Shock séptico por *Leptotrichia buccalis* en paciente neutropénico por quimioterapia

Septic shock caused by Leptotrichia buccalis *in a neutropenic patient secondary to chemotherapy*

Presentamos el caso de un varón de 55 años, fumador y bebedor importante con carcinoma epidermoide supraglótico T4aN1M0, portador de reservorio subcutáneo y acceso venoso periférico para tratamiento quimio-radioterápico. A la semana de recibir el primer ciclo de cisplatino ingresa en urgencias y es trasladado a la UCI por *shock* séptico (fiebre, hipotensión, disminución del nivel de conciencia, procalcitonina de 46 ng/ml y lactato de 5,47 mmol/l) con alteraciones hidroelectrolíticas severas (hiponatremia, hipopotasemia, hipocloremia, hiperglucemia y acidosis metabólica), fracaso renal agudo y bicitopenia severa (leucopenia de 300, con 60 neutrófilos y trombocitopenia de 19.000) sin coagulopatía.

Se inicia tratamiento de soporte con cristaloides, transfusión de plaquetas, aminas vasoactivas y antibioterapia endovenosa empírica con piperacilina-tazobactam y, posteriormente, con meropenem, amikacina y linezolid. Presenta una evolución tórpida, fibrilación auricular rápida e insuficiencia respiratoria con mala respuesta a pesar de la ventilación mecánica y amiodarona en perfusión. Fallece en pocas horas tras parada cardiorrespiratoria y fracaso multiorgánico.

En la radiografía de tórax destacaba un infiltrado bilateral (fig. 1).

En los hemocultivos obtenidos al ingreso creció en todos los frascos un bacilo gramnegativo largo, fusiforme y microaerófilo. El crecimiento fue lento y a las 48 h, la colonia era pequeña, gris y bien definida. Mediante la espectrometría de masas (MALDI-TOF) se identificó como *Leptotrichia buccalis*.

Leptotrichia spp., es un bacilo gramnegativo, a veces se ha descrito como gran variable, inmóvil, anaerobio facultativo, fusiforme, fermentador de hidratos de carbono y productor de ácido láctico. Algunas especies no crecen en medios convencionales y cuando lo hacen son de crecimiento lento. La identificación por métodos fenotípicos es difícil, y por ello se cree que sus infecciones están infradiagnósticadas[1] por identificarlas como *Fusobacterium* o *Lactobacillus*. Actualmente se identifica por espectrometría de masas o por secuenciación del gen del ARNr 16S. *Leptotrichia buccalis* habita fundamentalmente en la cavidad oral por lo que suele causar enfermedades odontológicas y abscesos bucales, aunque en pacientes inmunodeprimidos actúa como patógeno oportunista[2]. Posee una similitud taxonómica con las fusobacterias, por lo que antiguamente pertenecían a la misma familia[1–3]. La patogenicidad de *Leptotrichia* spp. se debe a la producción de LPS y secreción de endotoxinas que desencadenan una reacción inflamatoria mediante citoquinas[2].

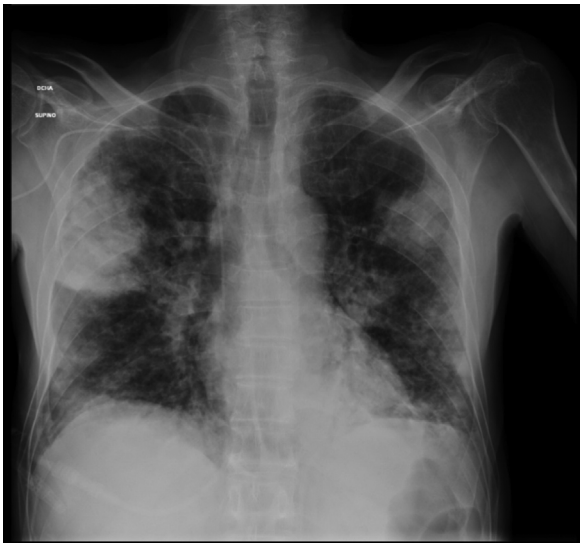

Figura 1. Infiltrado alveolar bilateral en radiografía de tórax al ingreso.

