

First reported case of a corneal abscess caused by *Massilia timonae*



Primer caso descrito de absceso corneal causado por *Massilia timonae*

To the Editor:

Massilia timonae was described for the first time in 1998 by La Scola *et al.* as a fastidious, slowly growing, gram-negative bacterium.¹ *M. timonae* was isolated from a blood culture of an immunocompromised patient.

Since then, only six other cases of human infections caused by this microorganism have been described in the literature: three patients with sepsis, two with wound and bone infection, and the last one with a generalized lymphadenopathy and malaria coinfection. Only two of these patients had a relevant underlying condition.^{2,3,4} Herein, we describe the first isolation of *M. timonae* in ocular samples of a healthy woman with a corneal abscess.

Thirty-one year old female, with no history of systemic or ocular disease of interest, arrived to our hospital due to pain and photophobia in the right eye during the last two days. The patient referred neither systemic treatment, usage of contact lenses nor previous trauma. Visual acuity was 20/20 in both eyes. In the examination of the anterior pole with the biomicroscopy, erythema, moderate ciliary injection, two corneal abscesses with dense corneal stromal infiltrate and indistinct borders with 1 mm approximately size, surrounding leukocyte infiltration and edema were observed. Both lesions had epithelial defect with positive fluorescence staining. No anterior chamber reaction was found. She preserved pupillary reflexes. Fundus and intraocular pressure was normal.

Corneal scraping with a hypodermic needle was performed, and the sample was sent to the microbiology laboratory. After that, empirical treatment with ciprofloxacin eye drops (3 mg/ml Q2 h) alternating with tobramycin eye drops (3 mg/ml Q2 h), night ointment of ciprofloxacin (3 mg/g), and cyclopentolate eye drops (10 mg/ml Q12 h) was initiated.

In the gram stain of the ocular sample, gram-negative rods were observed. The sample was cultured in blood agar, thioglycolate at

37 °C and Sabouraud agar at 30 °C. After 24-hour incubation, 2–3 mm flat, shiny, greyish coloured colonies were observed in blood agar. In thioglycolate medium, a white layer inside the aerobic zone was observed. (Fig. 1)

A MALDI-TOF (Bruker-Daltonics, Bremen, Germany) with 24 grow blood agar colony was performed, and the result was *M. timonae*. Catalase and motility test were positive, while the oxidase test was negative. Moreover, API20NE test (bioMérieux, Marcy l'Etoile, France) was performed and the following results: reduction of nitrates to nitrites, indole production and glucose fermentation negative, and esculin and gelatine hydrolysis positive. It utilized as sole carbon source arabinose, mannose, maltose, malate, trisodium citrate and phenylacetic acid, but not manitol, N-acetylglucosamine, potassium gluconate, capric acid and adipic acid. The only discrepant test with La Scola *et al.* was arginine dihydrolase, which was negative; this difference had been previously in four strains of *M. timonae*.^{1,2}

Bacterial identification was confirmed by DNA sequencing of the 16SrDNA. The DNA was extracted and PCR was performed with the following specific primers to amplify the 16S rRNA gene-coding region: 27F (5'AGA GTTGA TCC TGG CTC AG 3') and 1492R (5'GGT TAC CTTGTT ACG ACT T 3'). PCR was performed using the following program: 94 °C for 5 min, followed by 30 cycles of 94 °C for 40 s, 55 °C for 40 s, 72 °C for 80 s, and a final extension period of 72 °C for 7 min. 16S rDNA PCR products were sequenced and showed a 99% identity respect to that of the *Massilia timonae* strain 99A9205 (AY157761.1, GenBank).

The patient was re-examined within 24 hours, with significant subjective improvement. The two abscesses persisted with less infiltration and resolution of the epithelial defect. Given the objective and subjective improvement the same treatment was kept, except for cyclopentolate eye drops.

The antibiogram was performed twice, using a commercial microdilution (NM44 MicroScan, Siemens, USA) and no growth was observed. The antibiogram was then performed with Etest on Mueller Hinton agar plates containing 5% sheep blood (Oxoid, Basingstoke, United Kingdom). MICs values were: ampicillin <0.016 µg/ml, piperacillin-tazobactam 16 µg/ml, amoxicillin-clavulanic acid 2 µg/ml, clindamycin 0.125 µg/ml, ceftazidime 0.0125 µg/ml, ertapenem 0.25 µg/ml, meropenem 0.016 µg/ml,

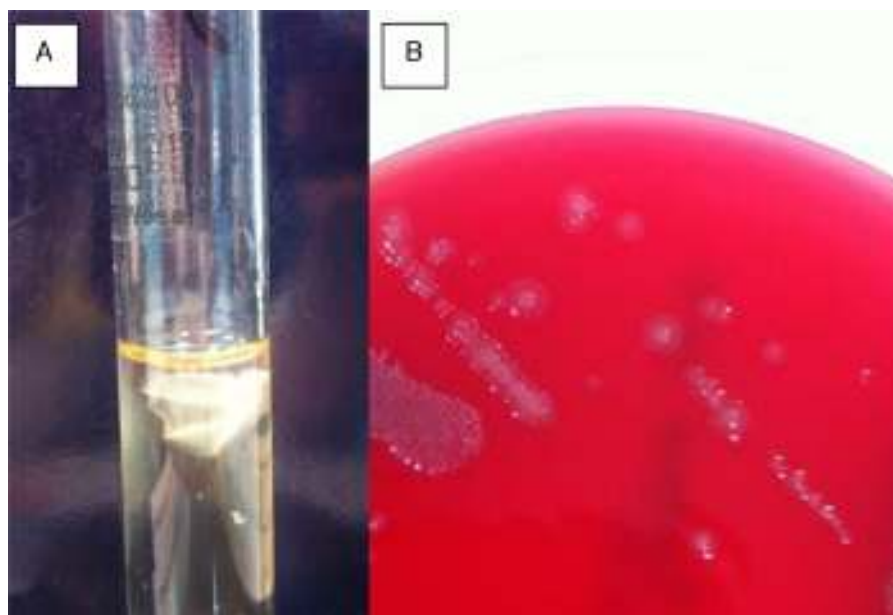


Figure 1. A) *M. timonae* inoculated in thioglycolate medium. They made a white layer inside the aerobic zone. B) 24-hours blood agar culture of *M. timonae*.

