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A case of bacteremia by *Streptococcus pseudopneumoniae*

Un caso de bacteriemia por Streptococcus pseudopneumoniae

Case report

A 70-year-old man with a history of polycystic kidney disease, presented to the Urology outpatient clinic with symptoms of chronic urinary obstruction. He was diagnosed with benign prostate hyperplasia and he was treated with photovaporization. Few hours after the procedure he presented with septic shock. Treatment with antibiotics (meropenem, linezolid and daptomycin) and vasoactive drugs was initiated with significant improvement after 72 h. *Streptococcus pneumoniae* was tentatively identified in one of two blood cultures. Urine antigen of *S. pneumoniae* (BinaxNOW, Abbott) and HIV serology were negative. There were no signs of lung consolidation in the chest radiography.

The presumptive identification of *S. pneumoniae* in the microbiology laboratory was performed by optochin disc diffusion test incubated in CO_2 and in ambient air (susceptible in both atmospheres), and mass spectrometry (MALDI-TOF, Bruker). Susceptibility testing was performed with disc diffusion according to EUCAST (v13.1) (www.eucast.org). The isolate was susceptible to cefotaxime, clindamycin and vancomycin, and susceptible with increased exposure to penicillin and levofloxacin. Treatment was deescalated to ceftriaxone with good clinical progress.

As part of a surveillance programme at the Madrid Autonomous Community, all isolates of *S. pneumoniae* are analyzed at the Regional Public Health Laboratory for characterization. These results showed that this particular isolate was non typable, and soluble in bile. The capsular polysaccharide biosynthesis A *(cpsA)* and autolysin *(lytA)* genes were not detected, while the amplification of the pneumolysin gene *(ply)* was positive. Given this variety in our findings, whole genome sequencing (WGS) was performed with MinION (Oxford Nanopore) leading to identification of *Streptococcus pseudopneumoniae*.

S. pseudopneumoniae is a bacterial species closely related to *S. pneumoniae*, first identified in 2004 as part of the *Streptococcus mitis* group.[1] It is considered an opportunistic pathogen associated with septicaemia and meningitis,[2,3] particularly in patients with haematologic disease.

Phenotypic characteristics can provide some clues for its identification, but these may not be definitive, as they can overlap with other streptococcal species. *S. pseudopneumoniae* colonies have a similar appearance to *S. pneumoniae* in blood agar plates with alpha-hemolytic activity, but unlike the latter, *S. pseudopneumoniae* lacks capsule, is often resistant to optochin (inhibition zones <14 mm) when incubated with CO_2 but susceptible to optochin (inhibition zones >14 mm) when incubated in ambient atmosphere, and not soluble in bile.[1,4] However, there are exceptions and a variable proportion of *S. pneumoniae* strains do not have a specific agglutination in the Quellung reaction due to lack of capsule (non-typeable), can be optochin resistant and bile insoluble.[5,6] Additionally, a proportion of *S. pseudopneumoniae* has also been reported as optochin susceptible when incubated in CO_2 (16.4%), or bile soluble (36.1%)[6] like in our case, although this does not represent the majority of the isolates. Moreover, commercial tests (such as antigen detection or DNA hybridization probes), might not easily discriminate between both species.[1,7]

The *lytA* and the *cpsA* genes are harbored by *S. pneumoniae* (although the latter may be absent in non-typeable strains), however none of these genes are present in *S. pseudopneumoniae*, hence being useful for discrimination between both species.[6,8] Nevertheless, there are some rare *S. pneumoniae* strains that show some molecular peculiarities of the *lytA* gene that confer an atypical bile insoluble phenotype.[9]

In contrast to the *lytA* and the *cpsA* genes absent in *S. pseudopneumoniae*, some isolates can carry the *ply* gene.[6,10]

Our isolate was non-typeable, optochin susceptible when incubated both in CO_2 and in ambient air, and bile soluble. The PCR was positive for *ply*, while negative for *lytA*.

Resistance rates are often higher in *S. pseudopneumoniae*, particularly for penicillin (60.7%) and erythromycin (42.6%),[6] therefore the correct identification could affect empiric treatment.