En una reciente revisión[4] se han descrito aislamientos de esta bacteria en casos de septicemia, fiebre neutropénica, trombocitopenia, disnea subaguda, halitosis y diversas enfermedades odontológicas (pulpitis o necrosis pulpar, periodontitis, placas dentales...) e incluso endocarditis[5]. Se ha descrito un mayor riesgo de bacteriemia por *Leptotrichia buccalis* en pacientes con neutropenia febril posquimioterapia y mucositis o infecciones periodontales[6,7]. El paciente que presentamos, tenía una boca séptica y déficit de piezas dentarias, además del tumor laríngeo con invasión local.

Existen casos publicados de síndrome de Lemierre por *Leptotrichia buccalis* en pacientes neutropénicos[8] con infiltrados radiológicos bilaterales y abscesos pulmonares en TC. En nuestro caso, tras el rápido desenlace fatal y la ausencia de consentimiento para necropsia, no se pudo completar el estudio, pero a pesar de su rareza, no descartamos esta posibilidad. En el diagnóstico diferencial incluimos también neumonía[9] bilateral atípica por *Leptotrichia buccalis* debido a la sepsis grave, insuficiencia respiratoria y radiología compatible.

Por lo general, es susceptible a múltiples agentes antimicrobianos como betalactámicos, carbapenémicos, clindamicina, metronidazol, rifampicina, tetraciclinas y cloranfenicol[1,4,6,7], y resistente a aminoglucósidos, macrólidos, vancomicina y fluoroquinolonas[4,10].

Creemos que nuestra aportación es importante porque no hay publicado ningún *shock* séptico por *Leptotrichia buccalis*. La mayor parte de los casos con bacteriemia descritos en la literatura también tenían neutropenia posquimioterapia, y la puerta de entrada era la cavidad oral. Sin embargo, todos ellos habían respondido a los antibióticos previamente mencionados, a diferencia de nuestro paciente.

Bibliografía

1. Harmon N, Mortensen JJ. Case Twenty-Four: Bacteremia Caused by an Uncommon Gram-negative Organism. Cont Education Topics & Issues. 2012;14:82–4.
2. Reig M, Baquero F, García-Campello M, Loza E. *Leptotrichia buccalis* Bacteremia in Neutropenic Children. J Clin Microb. 1985;22:320–1.
3. Hamilton RD, Zahler SA. A study of *Leptotrichia buccalis*. J Bacteriol. 1957;73:386–93.
4. Eribe ERK, Olsen I. *Leptotrichia* species in human infections. J Oral Microbiol. 2017;9:1368848, http://dx.doi.org/10.1080/20002297.2017.1368848
5. Duperval R, Marcoux J. A Infective endocarditis due to *Leptotrichia buccalis*: A case report. Can Med Assoc J. 1984;30:422–4.
6. Couturier MR, Slechta ES, Goulston C, Fisher MA, Hansona KEJ. *Leptotrichia* bacteremia in patients receiving high-dose chemotherapy. Clin Microb. 2012;50:1228–32.
7. Weinberger M, Wu T, Rubin M, Gill VJ, Pizzo PA. *Leptotrichia buccalis* bacteremia in patients with cancer: Report of four cases and review. Rev Infect Dis. 1991;13:201–6.
8. Hot A, Coppere B, Ninet J, Thiebault A. Lemierre syndrome caused by *Leptotrichia buccalis* in a neutropenic patient. Int J Infect Dis. 2008;12:339–40, http://dx.doi.org/10.1016/j.ijid.2007.08.009
9. Morgenstein AA, Citron DM, Orisek B, Finegold SM. Serious infection with *Leptotrichia buccalis:* Report of a case and review of the literature. Am J Med. 1980;69:782–5.
10. Pate JB, Clarridge J, Schuster MS, Waddington M, Osborne J, Nachamkin I. Bacteremia Caused by a Novel Isolate Resembling *Leptotrichia* Species in a Neutropenic Patient. J Clin Microb. 1999;37:2064–7.

