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Scientific letter

Vulvovaginitis due to *Neisseria meningitidis* in a 6-year-old girl☆

Vulvovaginitis por Neisseria meningitidis *en niña de 6 años*

Neisseria meningitidis is a gram-negative diplococcus that can act as a commensal in mucosa of the upper respiratory and anogenital tracts, or produce disseminated meningococcal infection. Cases of urogenital and anogenital infection have also been reported. Here, we present a case.

A six-year-old female patient with a previous diagnosis of severe pulmonary stenosis treated with percutaneous pulmonary valvuloplasty attended the paediatric clinic due to dysuria and the appearance of greenish-yellow discharge without other notable alterations. Her physical examination was unremarkable and a test strip was negative. A vulvar swab was sent to our laboratory, from which a Gram stain was performed in which <5 PMNLs/1000 magnification field and intra/extracellular gram-negative diplococci were observed. After 24 h of incubation at 37 °C with an atmosphere of 5% CO_2, translucent, greyish convex colonies, oxidase positive, were isolated on chocolate and Thayer-Martin agar, identified as *N. meningitidis* by MALDI-TOF (LSV 2.57) and Filmarray® BCID Panel. The strain was classified by agglutination (Pastorex® Meningitis) as serogroup C. The strain showed sensitivity to ampicillin, cefotaxime, meropenem, tetracycline and ciprofloxacin. A culture of the pharyngeal sample was performed 48 h after the vaginal sample, which resulted negative for *N. meningitidis*. Treatment with amoxicillin/clavulanic acid was started and the case was reported to the Public Health Service due to possible legal implications. Throat and vulvar cultures were repeated one month later, both being negative for meningococcus.

Šikanić-Dugić et al. carried out a study in 115 girls with symptoms of vulvovaginitis aged between 2 and 8 years. In 33.04% of the patients, a bacterium was identified as the causal agent: *S. pyogenes* (n = 21; 55.3%), followed by *H. influenzae* (n = 5; 13.2%) and *S. agalactiae* (n = 4; 10.5%), among others. *N. meningitidis* was not detected in any of the cases[1]. Isolation of *N. meningitidis* in genital samples is not uncommon[2], but it is an infrequent cause of vulvovaginitis in young girls[3]. There are case reports of meningococcal infection associated with sexual practices in both the heterosexual population and in men who have sex with men[2]. Offman et al. reported a case of vulvovaginitis in an adult patient complicated by meningitis and septic shock, highlighting the need for rapid and correct identification of the aetiological agent[4]. Meanwhile, different outbreaks of disseminated meningococcal infection associated with sexual transmission have also been described in Europe, the US and Australia[2]. The invasive capacity of *N. meningitidis* is therefore not limited to its nasopharyngeal location.

Given the phylogenetic relationship between *N. meningitidis* and *N. gonorrhoeae* and their phenotypic similarities, it is necessary to establish a correct aetiological diagnosis at the species level. The classic methods used to differentiate both species were eminently biochemical. Currently, mass spectrometry (MALDI-TOF) allows us to discriminate between both species. Although the isolation of greyish, oxidase and catalase positive colonies in culture of urogenital samples suggests infection by *N. gonorrhoeae, N. meningitidis* must be taken into account given the possible repercussions.

Three main ways for *N. meningitidis* to reach the genital mucosa have been proposed: sexual transmission, orogenital transmission, and autoinoculation from the upper respiratory tract[2,5,6]. The possibility of sexual abuse should not be ruled out[7]. In the case that we present, the origin of the infection could not be identified, since the oropharyngeal swab was negative on two occasions and no samples were taken in the patient's immediate environment.

There is a question as to whether vaccination against *N. meningitidis* would be useful for the prevention of urogenital infection. The ability of *N. meningitidis* to adapt to the urogenital mucosa may lead to loss of the polysaccharide capsule or a change in the expressed serogroup, the target of existing vaccines. Our patient was up to date on her vaccination schedule (including vaccines against serogroups B and C)[2]. More studies would be necessary to establish the most appropriate public health service measures for the prevention of this type of infection.

Currently, there are no clinical guidelines or bibliography that support the preferential use of a specific antibiotic. In the case we present, the patient was treated with amoxicillin/clavulanic acid, and responded favourably.

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Héctor Condado Condado [a,*], Tatiana Khaliulina Ushakova [a], María Pilar Acín Romero [b], Antonio Beltrán Rosel [a]

[a] *Servicio de Microbiología y Parasitología Clínica, Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain*
[b] *Servicio de Pediatría, Centro de Salud Universitas, Zaragoza, Spain*

* Corresponding author.
E-mail address: hcondado@salud.aragon.es
(H. Condado Condado).

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Mycoplasma genitalium: Analysis of mutations associated with macrolide resistance in Lleida, Spain

Mycoplasma genitalium*: análisis de las mutaciones asociadas a la resistencia a macrólidos en Lleida, España*

Mycoplasma genitalium is a sexually transmitted pathogen responsible for 10-30% of non- gonococcal urethritis in men. In women, it is associated with cervicitis and complications such as pelvic inflammatory disease (PID) and possible infertility and poor obstetric outcomes[1,2].

