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Listeria grayi Meningitis in a Polypathological Patient: A Case Report

Rachida Issa Moussa [1, 2], Ikram Habboubat [1, 2], Yassine Ben Lahlou [1, 2], Mariama Chadli [1, 2]*

1 Faculty of Medicine and Pharmacy, Mohamed V University, Rabat, Morocco.

2 Bacteriology Department, Mohamed V Military Training Hospital, Rabat, Morocco.

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ABSTRACT

Background: The various species of the *Listeria* genus are frequently isolated from food and drink products. They are classified into two categories according to their pathogenicity. Pathogenic species are frequently incriminated in infections of the elderly, immunocompromised and pregnant women. The *Listeria grayi* species is rarely isolated as a pathogen in human pathologies. We report a case of *L. grayi* meningitis in a polypathological patient. Antimicrobial susceptibility testing revealed resistance to ampicillin and susceptibility to Meropenem. Therapeutic failure was recorded despite in vitro sensitivity.

Methods: Conventional biochemical test and Api *Listeria* gallery was used for identification of the isolate.

Results: We report a case of *L. grayi* meningitis in a polypathological patient. Antimicrobial susceptibility testing revealed resistance to ampicillin and susceptibility to Meropenem. Therapeutic failure was recorded despite in vitro sensitivity.

Conclusion: Given its infrequent reporting, *Listeria grayi* meningitis warrants consideration, especially in elderly patients with multiple pathologies.

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*Corresponding Authors: Rachida Issa Moussa, Faculty of Medicine and Pharmacy, Mohamed V University, Rabat, Morocco. Bacteriology Department, Mohamed V Military Training Hospital, Rabat, Morocco.

Tel: +21-27-72378319, *E-mail:* issamoussar@gmail.com

Introduction

The *Listeria* genus includes several species widely distributed in nature (1,2). *Listeria monocytogene* is the most important *Listeria* species in human pathology. Clinical signs range from mild influenza-like illness to meningitis, frequently accompanied by septicemia, and meningoencephalitis, particularly in the immunocompromised, pregnant women and the elderly (3–5). Other species considered "non-pathogenic", such as *Listeria grayi*, are becoming increasingly lethal in immunocompromised populations or those suffering from multiple diseases.

Case presentation

The patient, a 65-year-old female, was admitted to the emergency department with a sudden loss of consciousness. Her medical history included hypertension complicated by heart failure, type 2 diabetes for 16 years complicated by diabetic nephropathy, chronic renal failure for one year on dialysis, and SARS-CoV-2 infection dating back one month before hospitalization. Her surgical history included tubal ligation.

The symptomatology that prompted the consultation was an altered general condition. On admission, the patient presented with a fever of 38.6 °C, a GCS of 12, eupneic with 97% saturation and a blood pressure of 21/13 mmHg. The patient subsequently presented with two convulsive seizures and deteriorating respiratory and cardiac function. Paraclinical examination revealed hyperglycemia at 6 g/l, acetonuria at 3g/l. Chest and brain CT scans revealed no abnormalities. In terms of infection, the patient presented with a hyperleukocytosis of 18,000 /mm3 and a CRP = 150 mg/l. A urine culture, two blood culture bottles (anaerobic + aerobic) and a lumbar puncture were realized. Given the positive infectious workup, the patient was initially started on rocephin and Flagyl.

Cytobacteriological examination of the cerebrospinal fluid (CSF) revealed a clear fluid, a cellular reaction estimated at 154 white blood cells/mm3 with a mixed formula: PNN = 48%, lymphocyte =22%, monocytes = 22%, and other at 7%. Direct microscopic examination of the CSF after Gram coloration was negative. Biochemistry showed glucorachia at 1.14 g/l, proteinorachia at 0.25 g/l, and normal chlorurachia. The patient, initially on rocephin and flagyl, was switched to vancomycin and Augmentin after transmission of the CSF cytology results.

CSF culture yielded thin, translucent, shiny, non-hemolytic colonies on fresh blood agar (fig. 1a). Microscopic examination after Gram staining revealed small Gram-positive bacilli (fig. 1b), positive for catalase and slowly positive for esculin. Isolated bacteria were motile at 22 °C and immobile at 37 °C.

Seeding an Api *Listeria* gallery confirmed that the nature of the species as *Listeria grayi*. The antibiogram showed a strain sensitive to meropenem and resistant to amoxicillin and ampicillin. The patient's condition worsened and she died sometime after hospitalization.

Discussion

The genus *Listeria* comprises two pathogenic species, *Listeria monocytogenes* and *L. ivanovii*, and eight nonpathogenic species that include *L. innocua*, *L. seeligeri*, *L. welshimeri*, *L. grayi*, *L. marthii*, *L. rocourtiae*, *L. fleischmannii*, and *L. weihenstephanensis* (1).

