

## CASE REPORT

# Co-infection with *Streptococcus pneumoniae* and *Listeria monocytogenes* in an immunocompromised patient

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A 34-year-old HIV-positive man with a history of chronic substance abuse was admitted with dual infection of *Streptococcus pneumoniae* and *Listeria monocytogenes*. Combined bacteraemia with *S. pneumoniae* and *L. monocytogenes* is very rare. To the best of our knowledge, this is the first such case documented at our institution and in South Africa. Ampicillin should be added to antibiotic regimens to improve patient outcome if *L. monocytogenes* infection is suspected. Co-infections that occur with *L. monocytogenes* may have conflicting antibiotic treatment options. This case report emphasises the need for a good relationship between the local microbiology pathologist and physician to select appropriate antibiotic treatment before definitive results are available.

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In September 2017, the National Institute for Communicable Diseases (NICD) released a statement reporting an unprecedented increase in the number of *Listeria* cases across South Africa (SA). The increase was noted in the private and public sectors, with 190 confirmed cases of listeriosis across the country between January and August 2017. The NICD also initiated enhanced surveillance at a number of hospitals nationally to gather additional information.<sup>[1]</sup> An increase in *Listeria monocytogenes* isolates was detected at our institution. Seven cases were reported at our laboratory in 2016. This figure increased to 14 confirmed listeriosis cases up to October 2017, with 12 of these clustering between June and October (unpublished data – Division of Medical Microbiology, Department of Pathology, Groote Schuur Hospital, Cape Town, SA, 2017). This case report increases awareness about *L. monocytogenes* and highlights the potential for co-infections.

## Case report

A 34-year-old man presented to a local hospital with a 3-week history of worsening cough and dyspnoea. He had a long-standing history of methamphetamine and cannabis use. The patient was also HIV-positive, with a recent absolute CD4+ count of 32 cells/ $\mu$ L. He was not on antiretroviral therapy and had not been admitted to hospital previously. He required intubation and ventilation because of respiratory distress, and the chest radiograph confirmed a multilobar pneumonia. The patient also required inotropes for septic shock and blood transfusion for severe anaemia (Hb 4.8 g/dL). Laboratory tests showed hypoglycaemia, hypocalcaemia and deranged liver enzymes, with normal kidney function. The patient was treated empirically with ceftriaxone and azithromycin before being transferred to a tertiary hospital intensive care unit.

## Management and investigations

A blood sample was taken on admission. After 14 hours, a Gram stain showed a combination of Gram-positive cocci in chains and small Gram-positive bacilli. The following day, based on preliminary laboratory results, the presence of *Listeria* and *Streptococcus pneumoniae* was suspected. Ampicillin was added to the patient's antibiotic treatment, which had in the interim been escalated to

imipenem by the attending clinicians owing to the severity of the illness and apparent concern about Gram-negative infection. The identification of both organisms was subsequently confirmed using routine laboratory methods (Fig. 1), including the Vitek 2 system (bioMérieux, SA). Both organisms were susceptible to penicillin, with minimum inhibitory concentrations (MICs) of <0.06  $\mu$ g/mL and 0.125  $\mu$ g/mL for *S. pneumoniae* and *L. monocytogenes*, respectively. MIC determinations were done using the Vitek 2 streptococcal antibiotic susceptibility test card (AST-ST01, USA), supported by oxacillin disc testing for *S. pneumoniae* and Epsilometer testing (E-test) (bioMérieux, SA) for *L. monocytogenes* (Fig. 2). *L. monocytogenes* was also cultured from a second blood sample taken on admission,