The lack of cell wall in *M.genitalium* precludes the use of ß-lactams and limits its treatment choice to antibiotics such as tetracyclines (doxycycline-DOX), macrolides (azithromycin-AZM) and quinolones (moxifloxacin-MXF). Due to the decrease in cure rates with DOX, AZM is the recommended first-line treatment against *M.genitalium*[3,4]. However, since Jensen et al. in 2008 reported AZM treatment failure due to single-nucleotide polymorphism (SNP) mutation at positions 2058 and 2059 (*Escherichia coli* numbering) in region V of the 23S rRNA gene[5], the implementation of macrolide-resistance mutations (MRMs) assays has become of importance in order to minimize treatment failures. MXF is the second-line treatment recommended in such cases[3,4].

To date, limited data has been published regarding the prevalence of AZM resistance-associated mutations in Spain[6,7], so the objective of this study is to report the mutations found in the sanitary region of the province of Lleida between May 2019 and January 2021.

During this time, a total of 2288 specimens were tested for *M.genitalium*. DNA of the specimens was extracted using EZ1 or QIASymphony equipment (QIAGEN®), and real-time PCR screening was performed using the AllplexTM STI-7 V1-1 kit (Seegene®). Positive *M.genitalium* specimens were tested for MRMs with the Allplex MG&AziR (Seegene®) assay, which consists in a multiplex qPCR for detection of *M.genitalium* and six AZM SNPs (A2058G, A2058T, A2058C, A2059G, A2059T, A2059C). Both techniques were run on the CFX96 qPCR instrument (Bio-Rad®).

Of the 2288 of specimens, 46 samples from 46 patients (36 men and 10 women), consisting of 19 urethral swabs (41.3%), 14 first-void urines (30.4%), 10 endocervical swabs (21.7%) and 3 rectal swabs (6.5%), tested positive for *M. genitalium*, representing 2.1% of prevalence. The request of sexually transmitted diseases (STD) testing of these samples were mainly urethritis (27) (58.8%), but also asymptomatic screening in high risk contacts (6) (13%), cervicitis (6) (13%), PID (4) (8.7%) and HIV pre-exposure prophylaxis (PrEP) (3) (6.5%).

The demographic and clinical data of the 39 infection episodes are described and classified by the sexual orientation in Table 1. Among them, 20 were men who have sex with women (MSW) (51.3%), 9 were men who had sex with men (MSM) (23.1%), and 10 were women (25.6%). Seven medical records, all from men, were not available.

Considering coinfections with other STDs, 9 *M.genitalium* cases (19.6%) were in coinfection with either *Ureaplasma urealyticum* (UU) (8.1%), *Chlamydia trachomatis* (CT) (6.9%), *Neisseria gonorrhoeae* (NG) (2.3%) and *Mycoplasma hominis* (MH) (2.3%).

Regarding MRMs, 37 episodes were classified as "wild type"/non-mutated (WT), whereas 9 cases (8 men and 1 woman) carried an AZM resistance mutation (3 urethral swabs, 4 first-void

Table 1
Demographic and clinical data of the positive *M. genitalium* episodes classified by the sexual orientation of patients.

Total no. = 39[a]	MSM (*n* = 9) 23.1%	MSW (*n* = 20) 51.3%	Women (*n* = 10) 25.6%
	No. (%)	No. (%)	No. (%)
Medical history			
HIV positive	2 (22.2)	–	–
Syphilis history	3 (33.3)	2 (10)	1 (10)
HIV and syphilis	2 (22.2)	–	–
Clinical findings[b]			
Total symptomatic	**4 (44.4)**	**17 (85)**	**10 (90)**
Urethritis	4 (44.4)	17 (85)	–
Cervicitis	–	–	6 (60)
PID	–	–	4 (44.4)
Total asymptomatic	**5 (55.5)**	**3 (15)**	–
HIV pre-exposure prophylaxis (PrEP)	3 (33.3)	–	–
High-risk contacts	2 (22.2)	3 (15)	–
Specimens[c]			
Urethral swab	4 (44.4)	11 (55)	–
First-void urine	3 (33.3)	8 (40)	–
Rectal swab	2 (22.2)	1 (5)	–
Endocervical swab	–	–	10 (100)
Macrolide resistance by specimen[d]			
23S rRNA mutant MG	**3 (33.3)**	**3 (15)**	**1 (10)**
Urethral swab	1 (11.1)	1 (33.3)	–
First-void urine	1 (11.1)	2 (66.7)	–
Rectal swab	1 (11.1)	–	–
WT MG	**6 (66.7)**	**17 (85)**	**9 (90)**
Urethral swab	4 (44.4)	11 (64.7)	–
First-void urine	1 (11.1)	5 (29.4)	–
Rectal swab	1 (11.1)	1 (5.9)	–
Total no. coinfection[e]			
CT	–	3	2
NG	1	–	–
MH	–	–	1
UU	2	1	2

[a] Medical records were missing in 7 patients. [b,c,d,e] comments are referred to these episodes.
[b] Six patients were tested for STD because of urethritis and one was because of a high-risk contact.
[c] Four samples were urethral swabs and 3 were first-void urines.
[d] Five samples were wild type (WT) (2 first-void urines and 3 urethral swabs) and two carried a MG mutation (1 first-void urine and 1 urethral swab).
[e] In four of these samples, MG was in coinfection with CT, UU, NG and both MH and UU.