

CASE REPORT

Listeria endocarditis: current management and patient outcome—world literature review

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Abstract

This is believed to be the 58th reported case of *Listeria monocytogenes* infective endocarditis. Published reports worldwide were reviewed as to treatment, outcome, and prognostic features. There is controversy over whether all patients with this condition should have surgery. Moreover the best antibiotic treatment is not known, which accounts for the heterogeneity of regimens used. *Listeria* endocarditis has a high mortality rate (37%). This was higher in men (41% v 32%) and in patients with valve prostheses (41% v 31%), though neither observation reached statistical significance. There was no significant difference in mortality between surgical and non-surgical treatment, but untreated listeria endocarditis proved universally fatal. From the data, treatment with ampicillin is recommended, with resort to surgery in cases where the infection cannot be eradicated or where haemodynamic compromise has occurred.

(Heart 1997;77:380-383)

Keywords: *Listeria monocytogenes*; bacterial endocarditis; treatment; prognosis

Listeria monocytogenes is widely distributed in nature. It has been isolated from soil, dust, animal feed, water, sewage, and almost every type of animal cultured, including asymptomatic humans. In humans it may be encountered as a pathogen, especially in immunocompromised individuals. In cardiology it usually manifests as valve endocarditis, most commonly on prosthetic valves. Since the first report in 1955 by Hoepfich¹ only 57 cases have been reported worldwide. There seems to be no consensus as to whether surgical treatment confers extra benefit in addition to antibiotic treatment alone. Despite the known sensitivity of *L. monocytogenes* to penicillin, a wide range of antibiotic regimens has been used. We present a further case report of *L. monocytogenes* prosthetic valve endocarditis, and review the world literature in an attempt to determine whether one antibiotic regimen is superior to others, and whether surgery, even in the context of an infected valve, is a neces-

sary adjunct to antibiotic treatment. We also assess the efficacy of different antibiotic regimens and the mortality with antibiotic and surgical treatment where the disease affects prosthetic or diseased valves as well as previously normal valves.

Case report

A 78 year old woman who had a Starr Edwards mitral valve replacement 10 years previously presented to her district general hospital with a one month history of malaise, pyrexia, shortness of breath, and purulent sputum. On questioning she admitted to weight loss but not to night sweats. Two weeks previously she had been treated with a course of cephalexin for a presumed chest infection, but showed no improvement. Her only other treatment was digoxin 0.125 mg daily for atrial fibrillation. On examination she had facial plethora, a temperature of 38.8°C, and a solitary splinter haemorrhage on her left foot. Cardiovascular examination showed an irregularly irregular pulse at a rate of 80 beats/min and blood pressure was 160/90 mm Hg. There was an ejection systolic murmur loudest at the left sternal edge. The jugular venous pressure was raised to 6 cm and she had mild bilateral ankle oedema. Her chest was clear and there were no abdominal or neurological abnormalities. Laboratory investigations showed a haemoglobin (Hb) of 114 g/l, a white cell blood count (WBC) of $12.9 \times 10^9/l$, a platelet count of $106 \times 10^9/l$, and an erythrocyte sedimentation rate (ESR) of 47 mm in the first hour. Urea and electrolytes, and liver function tests were normal. After four sets of blood cultures had been obtained, she was started on benzylpenicillin and gentamicin empirically for presumed endocarditis. Three of the four blood culture bottles subsequently grew *L. monocytogenes* (sensitive to erythromycin, penicillin, and gentamicin), establishing the diagnosis of listeria endocarditis. She made a steady recovery until she developed an episode of slow atrial fibrillation at a rate of 48 beats/min. It was felt that this may have represented the development of complete heart block and she was therefore transferred to St Mary's Hospital, London, for assessment of the need for surgical replacement of her prosthetic valve.

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Accepted for publication
13 December 1996

The slow atrial fibrillation resolved on reducing the dose of digoxin and she continued to improve clinically. Her ESR fell to 10 mm in the first hour, while the first estimation of C reactive protein two weeks into the treatment was found to be less than 5 IU/l. A transoesophageal echocardiogram showed moderate left ventricular function and a well

