clinical and laboratory values, treatments, and echocardiography findings at admission and patient mortality during the index admission and at the end of a 1-year follow-up period. Subsequently, after the exclusion of patients with end-stage disease in palliative care, patients with acute HF and hyperuricemia at admission were compared with those with normal UA concentrations. The UA was measured in the first 48 hours of emergency department admission; men and women were considered hyperuricemic with plasma concentrations of > 8 mg/dL and > 7 mg/dL, respectively. Quantitative variables are shown as means $\pm$ standard deviation and categorical variables as percentages. The characteristics of the 2 groups (hyperuricemic vs normouricemic) were compared using chi-square and Student t tests. Logistic regression analysis and multivariable Cox proportional hazard risk analysis were used to evaluate the in-hospital and 1-year mortality rates. Statistical significance was defined as $P < .05$.

A total of 244 consecutive patients admitted for acute HF were evaluated, 128 women (52.5%) and 116 men, with a mean age of 75 ± 10 years and moderate comorbidity (Charlson index of 2.6). In total, 144 (59%) showed a preserved left ventricular ejection fraction ($> 50\%$); 203 (83.1%) were receiving diuretics, and 180 (73.7%) patients were using angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers. A considerable majority—167 of the 244 patients (68.4%)—had hyperuricemia at admission, mainly women, and these hyperuricemic patients had a higher degree of functional dependence and higher serum creatinine concentrations than normouricemic patients with acute HF. Normouricemic patients showed a greater tendency for diabetes mellitus and obesity (Table).

During the index admission, 27 patients (11.1%) died, with 28 more patients dying during the first year, giving a cumulative 1-year mortality rate of 22.4%. There was no difference in the mortality rate during the index admission between acute HF patients with and without hyperuricemia (13.2% vs 6.5%; P = .780); however, 1-year mortality was significantly higher in patients with acute HF and hyperuricemia (26.9% vs 13.0%; P = .015). After the Cox regression analysis, high UA concentrations were still associated with 1-year mortality (hazard ratio [HR] = 1.091; 95% confidence interval [95%CI], 1.018-1.169) and the results indicated a protective effect of a better Barthel index at admission (HR = 0.979; 95%CI, 0.969-0.989).

Thus, hyperuricemia was a common finding in our patients requiring hospital admission for acute HF, although its cause is probably multifactorial, either due to the diuretic treatment received, its frequent association with renal dysfunction, or xanthine oxidase overexpression due to the proinflammatory status.[4,5] In line with the few available studies, our results show higher long-term risk of death for patients admitted for acute HF with hyperuricemia, although not of in-hospital death during the index admission. However, there is currently no consensus on whether hyperuricemia plays a direct pathogenic role in the myocardium or whether it acts as a simple surrogate marker of severity.

One question to consider is if the mere reduction in UA can be beneficial in patients with HF. Further work evaluating the effect of hyperuricemic treatment of these patients is required.[6]

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REFERENCES

1. Ponikowski P, Jankowska EA. Patogenia y presentación clínica de la insuficiencia cardiaca aguda. Rev Esp Cardiol. 2015;68:331–7.
2. Eisen A, Benderly M, Goldbourt U, Haim M. Is serum uric acid level an independent predictor of heart failure among patients with coronary artery disease? Clin Cardiol. 2013;36:110–6.
3. Radovanovic S, Savic-Radojevic A, Pekmezovic T, Markovic O, Memon L, Jelic S, et al. El ácido úrico y la actividad de gammaglutamil transferasa se asocian a los índices de remodelado ventricular izquierdo en pacientes con insuficiencia cardiaca crónica. Rev Esp Cardiol. 2014;67:632–42.
4. Hare JM, Mangal B, Brown J, Fisher Jr C, Freudenberger R, Colucci WS, et al.; OPT-CHF Investigators. Impact of oxypurinol in patients with symptomatic heart failure. Results of the OPT-CHF study. J Am Coll Cardiol. 2008;51:2301–9.
5. Kaufman M, Guglin M. Uric acid in heart failure: a biomarker or therapeutic target? Heart Fail Rev. 2013;18:177–86.
6. Tamariz L, Hare JM. Xanthine oxidase inhibitors in heart failure: where do we go from here? Circulation. 2015;19:1741–4.

