Osteomyelitis and possible endocarditis secondary to *Lactococcus garvieae*: a first case report

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Abstract

Although osteomyelitis is commonly caused by staphylococcal infection, the first case of a lumbar osteomyelitis secondary to *Lactococcus garvieae* is reported. The case was complicated by possible endocarditis of an aortic valve prosthesis.

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Keywords: *Lactococcus garvieae*; osteomyelitis

Lactococci are often believed to be of low virulence. We report a first case of osteomyelitis secondary to *Lactococcus garvieae* in a previously well, middle aged woman.

Case report

A 56 year old woman was referred to a rheumatology clinic with a nine week history of lower back pain and a five week history of rigors and night sweats. She was anorexic and had lost approximately 3.5 kg in weight in six weeks. Systems review was unremarkable. Her past medical history included a xenograph aortic valve replacement for aortic stenosis 12 years earlier (Ionesu-Shiley valve) and she was known subsequently to have mild aortic regurgitation. She took no prescribed medication and until this illness had been fit and well. Examination was unremarkable other than tenderness over L5/S1 and a soft early diastolic murmur at the left sternal edge in keeping with the aortic regurgitation. Results of routine tests were as follows: haemoglobin 99 g/l (mean corpuscular volume 92 fl), white cell count 6.1×10^9/l, erythrocyte sedimentation rate 74 mm/hour, and C reactive protein 12.6 mg/l; urea, electrolytes, creatinine, liver function tests, and a bone profile were all normal. The urine culture was negative, the chest radiography was normal, an electrocardiogram showed sinus rhythm with a normal axis and deep T wave inversion in the inferolateral territory. This was unchanged from earlier electrocardiograms (previous history of aortic stenosis). Thoracic and lumbar spine radiographs showed a thoracolumbar scoliosis with loss of disc height at L2/L3 and subchondral bone loss. A bone scan revealed increased tracer activity in the mid-lumbar region (fig 1).

Three days later she was admitted with increasing back pain and spiking temperatures. A diagnosis of presumed osteomyelitis was made and she was treated with analgesics and bed rest, while blood cultures were repeatedly taken during temperature spikes. A computed tomographic guided vertebral biopsy was arranged.

On day 6 after admission, pale splinter haemorrhages were noted in several nails of her hands and toes, not previously documented. There was no splenomegaly or microscopic haematuria and there was no other evidence of embolic phenomena. The murmur of aortic regurgitation was unchanged. A transthoracic echocardiogram revealed a well seated valve replacement in the aortic position, with thin mobile leaflets and mild to moderate transvalvular aortic regurgitation. Other valves appeared normal and no vegetations were identified. In view of the high suspicion of infective endocarditis, a transoesophageal echocardiogram was undertaken. No vegetations or changes consistent with an aortic root abscess were identified. The aortic regurgitation remained unchanged in severity and no further splinter haemorrhages subsequently developed.

All blood cultures, in addition to the biopsied bone, grew Gram positive cocci growing in chains on blood agar. They were identified as *Lactococcus garvieae* and were found to be indistinguishable from one another by API Strep (bioMerieux, Basingstoke, Hants, UK), sensitivity testing and their identity was confirmed by the Streptococcal Reference Laboratory (Respiratory and Systemic Infection Laboratory, London, UK). Vancomycin had been started after the bone biopsy, which was subsequently replaced by teicoplanin to which the organism was sensitive. With antibiotic treatment her clinical course improved and her remaining admission was uneventful. She was discharged after one month of intravenous treatment, with a temperature chart, to complete a further two months of teicoplanin at home via a Hickman line. She has remained well and continues under active follow up.