Listeria species are commonly found in the environment and can be transmitted through various sources such as food, beverages (including pasteurized milk), and water. Interestingly, pathogenic properties have been identified in some nonpathogenic *Listeria* (3). A study conducted on a dairy farm revealed that the prevalence of *Listeria grayi* contamination was approximately 10.3%, with water being the primary source of contamination (6).

Very few studies have been reported on the involvement of *Listeria grayi* in human pathologies, leading to long laboratory identification times. The cases of *Listeria* meningitis described in the literature generally concern *Listeria monocytogenes*. *L. monocytogenes* is the third most common cause of bacterial meningitis, after *Streptococcus pneumoniae* and *Neisseria meningitidis* (7). Its diagnosis should be considered in all elderly patients (8,9) immunocompromised patients (10), patients receiving long-term glucocorticoids, HIV-positive patients, patients with chronic alcoholism/liver disease, patients with malignant tumors, transplant patients, diabetics (11). The prevalence of *L. monocytogenes* meningitis is considerably higher in these populations. Our patient was at increased risk of *Listeria* infection due to her multiple risk factors.

L. monocytogenes is widely regarded as the causative agent of meningitis and sepsis, particularly in immunocompromised patients (10). Alteration of consciousness and fever are frequently reported in neurolisteriosis cases. Nuchal rigidity can be observed in about 60% of these cases. The classic triad (nuchal rigidity, fever, and impaired consciousness status) was reported in about 50% of them. Respiratory failure within 48 hours from admission is reported less frequently in *Listeria* meningitis patients (10). Our patient's symptoms were the same as those described in the literature for *L. monocytogenes* infection. To our knowledge, this is the first case report of *Listeria grayi* meningitis reported in a patient with multiple comorbidities.

Common biochemical characteristics of the *Listeria* genus are positive catalase, indole and negative oxidase, esculin hydrolysis, but negative urea (1) mobility at 25 °C and immobility at 37 °C. In addition to shared biochemical characteristics, *Listeria grayi* has other features such as a non-hemolytic character (6).

The bacterium has been identified in the laboratory using a variety of conventional techniques. These include Gram staining, catalase reaction (positive), oxidase reaction (negative), esculin hydrolysis (positive), which can be observed in bile-esculin agar, motility (positive) at 25 °C and immobility at 37 °C. Considering the lack of information regarding its non-hemolytic nature, we conducted a seeding of an Api *Listeria* gallery, which resulted in confirmed identification of *Listeria grayi*.

Considered non-pathogenic, there is an absence of sensitivity profile to antibiotics determined by CA-SFM and pre-established guidelines. They do not have antibiotic susceptibility profiles determined by CA-SFM and pre-established guidelines. The treatment of infections caused by opportunistic bacteria can pose a serious challenge, as these bacteria, despite having low virulence, exhibit natural resistance to many antibiotics (3). All *Listeria* species were found to be naturally sensitive or intermediate to tetracyclines, aminoglycosides, penicillins (except for oxacillin), first and second generation cephalosporins, carbapenems, macrolides, lincosamides, glycopeptides, and chloramphenicol. *Listeria* spp. were naturally resistant or intermediate to most `modern'cephalosporins, aztreonam and sulfamethoxazole (3). *L. grayi* was naturally resistant to trimethoprim, and consequently, to cotrimoxazole (Trimethoprim/sulfamethoxazole). It displayed least susceptibility to rifampicin, while being most susceptible to quinolones (3). Given the mixed cerebrospinal fluid (CSF) composition, it was determined to discontinue the administration of rocephin and flagyl in our patient, and instead initiate the use of vancomycin and augmentin. *L. monocytogenes* has been found

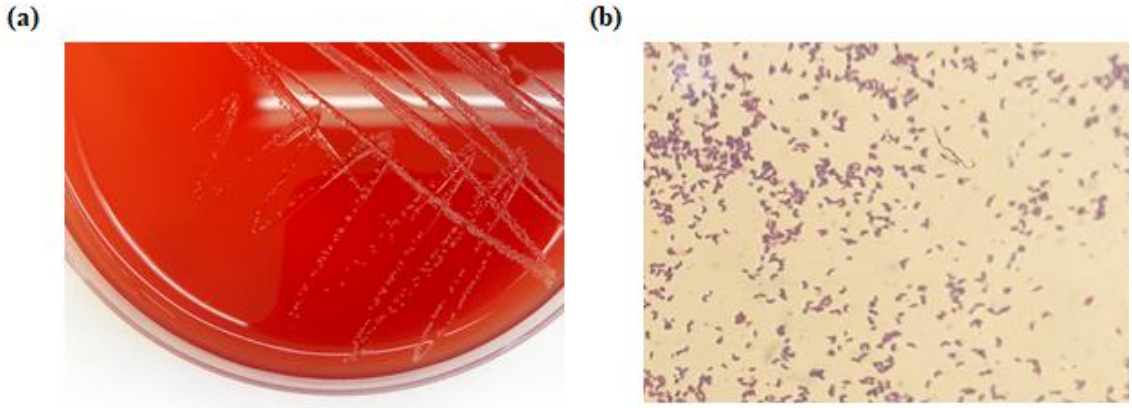

Fig 1. Non-hemolytic colonies on blood agar (a) and Gram-positive bacilli after Gram staining (b).