Infective Endocarditis due to *Listeria Monocytogenes*: A Report of 4 Patients

Endocarditis infecciosa por Listeria monocytogenes: a propósito de 4 casos

To the Editor,

Although the incidence of *Listeria monocytogenes* infections is increasing,[1] infective endocarditis (IE) is still an uncommon and poorly studied disease, with only case reports and reviews reported in the literature.[2,3]

Listeria is a nonsporulating, aerobic, Gram-positive coccobacillus. *Listeria. monocytogenes* is only considered pathogenic in humans, behaving as a zoonosis. It is usually acquired from food and causes disease as an opportunistic infection in newborns, pregnant women, and immunocompromised patients, although it can also affect healthy individuals. Its clinical presentation is diverse; miscarriage, sepsis, and meningoencephalitis are common, and it is generally associated with high morbidity and mortality.[2]

The aim of this work was to describe the characteristics of patients with IE caused by *L. monocytogenes* who were treated in 3 Spanish hospitals considered referral centers for this disease. From a multipurpose database containing 1374 IE episodes consecutively diagnosed between January 1995 and November 2015, we selected those caused by *L. monocytogenes*. The characteristics of the 4 patients (0.3%) identified are described in the Table.

Although we cannot draw any conclusions because of the small number of patients, our patients do show some common features. The patients were all elderly, older than previously reported ages for infections of this bacteria.[1,2] Although *L. monocytogenes* typically affects women, IE is more frequent in men, particularly in the setting of prosthetic endocarditis.[2] Three of the 4 patients in our series were diabetic, and all had received a valve prosthesis, although the IE exclusively affected a native valve in 1 of the

Table

Summary of the Characteristics of the Patients With *Listeria monocytogenes*

	Patient 1	Patient 2	Patient 3	Patient 4
Age, y	84	84	80	79
Sex	Male	Male	Female	Male
Type of endocarditis (postoperative interval)	Prosthesis Early (10 mo)	Prosthesis Late (14 y)	Prosthesis Late (2 y)	Native
Comorbidities	DM, immunosuppression,[a] chronic renal failure, collagenopathy	No	DM	DM
Form of presentation	Heart failure	Ischemic stroke	Fever and malaise	Fever and malaise
Clinical features during admission				
Embolism	No	Yes	No	No
Heart failure	Yes	Yes	No	No
Kidney failure	Yes	No	No	No
Persistent infection[b]	No	No	No	No
Septic shock	No	No	No	No
Vegetation diameter, mm	4,7	7	12	5,4
Periannular complication	No	No	No	No
Localization	Biological mitral prosthesis	Mechanical mitral prosthesis	Biological mitral and aortic prostheses	Native mitral valve (aortic prosthesis not affected)
Antibiotic therapy (weeks of treatment)	Meropenem (6) Daptomycin (6)	Ampicillin (6) Gentamicin (2)	Ampicillin (6) Gentamicin (2)	Ampicillin (6) Gentamicin (2)
Operation	No	No	No	No
In-hospital death	No	No	No	No
Follow-up, y	3 Asymptomatic Without cardiac surgery	5 Death from lung cancer Without cardiac surgery	7 Noncardiac death Without cardiac surgery	10 Asymptomatic Without cardiac surgery

DM, diabetes mellitus.

[a] Immunosuppression due to collagenopathy-related chronic corticoid use.

[b] Persistent fever or positive cultures after 1 week of adequate antibiotic therapy, without another infection focus.

patients. Both factors (diabetes mellitus and prosthesis) have been associated with IE due to *L. monocytogenes*,[2] probably because of the tendency of this bacterium to affect immunocompromised patients and those with predisposing factors. All of our patients showed mitral valve involvement, the most commonly affected site in prosthetic disease (52%).[2] Regarding the mechanism of transmission, there is little information in the literature on the history of the consumption of possibly contaminated food, and we were also unable to verify this datum in our patients.

The most frequent focus of *L. monocytogenes* infection is the central nervous system.[1] In the case of IE, various forms of presentation have been described in the literature, from localized infections to systemic symptoms with a fulminant course.[3] Our 4 patients showed diverse forms of presentation, with a relatively benign clinical course. Notably, despite the evidence of IE,[4] all 4 patients received medical treatment, without increased in-hospital mortality or long-term follow-up. Although *L. monocytogenes* infections are associated with elevated mortality,[1] particularly in the setting of IE,[2] lower mortality has been described in patients with prosthetic endocarditis than in those with native valve endocarditis.[2] The antibiotic therapy recommended for *Listeria* infections is based on a combination of ampicillin and gentamicin. The evidence for this approach is weak: there are no comparative studies, only the results of large series[5] and a theoretical synergistic effect in in vitro studies.[6] This antibiotic regimen was used in our patients, except in patient 1, who was allergic to penicillin and had chronic renal failure. This patient was thus treated with combination meropenem and daptomycin in accordance with the antimicrobial susceptibility profile.

In conclusion, IE due to *L. monocytogenes* is an uncommon condition tending to affect elderly patients and those with diabetes and prosthetic valves. Antibiotic therapy with ampicillin and gentamicin is a suitable therapeutic option, at least in patients with a good clinical course.