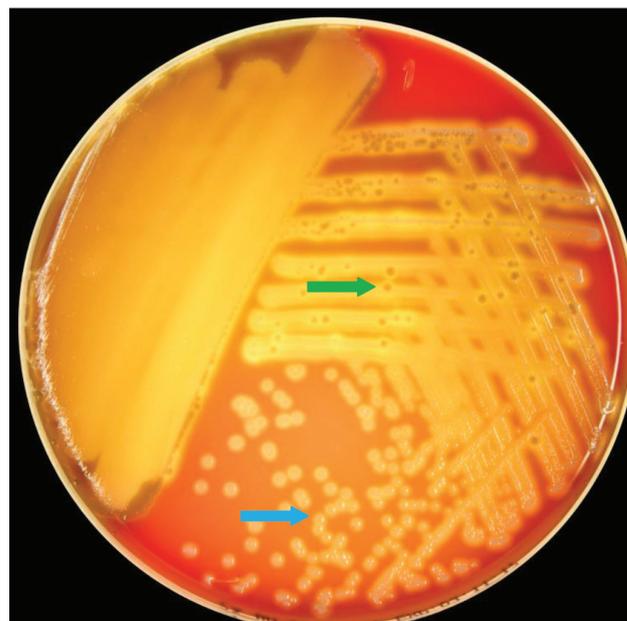


Fig. 1. Mixed culture of *Streptococcus pneumoniae* and *Listeria monocytogenes* on a 2% blood agar plate after 24 hours of incubation. There is alpha-haemolytic activity owing to *S. pneumoniae* (green arrow), and beta-haemolytic activity produced by *L. monocytogenes* (blue arrow).

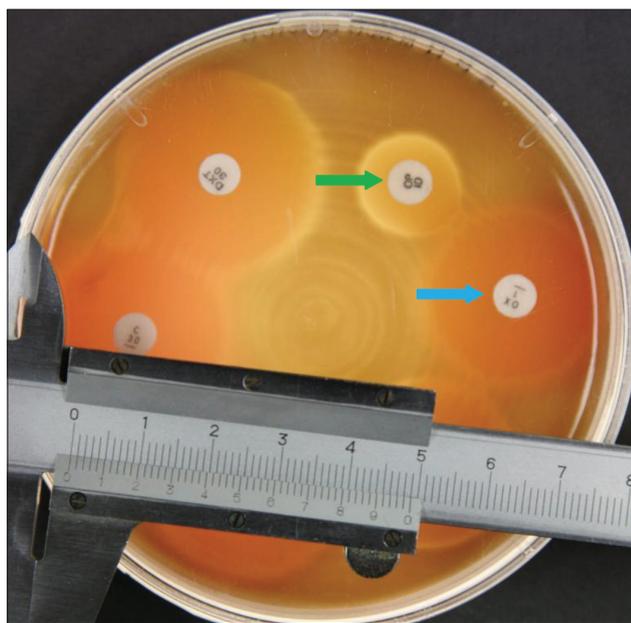


Fig. 2. Disc diffusion susceptibility testing of a *Streptococcus pneumoniae* isolate on Mueller-Hinton, with 5% sheep blood agar (optochin (OP) (green arrow) and oxacillin (OX) (blue arrow)). Based on the zones of inhibition observed, it was possible to make the presumptive identification of penicillin-sensitive *S. pneumoniae*.

which showed growth after 35 hours. Once antibiotic susceptibility results were available, definitive treatment with ampicillin and co-trimoxazole was initiated and administration of other antibiotics was discontinued. Acute renal failure at the time precluded the use of gentamicin. Meningo-encephalitis was not suspected, as no cells or organisms were present in the cerebrospinal fluid and there was no subsequent growth of bacteria. No pathology was noted on a computed tomography scan of the brain. No additional pathogens were detected and results of laboratory tests for *Mycobacterium tuberculosis* and *Legionella* serogroup 1 were negative. An echocardiogram revealed cardiomegaly with signs of biventricular failure, conduction abnormalities and an akinetic septum. An ischaemic hepatic liver injury was suspected. Multi-organ failure followed an acute kidney injury secondary to sepsis, with a metabolic acidosis. A poor response to adequate treatment, decline in clinical presentation, two resuscitating events in the intensive care unit and poor prognosis with multi-organ failure prompted the withdrawal of active treatment. The patient passed away within 7 days of initial admission to hospital.