In our patient, who presented with an invasive disease (bacteraemia), the urinary tract seemed the most likely focus, although urine culture was sterile. Nevertheless, routine culture media used for urine are not suitable for *Streptococcus* spp. and culture in enriched media was not performed. To our knowledge, no cases of urinary tract infection caused by *S. pseudopneumoniae* have been described previously.

In conclusion, it is important to note that relying solely on phenotypic characteristics for the identification of *S. pseudopneumoniae*

can be inconclusive and may lead to misidentification. Molecular methods, such as WGS, might be needed for accurate identification.

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Tolerance of Atovacuona/proguanil in off-label indication in children

Tolerancia de Atovacuona/proguanil en niños con indicación fuera de ficha técnica

Dear Editor,

Malaria is a severe disease caused by a parasite of *Plasmodium* genus, transmitted by the bite of an Anopheles mosquito vector.[1] Malaria is endemic in many tropical countries; in 2022, 93.6% of cases and 95.4% of deaths (more than 78% of these in children under 5 years old) occurred in Africa.[2] It is the leading cause of fever in tropical travellers and it can cause severe illness.[1] Globally, in 2022, there were 249 million cases and 608,000 deaths.[2] Therefore, the World Health Organization (WHO) and the Centers of Disease Control and Prevention (CDC) recommend antimalarial chemoprophylaxis for all travellers visiting endemic areas.[2,3] With the major roll-out of malaria prevention and treatment measures, more than 11 million deaths were averted globally since 2000.[1] Malaria deaths in Africa reduced by 36% between 2000 and 2021.[1] Although malaria prevention in children is a significant challenge, Atovacuona/proguanil (A/P) is only authorised for those whose weight is ≥11 kg according to its technical datasheet.[4]

We conducted a retrospective study to determinate tolerance and side effects (SE) during and after travel in children under 11 kg taking paediatric A/P (25 mg/62.5 mg) as an off-label prophylactic measure.

Children weighing under 11 kg, who attended an International Vaccination Centre at a reference hospital in Madrid between 2018 and 2022 and were recommended chemoprophylaxis with paediatric A/P according to their weight, were included. Children weighing 5 kg to <8 kg received ½ pediatric tablet daily; those weighing 8 kg to <10 kg received ¾ pediatric tablet daily and those weighing 10 kg to <20 kg received 1 pediatric tablet daily. The medication was administered one to two days prior to exposure, during exposure, and for one week following exposure. If needed, tablets could be broken or crushed and mixed with a drink. We recommended taking it in the morning with food beginning and with a milk drink.

Parents were informed that we rely on recommendations from the Spanish Ministry of Health, CDC and WHO, which indicate chemoprophylaxis in children weighing 5–11 kg when travelling to high-risk countries.[2,3,5] A contact telephone number was provided in case of any SE, and a follow-up telephone call was made to all families after their travel.

A total of 32 children received a chemoprophylaxis recommendation, but 4 (12.5%) did not take the drug due to parental decision. In 9 cases (28.1%), none of the parents answered the follow-up telephone call and, although none reported SE, they were considered lost to follow-up. The remaining 19 children were analysed. As they were infants, all parents followed the recommendations closely and did not miss any doses.

Ten (52.6%) were girls, the median age was 9 months (interquartile range [IQR] 6–13), and the median weight 9 kg (IQR 8–10). The majority, 16/19 (84.2%), were healthy; two were late preterm and one was a carrier of sickle-cell anaemia. All were well vaccinated and without allergies. They were all born in Spain and in 17 cases (89.4%) it was their first trip to a high-risk area, making it crucial to prescribe malaria prophylaxis and split the tablets if necessary. Two infants (10.5%) had previously travelled to the same country and also received chemoprophylaxis on that occasion. The most common reason for travel was visiting friends and relatives (16 cases, 84.2%). All travelled to highly endemic areas, with Africa being the most frequent destination (18 cases, 94.7%). The median duration of the travel was 30 days (IQR 15–90). The most frequent travel periods were summer (7 cases, 36.8%) and autumn (7 cases, 36.8%), corresponding with the months of June to November, when the rainy season occurs in African countries, leading to a higher risk of