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REFERENCES

1. Sedano R, Fica A, Guíñez D, Braun S, Porte L, Dabanch J, et al. Infections by Listeria monocytogenes. Rev Chilena Infectol. 2013;30:417–25.
2. Fernández Guerrero ML, Rivas P, Rábago R, Núñez A, de Górgolas M, Martinell J. Prosthetic valve endocarditis due to *Listeria monocytogenes*. Report of two cases and reviews Int J Infect Dis. 2004;8:97–102.
3. Pocar M, Passolunghi D, Moneta A, Donatelli F. Fulminant prosthetic valve endocarditis caused by Listeria monocytogenes. Eur J Cardiothorac Surg. 2009;36:1077.

4. Carrasco-Chinchilla F, Sánchez-Espín G, Ruiz-Morales J, Rodríguez-Bailón I, Melero-Tejedor JM, Ivanova-Georgieva R, et al. Influencia de una estrategia de alerta multidisciplinaria en la mortalidad por endocarditis infecciosa izquierda. Rev Esp Cardiol. 2014;67:380–6.

5. Mylonakis E, Hohmann EL, Calderwood SE. Central nervous system infection with _Listeria monocytogenes:_ 33 years' experience at a general hospital and review of 776 episodes from the literature. Medicine (Baltimore). 1998;77:313–36.

6. Azimi PH, Koranyi K, Lindsey KD. _Listeria monocytogenes:_ synergistic effects of ampicillin and gentamicin. Am J Clin Pathol. 1979;72:974–7.

The Importance of Family-genetic Screening: The Phenotype Caused by the p.L3778F Ryanodine Receptor Mutation is Likely Less Severe Than Previously Thought

La importancia del estudio familiar y genético: la mutación p.L3778F en el receptor de la rianodina probablemente no cause un fenotipo tan grave

To the Editor,

We present the case of a family with a history of sudden cardiac death at a young age. The initial diagnosis was catecholaminergic polymorphic ventricular tachycardia (CPVT) caused by the p.L3778F mutation in the cardiac ryanodine receptor gene (_RyR2_). Several years after this initial diagnosis, a comprehensive family genetic study by next generation sequencing (NGS) has now identified a second pathogenic mutation, this time in _KCNQ1_ and linked to type 1 long QT syndrome (LQTS1). The severe phenotype is likely due to the presence of both mutations and not exclusively to the p.L3778F mutation in _RyR2_ as previously reported.[1]

The proband (III:5) had a cardiac arrest at the age of 8 years while swimming but recovered fully after resuscitation. His brother had died suddenly, also while swimming, at 10 years of age (no abnormalities were detected on autopsy).

An electrocardiogram (ECG) of the proband showed sinus bradycardia with a QTc of 440 ms, whereas the results of echocardiography, Holter recording, and exercise stress testing were normal. The context of the cardiac arrest suggested LQTS1, and the patient was prescribed beta-blockers. An electrophysiological study was conducted without arrhythmia induction, and the patient was fitted with a subcutaneous Holter monitor. At the age of 10 years, he had an exertion-induced syncopal episode, and ECG revealed self-limiting polymorphic ventricular tachycardia (Figure A).

The patient was referred for further investigation to a center with expertise in cardiac channelopathies. A mutational screen was conducted of the _RyR2, KCNQ1, KCNH2, SCN5A, KCNE1,_ and
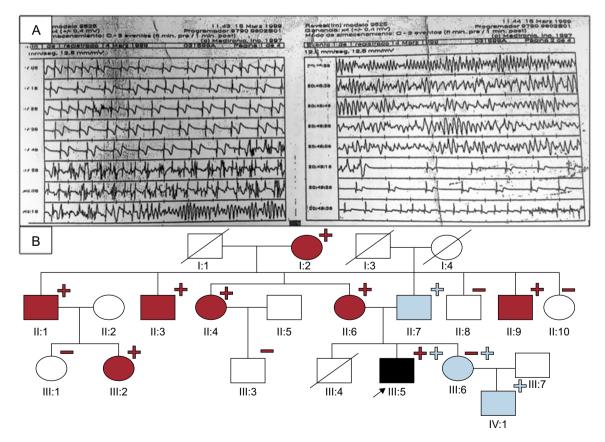

Figure. A: Recording of the polymorphic tachycardia in the proband. B: Family tree. /, deceased; –, noncarriers, lacking the L3778F mutation in _RyR2_ (blue) or the E449R*14 mutation in _KCNQ1_ (red); +, carriers, heterozygous for L3778F in _RyR2_ (blue) or E449R*14 in _KCNQ1_ (red); circles, women; boxes, men; arrow, proband; blue fill, patient with CPVT (according to the European and US consensus statement)[3]; black fill, patient clinically affected by LQTS1 and CPVT; red fill, patient with LQTS1; _RyR2_, ryanodine receptor gene; LQTS1, type 1 long QT syndrome; CPVT, catecholaminergic polymorphic ventricular tachycardia.