## Discussion

Dual infection with *S. pneumoniae* and *L. monocytogenes* is rare, but not unknown. A retrospective Danish study between 1997 and 2012 reviewed 231 patients with *L. monocytogenes* bacteraemia and/or meningitis. The investigators documented 4 polymicrobial patients, 2 of whom were co-infected with *S. pneumoniae*. One patient died after 2 days of definitive treatment with ampicillin in combination with gentamicin. The other patient received benzylpenicillin as monotherapy and survived. The remaining 2 co-infected patients were also infected with *Escherichia coli*.<sup>[2]</sup> *L. monocytogenes* has been documented as a rare concomitant infection in an immunocompetent patient with cryptococcal disease.<sup>[3]</sup> Interactions between bacteria and viruses are an emerging topic in human infections, with evidence that an indirect interaction between the measles virus and *L. monocytogenes* promotes their co-infection.<sup>[4]</sup>

The mortality rate associated with *L. monocytogenes* is high – ranging from 20% to 30%, even with adequate antibiotic treatment. The variability in mortality can be explained by differences in risk factors, delay in diagnosis and inadequate empirical antibiotic treatment.<sup>[2,5]</sup> Significant risk factors associated with 30-day mortality in the above-mentioned Danish study included septic shock, altered mental state and inadequate treatment, especially with the cephalosporins.<sup>[2]</sup> The Multicentric Observational NATIONAL Study on LISTERIOSIS and Listeria (MONALISA)<sup>[6]</sup> was a national prospective observational cohort study performed in France between 2009 and 2013. It showed that the most important mortality prognostic factors for both *Listeria* bacteraemia and neuroinfection are multi-organ failure, aggravation of any pre-existing organ dysfunction, ongoing cancer, and monocytopenia.<sup>[6]</sup> It is unfortunate that our patient had multi-organ failure, anaemia, septic shock and an altered mental state, despite being on adequate antibiotic treatment.

Therapeutic guidelines for the treatment of *Listeria* lack a strong evidence base, as no clinical trials have been done regarding this disease, which is considered rare. The incidence of listeriosis is estimated at 3 - 6 cases per million population per year in the western hemisphere.<sup>[6,7]</sup> *Listeria* is intrinsically resistant to cephalosporins, while ampicillin and benzylpenicillin remain the preferred antibiotics for treatment.<sup>[8,9]</sup> The addition of a second agent, usually gentamicin, is recommended in cases of meningitis/encephalitis, endocarditis or bacteraemia in immunocompromised hosts.<sup>[10,11]</sup> Co-trimoxazole is an acceptable alternative, either as monotherapy in patients with anaphylactic reactions to penicillins, or as combination therapy when gentamicin is not tolerated.<sup>[12-14]</sup>

The diagnosis of *Listeria* organisms is made by culturing clinical specimens such as blood, cerebrospinal fluid, amniotic fluid, placenta or other sterile body fluids. Ideally, these specimens should be taken before administering antibiotics. In our case, ampicillin was added early, based on the provisional detection of *Listeria* co-infection. Blood cultures were done before starting antibiotics, and the broad-spectrum antibiotics were subsequently de-escalated to narrow-spectrum agents once the organisms had been identified.

## Conclusion

It can be concluded from this case that ampicillin may be added to the antibiotic cover if listeriosis is suspected in a high-risk group. Vulnerable patients include those who are immunocompromised, pregnant women, neonates and the elderly. However, in the setting of the current national listeriosis outbreak, ampicillin should be added to ceftriaxone/cefotaxime for the empirical treatment of suspected bacterial meningitis in all patients.<sup>[15]</sup> Challenging empirical antibiotic choices might have to be made regarding co-infections, which require consultation with an infectious diseases specialist or microbiology pathologist. The current case report also highlights the importance of a close relationship between the local microbiologist and physician to select appropriate antibiotic therapy and potentially improve patient outcome.

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