Table 1 Summary of worldwide reports of listeria endocarditis cases

Case No (reference)	Age/sex	Previous cardiac pathology	Underlying condition	Valve(s) involved	Surgical or medical treatment	Outcome	Antibiotics
1 Hoeprich 1955 ¹	42/M	RHD	None	A + M	Medical	Survived	Pen + strept + erythr
2 Seeliger 1961 ³	NK/F	None	Severe anaemia	NK	Medical	Survived	"Supronalium"
3 Seeliger 1961 ³	35/F	NK	Chorea, septic abortion	M	Medical	Died	Pen + strept + erythr
4 Baker and Muchmore 1961 ⁴	28/M	Rheumatic fever	None	NK	Medical	Survived	Pen + strept
5 Baker and Muchmore 1961 ⁴	55/M	None	Alcoholism, metastatic pancreatic carcinoma	M	None (PM diag)	Died	None
6 Brecht 1962 ⁵	40/F	RHD	None	A + M	Medical	Survived	Reverin + strept*
7 Simpson and Hare 1967 ⁶	22/F	None	Hodgkin lymphoma, steroid treatment	A + M	None	Died	None
8 Buchner 1968 ⁷	49/M	RHD	Alcoholism, diabetes mellitus	M	Medical	Died	Pen + erythr (INH + strept)
9 Elston 1969 ⁸	56/M	None	Alcoholism, facial carcinoma	A + M	Medical	Survived	Pen + erythr
10 Goasguen 1969 ⁹	10/M	None	Kwashiorkor	A	Medical	Survived	Pen + chloramph
11 Latour 1970 ¹⁰	23/M	Aortic stenosis	None	A	Surgical	Died	Pen + strept
12 Degeorges 1971 ¹¹	31/M	Aortic stenosis	None	A + M	Surgical	Died	Amp + strept followed by amphot B
13 Quiret 1972 ¹²	64/M	Angina pectoris	NK	A + M	Medical	Died	Pen + gent
14 De Soldati 1972 ¹³	32/M	CHF	None	A + M	Medical	Survived	Chloramph + oleand + erythr
15 Bowmer 1973 ¹⁴	54/M	NK	NK	NK	NK	Survived	Pen + strept
16 Bowmer 1973 ¹⁴	76/M	NK	Autoimmune radiculitis and haemolytic anaemia, steroid therapy	NK	None	Died	None
17 Leonard 1973 ¹⁵	27/F	None	Haemodialysis, renal transplant	A	Medical	Survived	Amp + gent
18 Leonard 1973 ¹⁵	69/M	AVD, CHF, myocardial infarction	Haemodialysis, renal transplant	A + T	Medical	Died	Oxacil + amp
19 Bassan 1975 ¹⁶	75/M	Atrial fibrillation	None	?M	Medical	Survived	Pen
20 Weinstein 1975 ¹⁷	72/F	VP	None	A	Surgical	Died	Pen + kanamycin
21 Humbert 1977 ¹⁸	64/M	Angina pectoris	NK	NK	NK	Died	NK
22 Humbert 1977 ¹⁸	23/M	Aortic stenosis	NK	A	NK	Died	NK
23 Clark 1977 ¹⁹	67/F	RHD, streptococcal endocarditis	Milroy disease	A	Medical	Died	Cephalothin
24 Bayer 1977 ²⁰	16/F	RHD	None	M	Medical	Survived	Pen
25 Kaplan 1977 ²¹	55/M	RHD	None	A + M	Medical	Survived	Pen
26 Holshouser 1978 ²²	25/F	None	Diabetes mellitus, pregnancy	NK	Medical	Survived	Amp
27 Breyer 1978 ²³	64/M	VP	None	A	Medical	Died	Pen
28 Pitcher 1978 ²⁴	53/M	Hypertrophic cardiomyopathy	None	A + M	Medical	Survived	Pen
29 Saravolatz 1978 ²⁵	58/F	RHD, VP	None	M	Medical	Survived	Pen + tobr
30 Saraiva 1979 ²⁶	23/F	None	Septic abortion	?M	Medical	Died	Pen + cefalothin + strept
31 Cremades 1980 ²⁷	NK/M	NK	NK	A	Surgical	Survived	NK
32 Gelber 1980 ²⁸	66/M	None	Chronic lymphocytic leukaemia	A	Medical	Survived	Pen + strep
33 Skidmore 1981 ²⁹	27/M	VP	Marfan syndrome, peritoneal dialysis	A	Medical	Died	Pen
34 Winslow 1981 ³⁰	56/F	Mitral valve prolapse	None	M	Medical	Survived	Pen
35 Higgins 1983 ³¹	63/M	VP	Chronic rectal fistula	M	Medical	Survived	Pen + strep
36 Davis 1983 ³²	69/F	VP	None	M	Medical	Survived	Amp + gent
37 Arruda 1984 ³³	34/F	None	None	A	Medical	Survived	Pen G
38 Povoia 1984 ³⁴	43/M	VP	Redo VP	M	Medical	Died	Amp + amik
39 Sheinman 1985 ³⁵	74/M	Atrial fibrillation	None	A + M	Medical	Died	Amp + nelt
40 CDR 1985 ³⁶	68/M	NK	Diabetes mellitus	NK	NK	Survived	NK
41 CDR 1986 ³⁷	72/F	VP	NK	M	NK	Survived	NK
42 Gallagher 1986 ³⁸	69/F	Myocardial infarction	Diabetes mellitus, haemodialysis, vascular infection	A	Medical	Died	Vanc
43 CDR 1986 ³⁹	77/F	NK	NK	NK	NK	Survived	NK
44 Alonso 1988 ⁴⁰	55/M	MI 6 years before	None	A + M	Surgical	Survived	Nelt + pen
45 Carvajal 1988 ⁴¹	58/M	None	Colon adenocarcinoma	A	Surgical	Died	Amp + nelt
46 Carvajal 1988 ⁴¹	75/F	AVD, streptococcal endocarditis	Lung adenocarcinoma	A	Medical	Died	Amp + gent
47 Carvajal 1988 ⁴¹	83/F	AVD	Colon adenocarcinoma	A	Medical	Died	Amp
48 Jackson 1988 ⁴²	52/F	None	Cirrhosis	M + ?A	Medical	Survived	Amp + gent
49 Riancho 1988 ⁴³	55/M	IHD	HIV + ve	A + M	Surgical	Survived	NK
50 Aparici 1988 ⁴⁴	69/M	VP	None	M	Surgical	Survived	Amp + strept
51 Rao 1989 ⁴⁵	73/F	VP	None	M	Surgical	Survived	Amp + gent
52 Lazanas 1990 ⁴⁶	46/M	VP	None	A + ?M	Medical	Survived	Amox + nelt
53 Ochoteco 1990 ⁴⁷	55/NK	MI 6 years	HIV + ve	M + A	Surgical	Survived	Pen + nelt
54 (Berenguer 1991 ⁴⁸)	35/M	None	Liver cirrhosis, HIV + ve	NK	Medical	Died (GI bleed)	Co-trimoxazole
55 (Segura 1992 ⁴⁹)	67/M	VP + LA thrombus	Colon adenocarcinoma	M	Medical	Survived	Vanc + gent
56 (Lifshitz 1993 ⁵⁰)	78/M	VP + Perm Pacemaker	None	?A + M	Surgical	Survived	Amp + (toibr)
57 (Speeleveld 1994 ⁵¹)	71/M	VP	None	A	Surgical	Survived	Amp + amik
58 (Case)	78/F	VP	None	A	Medical	Survived	Amp