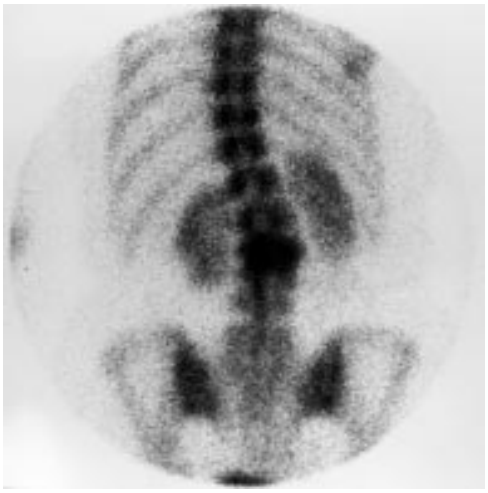

Figure 1 Bone scan showing increased tracer uptake in mid-lumbar region.

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Box 1: The Duke endocarditis service criteria for the diagnosis of infective endocarditis[5]

Definite infective endocarditis:
- Identification of micro-organisms from a vegetation by culture or histology, or from an intracardiac abscess.
- Histology from a vegetation or intracardiac abscess which confirms active endocarditis.
- Two major criteria or one major plus three minor or five minor criteria (see box 2).

Possible infective endocarditis:
Findings consistent with infective endocarditis but which do not satisfy "definite" or "rejected".

Rejected:
- The presence of a firm alternative diagnosis.
- Resolution of clinical manifestations within four days of antibiotic treatment.
- Absence of pathology evidence at surgery or postmortem within four days of antibiotic treatment.

Box 2: Definitions of major and minor criteria[5]

Major criteria:
- Detection of an organism *typical* for infective endocarditis—for example, *Streptococci viridans* species, *Streptococcus bovis* from two separate blood cultures.
- Persistently positive blood cultures for an organism *consistent* with infective endocarditis in samples drawn more than 12 hours apart or if three out of four separate cultures are positive and the first and last were drawn at least an hour apart.
- Evidence of endocardial involvement—for example, identification of vegetations or abscesses with echocardiography, new partial dehiscence of a prosthetic valve, new valvular regurgitation.

Minor criteria:
- Predisposition to infective endocarditis—for example, pre-existing heart condition, intravenous drug misuse.
- Fever $\geq 38^{\circ}$C.
- Vascular phenomena—for example, septic pulmonary infarcts, arterial emboli, mycotic aneurysm, intracranial or conjunctival haemorrhages, Janeway lesions.
- Immunological phenomena: glomerulonephritis, Osler's nodes, Roth spots, presence of rheumatoid factor.
- Positive blood cultures not meeting major criteria or serological evidence of active infection with an organism consistent with infective endocarditis.
- Echocardiogram consistent with infective endocarditis but not meeting major criteria.

Discussion

This is the first report of osteomyelitis secondary to infection with *L garvieae*, an emerging zoonotic pathogen.[1] Although first isolated from bovine sources, mainly involving cases of mastitis,[2] *L garvieae* has subsequently been isolated from both fish and humans.[1] Lactococci are facultatively anaerobic, catalase negative, Gram positive cocci that occur singly, in pairs, or in chains. They are most often confused with enterococcus species but can be differentiated by biochemical tests.[3] In contrast to streptococci and enterococci, lactococci are unusual pathogens and are considered to be opportunistic and of low virulence in humans. They have previously been recovered from urine and blood.[4] We are unaware, however, of any previous reports of osteomyelitis secondary to *L garvieae*, a condition where *Staphylococcus aureus* remains the commonest causative organism.

The complicating issue in this case was the finding of splinter haemorrhages in the presence of bacteraemia and a prosthetic heart valve. There should be a high index of suspicion for infective endocarditis in the presence of heart valve replacements, but there was no evidence on transthoracic or transoesophageal echocardiography of valve prosthesis or aortic root infection. The aortic regurgitation had previously been noted and was transvalvular rather than paraprosthetic. Using the criteria published by the Duke endocarditis service, the diagnosis of endocarditis in this case remains possible (see boxes 1 and 2).[5] This method for assessing the likelihood of infectious endocarditis employs clinical, microbiological, serological, and echocardiographic parameters as major and minor criteria rather similar to the Jones criteria used in the diagnosis of acute rheumatic fever. This yields a high specificity and hence a low chance of a false negative result[5].