Table 1. Result of the biochemical tests of the *Listeria* species, isolated from dairy farms in Khartoum State (6).

Bacteria suspected / Biochemical test		*L. monocytogenes*	*L. innucua*	*L. seeligeri*	*L. welshimeri*	*L. inovii*	*L. grayi*	*L. murrayi*
Catalase test		+	+	+	+	+	+	+
Mobility test	**25 °C**	+	+	+	+	+	+	+
	37 °C	-	-	-	-	-	-	-
MR		-	-	-	-	-	-	-
VP		+	+	+	+	+	+	+
β-hemolytic		h.β+ve	-ve Non h.	-ve Non h.	-ve Non h.	h.β+ve	-ve Non h.	-ve Non h.
hydrolysis of esculin		+	+	+	+	+	+	+
CAMP test		+	-	+	-	-	-	-
Xylose		-	-	+	+	+	-	-
Glucose		+	+	+	+	+	+	+
Sucrose		-	+	-	+	+	-	-
Rhamose		+	+	-	+	+	-	+
Mannitol		-	-	-	-	-	+	+

h.β: β-hemolytic; +ve: positive; -ve: negative; Non h.: non hemolytic.

to be susceptible to various antibiotics. The commonly prescribed antibiotics for this infection are penicillin, amoxicillin, and ampicillin, as per the guidelines and expert recommendations (10). While amoxicillin has shown better efficacy in laboratory studies, ampicillin is currently considered the preferred treatment option for listeriosis. Additionally, studies have

demonstrated a synergistic effect when these antibiotics are combined with aminoglycosides such as gentamicin or streptomycin (12,13). The study by Mary E Temple and Milap C Nahata (14) recommended a combination of penicillins (penicillin or ampicillin or amoxicillin) with gentamicin for all patients over 50 years old and those with comorbidity. The doses of gentamicin should not exceed 2.5 mg/kg/day (14). In the situation of *Listeria monocytogenes* meningitis, it is recommended to administer an adult with a dose of ampicillin exceeding 9 g/day for a minimum treatment period of 21 days (10). As an alternative therapy for *Listeria monocytogene* infection, Cotrimoxazole (Trimethoprim/sulfamethoxazole) is also utilized due to its effective penetration into the cerebrospinal fluid (CSF) (10,14). However, it is important to note that *Listeria grayi* naturally possesses resistance against this compound. The efficacy of Vancomycin against *Listeria* strains varies, and its usage is restricted because its cannot cross the blood-brain barrier and achieve therapeutic concentrations (10,14). Antibiotic susceptibility testing in accordance with CA-SFM guidelines for *L. monocytogenes* revealed resistance to ampicillin and susceptibility to meropenem. An adaptation of the antibiotic therapy was carried out immediately. The clinical case reported by Rapose et al (15) also isolated a species of *Listeria grayi* with reduced sensitivity to ampicillin. Unfortunately, our patient died after the introduction of meropenem, without any improvement in her condition. According to the study by Thønnings et al. (16) the use of meropenem as a definitive treatment was correlated with a high mortality rate. The death of our patient a few days after the introduction of meropenem testifies to a therapeutic failure. A clinical case reported at the University Children's Hospital in Belgrade reported therapeutic failure with meropenem during bacteremia despite demonstrated in vitro sensitivity (17).

Conclusion

Listeria grayi meningitis is an uncommon occurrence, however, due to the compromised health condition of our patient, she became susceptible to opportunistic infections. The rise in immunosuppressive diseases is contributing to the increased prevalence of opportunistic infections.

Considering alternatives like quinolones for treatment is reasonable; however, it is disappointing that they are not currently included in the recommended antibiotics for testing against *Listeria monocytogenes*, the more common pathogenic species within the genus. This gap in knowledge highlights an area for future investigation and potential refinement of treatment protocols for *Listeria* infections. The case of *Listeria grayi* meningitis in our patient serves as a reminder of the complexities involved in managing infections in immunocompromised individuals. Continued research into both the epidemiology and treatment options for *Listeria* infections, including alternative antibiotics like quinolones, is crucial for improving clinical outcomes in such cases.

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Ethics approval and consent to participate

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Conflict of interest

None declared.

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