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Carbapenemase-producing *Enterobacteriaceae* infections in General Surgery patients: Our experience☆

Infecciones por Enterobacterias productoras de carbapenemasas en pacientes de Cirugía General: análisis de nuestra experiencia

During the last decade, infections caused by carbapenemase-producing *Enterobacteriaceae* (CPE) have been dramatically increased worldwide. Numerous publications have focused on the epidemiology and risk factors for CPE-related infections,[1–3] although studies about surgical patients are scarce. Recognizing patterns in patients admitted to a General Surgery Department (GSD), could be essential to ensure a more rational antibiotic use in this specific setting. We performed a retrospective review including nosocomial CPE infections inpatients admitted to the GSD from January 2013 to December 2016. We analyzed patients with at least one (new) positive culture 48 h after admission for a CPE at any location and associated clinical signs or symptoms of infection. The probable infectious source was defined according to microbiological results and the analysis of clinical findings by two physicians in accordance with Centers for Disease Control definitions.[4] Patient's samples were collected and incubated based on standard recommendations.[5] We investigated the clinical and microbiological characteristics, treatment, complications, antimicrobial susceptibility and risk factors for mortality.

We included 40 patients with a CPE clinical infection: 50% were male, with a mean age of 69.4 ± 13.4 years. Charlson's comorbidity index median value was 3 (range 1–5). The rate of CPE infections in the GSD increased annually from 1.2% in 2013, to 4.7% in 2016.

Carbapenemase-producing *Klebsiella pneumoniae* strains were the most commonly identified (92.5%), all with the OXA-48-like carbapenemase. Prior to the CPE infection, other non-resistant microorganisms isolated were Gram-negative bacteria (52.5%), Gram-positive bacteria (65%), and fungi (40%). Intra-abdominal site was the most frequent source of infection (55%), followed by surgical wound (22.5%). CPE were susceptible to amikacin (100%), tigecycline (97%), and colistin (76%), and showed increased MICs but acceptable susceptibility to meropenem (64.3%) and imipenem (52.5%). CPE isolates showed low susceptibility rates to ertapenem (8.8%) and ciprofloxacin (5.3%).

Median hospital stay was 41.5 days (range 26.2–74.5). A surgical procedure had been performed in 35 patients in the previous 30 days, including emergency surgery in 15 cases. A major complication occurred in 23 patients, with a mortality rate of 17.1% in patients who underwent a surgery. A postoperative intra-abdominal infection (IAI) was present in 19 cases. The reoperation rate was 32.5%, without differences regarding mortality compared to non-reoperation. All patients received antibiotic therapy, of which 28 patients received carbapenem therapy. Table 1 shows the analysis of factors associated with mortality. Six patients received an appropriate empirical antibiotic regime, according to the *in vitro* activity. Appropriate definitive antimicrobial treatment was administered to 32 patients. The mortality rate at 30 days was 15%. Factors associated with mortality were: blood transfusions ($p = 0.021$), and lower rate of major complications (Clavien-Dindo ≥ III) ($p = 0.031$). A combined definitive two-drug targeted scheme was protector for mortality ($p = 0.048$).

This study summarizes the outcomes of patients with CPE infections in a GSD. The specific characteristics of this population were age >65 years, previous comorbidities (solid tumor, diabetes, and renal insufficiency), some risk factors for multidrug-resistant infections (including prior hospitalization and antibiotic therapy), all previously described.[1,2,6] In our series, antibiotic therapy had been previously prescribed in all patients (carbapenem therapy in 70%), with high rates of previous hospitalizations, surgery and endoscopic procedures. These findings agree with those of a recently published study of patients admitted in a surgical ICU from a tertiary-care Spanish hospital.[6] In addition, other investigations detailed that factors related with the acquisition of a CPE infection in solid organ recipients are poor functional status and frequent antimicrobial therapy, which more frequently occurs in the early post-transplant period.[7]

Intra-abdominal location was the most common source of CPE infection in our patients (the majority of patients had undergone an abdominal surgery). A two-drug scheme was a protective factor for mortality, and this combination is recommended by current guidelines on the treatment of IAI.[8,9] Despite this, several studies have not identified these differences in all patients and propose appropriate monotherapy for patients with low-mortality risk scores.[10]

Although this study only represents a review of an experience in a GSD of a single-institution with a limited number of patients, it shows a current vision of an increasing problem in a less analyzed population. As physicians prescribing antimicrobials, we may need to pay attention to patients with a specific clinical profile, using a targeted treatment for each patient. Future studies on CPE-related intra-abdominal infections could determine more definite features and outcomes in specific settings with surgical patients.

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