ciprofloxacin 0.064 µg/ml, gentamycin 2 µg/ml, tobramycin 2 µg/ml, and trimethoprim-sulfamethoxazole 0.003 µg/ml. Since there are not clinical breakpoints for this microorganism, MICs values were considered as susceptible according to CLSI breakpoints for non-*Enterobacteriaceae*.

A week later the patient continued improving. fluorometholone (2.5 mg/ml) eye drops Q6 h were added and frequency of antibiotics administration was decreased to 3 mg/ml Q6 h. A week later, there was a complete remission of symptoms and the treatment was concluded.

The genus *Massilia* belongs to the family *Oxalobacteraceae* (*Betaproteobacteria*), and up to now comprises twenty-five species.⁵ Members of the genus are characterized as aerobic, gram-negative and non-spore forming rods. This environmental microorganism has been previously described as the main cause of infection in humans in other samples, such a cerebrospinal fluid, blood, soft tissues and bone, but this is the first case where *M. timonae* is isolated from cornea.^{5,6,7,8}

Despite the lack of virulence of this microorganism and the absence of resistance to the majority of antibiotics, it is important to achieve a correct identification of that pathogen in all types of samples. *M. timonae* has proved to cause infection in different locations, independently of the underlying condition of the patients. Due to all these reasons, correct isolation and identification should routinely be performed.

In summary, this is the first case described of corneal abscess caused by *M. timonae* in a healthy woman.

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Mónica Ballesterio-Téllez^{a,*}, Teresa Laborda Guirao^a,
Nínive Batista Díaz^a, Álvaro Pascual Hernandez^{a,b}

^a Hospital Universitario Virgen Macarena, Sevilla, Spain

^b Universidad de Sevilla, Sevilla, Spain

* Corresponding author.

E-mail address: m.ballesterio.t@gmail.com

(M. Ballesterio-Téllez).

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Severe thrombocytopenia caused by linezolid poisoning in an overweight critically ill patient with renal impairment treated with the recommended doses



Trombocitopenia severa causada por intoxicación de linezolid en paciente crítico con insuficiencia renal y bajo peso utilizando las dosis recomendadas

Dear Sir,

We report the case of an 82-years-old woman moderately underweight (weight, 34.4 kg; BMI, 16.8 kg/m²), one kidney patient who was admitted to hospital for presenting fever and abdominal pain. At admission, a hydatidic cyst with calcification and fistulization to a new perihepatic collection was observed. Ten hours later, the patient was moved to the intensive care unit (ICU) due to severe hypotension and no response to the administration of fluids. Serum creatinine increased from 250.07 µmol/L to 365.98 µmol/L, and glomerular filtration rate (GFR) decreased from 0.28 mL/s/m² to 0.18 mL/s/m².

On the same day, a turbid fluid collection from the peritoneal drainage appeared and oral albendazole 400 mg twice daily, intravenous imipenem 500 mg twice daily and intravenous linezolid (LZD) 600 mg twice daily (34.9 mg/kg/day) were prescribed. After 5 days of treatment, her clinical situation improved without normalization of renal function (GFR 0.23 mL/s/m²). However, a decrease of 48.6% in the platelet count was observed and the patient experienced a mild hand tremor.

Due to suspicion of a possible overexposure to LZD, plasma concentrations were measured and a trough (pre-dose) and peak (at the end of 1 h infusion) samples were obtained. Trough and peak concentrations of LZD were 52.1 mg/L and 93.2 mg/L, and LZD treatment was stopped. Serial blood samples were obtained at 24, 48, 72, 96, 120 and 144 h after the discontinuation of LZD.

Linezolid plasma levels and platelet count are shown in Fig. 1.

Patient's serum haemoglobin also decreased from 129 g/L at the start of the LZD treatment to a nadir value of 88 g/L at the 11th day after the LZD discontinuation. An inverse lineal correlation was observed between the platelet count and LZD plasma levels (Pearson's correlation coefficient: −0.893 ($p = 0.041$)) but not with haemoglobin. The patient did not receive any blood nor platelet transfusion.

On 10th day of ICU admission, patient's clinical evolution improved and she was moved to a surgery ward. However, 7 days after, she was diagnosed with a septic shock due to a complicated intra-abdominal infection. The patient did not respond to fluid resuscitation and inotropic drugs and finally died 24 h later.

LZD is commonly used in the treatment of infections caused by multidrug-resistant Gram-positive cocci in critically ill patients. In this population, due to a high variability in the LZD pharmacokinetics, therapeutic drug monitoring (TDM) has been recommended.^{1,2}

LZD use has been related to haematological toxicity (thrombocytopenia, anaemia), neuropathy (peripheral and optical), lactic acidosis and gastrointestinal disturbances.^{3,4} Different risk factors of haematological toxicity, which is dose-dependent and reversible, have been identified: age, baseline platelet count <200 × 10⁹ cells/L, renal dysfunction, low body weight, treatment >14 days and chronic liver disease, being two of them present in our patient.^{3–5}