VP, valve prostheses; RHD, rheumatic heart disease; A, aortic; M, mitral; T, tricuspid; NK, not known; VD, valve disease; IHD, ischaemic heart disease; CHF, congestive heart failure; PM, postmortem. amik, amikacin; amp, ampicillin; amox, amoxicillin; amphot B, amphotericin B; chloramph, chloramphenicol; erythr, erythromycin; INH, isoniazid; nelt, neltimycin; oleand, oleandomycin; oxacil, oxacillin.

Table 2 Survival following surgical or medical treatment

	Surgical*	Medical	None
Survived	10	24	0
Died	4	13	3

*Antibiotics plus valve replacement.

seated mitral prosthesis with no evidence of a paravalvar leak. There was mild to moderate aortic regurgitation. Two small echogenic masses were seen on the ball of the Starr Edwards prosthesis.

She was treated with intravenous ampicillin and gentamicin for six weeks. She remained in hospital for a further week. Off antibiotics she remained well, her ESR and C reactive protein remain low, and a repeat transoesophageal echocardiogram could not detect the previously noted masses. Eighteen months later she was alive and well.

Review of published reports

For our literature search, the Silver Platter Medline identified many of the cases. Others were found in references from previous reports, and in some cases we used the *Index Medicus*. Statistics were carried out using the Statsview package. We found reports of 57 cases. Some of the information in these reports is rather limited. The main points of interest in each case are shown in table 1.

The mean age of patients was 53 years (range 10 to 83). More males were affected, with a male to female ratio of 1.6:1. Mortality was 37% (males 41%, females 32%) which is well over double the figure of 14% quoted by Bayliss *et al*² as the overall mortality rate from bacterial endocarditis from all causes. Though male mortality was apparently higher than female, the difference was not found to be significant using a χ^2 test ($P = 0.48$). Patients who had a previous valve prosthesis had a higher mortality (41%) than patients without a prosthesis (31%). This difference was not statistically significant ($P = 0.68$).

