; this was accompanied by teeth chattering and my body shaking uncontrollably. By this time, I was getting the night sweats every night at least twice a night.

I continued to see the GP for results of tests but he was unable to throw any light on these symptoms, at one point he recommended a strong antiperspirant. On one occasion, I saw him I believe on the 12 December he listened to my heart but nothing of concern was brought to my attention.

I saw him again on 21 December to discuss the results of ultrasound test on my abdomen. It was at this consultation he sent me to LRI GP assessment centre for investigation where it was found I had a heart murmur probably caused by endocarditis. Almost immediately I was given a dose of intravenous antibiotics and referred to CDU at Glenfield. Following admission to Glenfield and starting 6-week antibiotic course, I had no more fevers but was still getting the occasional night sweats, which receded as the course continued.

Stay in hospital

While in CDU, I was asked about lifestyle in regard to intravenous drug use, poor sexual health, possible HIV infection, none of which in any way applied to me, I was also spoken to about dental health (I visit dentist 6 monthly), consumption of seafood was also discussed as was exposure to domestic animals. I have consumed cooked seafood and have some contact with dogs, there were also a lot of feral cats around the hotel in Gran Canaria, some of which were around food serving areas.

During the first 4 weeks in Glenfield, I was feeling gradually better and my appetite returned up to surgery on 18 January 2017 to fit two mechanical heart valves which had been affected by the infection. Postsurgery I was in pain, but the symptoms of endocarditis had receded to a point where I did not feel ill other than with pain from the surgery and other pain associated with my still damaged ribs.

Return home

I was discharged on 2 February 2017 when my antibiotic course ended. Since being at home, I have not had any symptoms of endocarditis I experienced previously, my appetite is normal.

Learning points

- ▶ *Lactococcus garvieae* infection in humans is being increasingly reported, with endocarditis being the most common type of infection.
- ▶ Advances in clinical microbiology laboratory diagnostic methods have facilitated recognition of this organism.
- ▶ Antibiotic treatment with amoxicillin, possibly in combination with gentamicin and surgery as appropriate, appears to be an effective treatment of this organism as evidenced by negative culture results on the removed mitral valve.

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