Learning points
- *Lactococcus garvieae* is a rare cause of osteomyelitis.
- The presence of bacteraemia and a prosthetic heart valve requires a high index of suspicion for infective endocarditis.
- The Duke endocarditis service have published criteria for the diagnosis of infective endocarditis using major and minor criteria.

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Phaeochromocytoma unearthed by fluoxetine

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Abstract
Non-specific noradrenaline reuptake inhibition by high dose selective serotonin reuptake inhibitors, along with catecholamine release from phaeochromocytoma, may lead to a hypertensive paroxysm. This may unmask a clinically silent phaeochromocytoma. Hypertensive paroxysm induced by paroxetine leading to detection of phaeochromocytoma has been reported. The first patient in whom fluoxetine unmasked a phaeochromocytoma is reported.
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Keywords: selective serotonin reuptake inhibitor; fluoxetine; phaeochromocytoma

Learning point

Phaeochromocytoma or drug interactions should be suspected when hypertension is detected during treatment with fluoxetine.

Case report

A 29 year old man was prescribed fluoxetine (selective serotonin reuptake inhibitor) 20 mg/day for depression. In view of his poor response the fluoxetine dose was doubled to 40 mg/day. A few days later he presented with paroxysmal attacks of palpitations, nausea, headache, pallor, perspiration, and headache. His other medication was diazepam. On examination the patient was agitated, apprehensive, and had marked peripheral vasoconstriction. His blood pressure varied between 250/140 and 80/30 mm Hg. There was no postural hypotension. Phaeochromocytoma was considered in view of paroxysmal nature of symptoms and fluctuations of blood pressure. Blood pressure recorded earlier was normal. Twenty four hour excretion of noradrenaline was 10.3 nmol/day (normal range 0.06–0.47), adrenaline 32 nmol/day (normal <0.016), and vanillylmandelic acid 134 μmol/day (normal <30).

Magnetic resonance imaging of the abdomen for a suspected pheochromocytoma revealed a 3 cm diameter mass in the right adrenal gland. After surgical removal of the right adrenal gland, histological examination confirmed the presence of a phaeochromocytoma. The patient has been normotensive since then, and has no symptoms.

Discussion

Tricyclic antidepressant drugs lead to increased concentrations of noradrenaline due to inhibited presynaptic reuptake of noradrenaline. Although this effect is beneficial, it can lead to haemodynamic abnormalities, particularly when used with monoamine oxidase inhibitors or in a patient with phaeochromocytoma.[1] Similar haemodynamic effects are seen when selective serotonin reuptake inhibitors are used along with a monoamine oxidase inhibitor.[2]

A difference in selectivity has been seen in animal studies between various serotonin reuptake inhibitors, regarding dose dependent inhibition of noradrenaline uptake. In humans, such inhibition in therapeutic dosage has not been shown.[3]

Activity of cytochrome *P*-450 (CYP2D6) determines the rate of fluoxetine metabolism; this differs between poor and prolific metaboliser patients.[4] Non-specific noradrenaline reuptake inhibition by high dose serotonin reuptake inhibitors, along with catecholamine release from phaeochromocytoma, may explain the haemodynamic abnormalities seen in this patient. Inhibition of serotonin reuptake by platelets may result in increased plasma serotonin concentrations. This in turn leads to higher sensitivity of noradrenaline receptor, thus providing an alternative explanation for paroxysms of haemodynamic abnormalities.[5]

Paroxetine has been implicated in such adverse effects in a patient with pheochromocytoma.[6] There is no report of fluoxetine leading to such effects until now. Clinicians should suspect phaeochromocytoma or drug interactions when hypertension is detected during treatment with selective serotonin reuptake inhibitors.

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