Table 2 shows the number of patients receiving no treatment, medical treatment only, and what is labelled "surgical treatment" (which includes antibiotic treatment followed by replacement of the affected valve). Of the reported cases only three did not receive any treatment and this proved to be universally fatal ($P = 0.045$, χ^2 test). Survival rate was similar in the antibiotic treated group and in those in whom medical treatment was followed by surgery. Since patients were not randomly allocated to treatment, the possibility of

bias affecting which patients were selected for surgery must be considered. The selection bias could act in either direction, with either the most severe cases being put forward for surgery or those who are haemodynamically unstable being refused surgery.

As can be deduced from table 1, a vast array of antibiotic regimens has been used. Numerous changes took place in many of the patients' treatments through their illness, but we have tabulated the antibiotic regimen that was used for most of the time or that actually effected a cure. In table 3 we have simplified the antibiotic treatments by grouping similar antibiotic regimens together as one category. There is no statistically significant difference in the survival rate by the use of one or the other antibiotic regimen. This reflects the small number of patients in each treatment group. Three different regimens had 100% survival rate, but each group included only one patient. The combination of streptomycin and penicillin produced a survival rate of 73% (8 of 11), while the combination of aminoglycoside and penicillin showed a survival rate of 63% (10 of 16), which was the same as with penicillin alone (7 of 11).

Discussion

L. monocytogenes endocarditis is rare but an increase in incidence may be expected in view of the increase in the population of patients with valve prostheses, and as HIV infected patients survive longer and increase in numbers. Also the expertise in identifying this infection is growing. A reported mortality of 37% means that this type of infective endocarditis has a grave prognosis. In view of the small number of reported cases, and because of the wide variety of treatments used, it is extremely difficult to ascertain the best course of treatment. We can infer, however, that surgical treatment can be reserved for resistant cases, or in cases where significant valve damage has occurred which results in haemodynamic compromise.

We did not find that any antibiotic treatment was statistically superior to another. Of statistical significance in our results is the fact that untreated listeria endocarditis is universally fatal. The absence of controlled studies is not limited to the endocarditis form of listeriosis but extends to the other syndromes such as septicaemia, meningoencephalitis, and pregnancy related infections. From experimental laboratory studies it has been shown that there is synergism between ampicillin or penicillin and aminoglycosides against *L. monocytogenes*. The combination of streptomycin and penicillin seems to be the treatment resulting in the greatest survival (excluding the three categories with 100% survival, but with only a single patient treated in each of these). This could be a real or a historical difference, as streptomycin was rarely used after 1970. As streptomycin has to be given intramuscularly and has significant ototoxicity and nephrotoxicity, it should be reserved for second line treatment. It seems that a penicillin alone, such as ampicillin, pro-

Table 3 Antibiotic treatment and survival

Antibiotics	Survived	Died	% Survival
Chloramphenicol + penicillin	1	0	100
Erythromycin + chloramphenicol + oleomycin	1	0	100
Co-trimoxazole	1	0	100
Streptomycin + penicillin*	8	3	73
Penicillin*	7	4	64
Penicillin + aminoglycoside	10	6	63
Erythromycin + penicillin	1	1	50
Vancomycin	1	1	50
None	0	3	0

*Includes all types of penicillin, ie, benzyl penicillin, penicillin G, amoxicillin, and ampicillin.

vides the best treatment option. Adding an aminoglycoside does not seem to increase survival despite the synergism shown in the laboratory. Chloramphenicol has been used only twice and both patients survived. This may also prove to be an effective treatment, but as the numbers are so few and because of the well documented toxicity of chloramphenicol, this should be a treatment of last resort.

In summary we have presented another case of prosthetic valve bacterial endocarditis and reviewed the published reports. *Listeria endocarditis* has a high mortality rate of 37%, compared with 14% for other types of bacterial endocarditis. Anecdotally it had been suggested that patients with listeria endocarditis should have the affected valve replaced. We have not found any evidence to support this belief. Instead we suggest medical treatment with ampicillin if the organism is sensitive in cultures, and reserve surgery for cases where significant disruption of the valve apparatus has occurred, or when the fever is resistant to antibiotics.

Special thanks to Dr Robert Heyderman, Lecturer in Infectious Diseases, St Mary's Hospital, for his advice and critical comments.

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