



Extensively drug-resistant *Haemophilus parainfluenzae* in a patient from preexposure prophylaxis program

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M. Garreta-Esteban¹, R. Rubio-Casino¹, M. Cairo², R. Font², A. Boronat¹, M. Rajadell¹, M. Ballester-Tellez¹, E. Jimenez-Morgades¹, E. Calbo², J. Perez¹.

¹Catlab –Terrassa (Spain), ²Hospital Universitari MutuaTerrassa -Terrassa(Spain)

BACKGROUND

H. parainfluenzae is an opportunistic pathogen associated with sexually transmitted infections. The first extensively drug-resistant strain was described in Belgium in 2013, since then the spreading of MDR and XDR strains including the emergence of CTX-M-15 extended-spectrum-b-lactamase (ESBL) have been observed.

CASE DESCRIPTION

We report a case of XDR *H. parainfluenzae* urethritis on a patient under the preexposure prophylaxis program. The patient was a 30-year-old man having sex with men. Since 2019 the patient has been treated of six episodes of urethritis with ceftriaxone, azithromycin and doxycycline. In September 2023, *Mycoplasma genitalium* was identified as the causative organism of the urethritis. The patient was treated with moxifloxacin, which was repeated at the end of September due to the recurrence of symptoms and suspicion of reinfection. In November 2023, after a new episode of urethritis, urethral culture was performed, isolating a strain of *H. parainfluenzae* resistant to β -lactams including 3rd-generation cephalosporins, macrolides, tetracycline, fluoroquinolones, and cotrimoxazole, being ertapenem the only viable alternative for treatment (Table 1). Among the patient's previous isolates there were three *H. parainfluenzae* β -lactamase negative, susceptible to amoxicillin/clavulanic and cephalosporins. Antibiotic susceptibility was studied using a disc diffusion method. For the study of beta-lactam resistance mechanisms, the presence of TEM-1 β -lactamase was excluded by the cefinase-test (BD BBL Cefinase) and ESBL by the double-disk synergy test (DDST) and qPCR (eazyplex® SuperBugCRE) (Image 1). All procedures for susceptibility studies were performed following the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria for *H. influenzae*. To fully characterize the molecular determinants of resistance, NGS remains to be performed.

Table 1- Sensitivity of <i>H.parainfluenzae</i> isolated from urethral sample			
Antibiotic	Interpretation	Antibiotic	Interpretation
Ampicillin	R	Acid nalidixic	R
Oral amoxicilin	R	Levofloxacin	R
Penicillin G	R	Moxifloxacin	R
Amoxicilin/clavulanic	R	Azitromicine	R
Oral cefuroxime	R	Cotrimoxazole	R
Cefotaxime	R	Fosfomycin*	
Cefixime	R	Ertapenem*	

*There aren't clinical breakpoints established for EUCAST of these drugs for this microorganism.



Image 1. qPCR Eazyplex® SuperBug CRE

DISCUSSION

There is great concern about preventing the spread of resistant strains in some pathogenic STD species such as *N. gonorrhoeae*. However, other potential pathogens including *H. parainfluenzae* are emerging with resistance mechanisms that may become very complex to treat. Preexposureprophylaxis program patients suffer a high number of STDs due to unprotected sex and are candidates for selection of MDR mutants by repeated administration of successive antibiotics. We should monitor beta-lactam resistance in these microorganisms related, or not, to ESBL production.