y/o anestésicos locales junto con un seguimiento clínico estrecho después de este tipo de cirugías se antoja fundamental.

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Autoría

Domingo Fernández Vecilla: escribió la carta científica, revisó bibliografía.

Silvia López-Plandolit Antolin: ayudó a redactar el caso clínico, revisó bibliografía y proporcionó las imágenes.

Miren Josebe Unzaga Barañano: ayudó con la concepción del caso, revisó el caso y ayudó a modificarlo.

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Los autores declaran no tener ningún conflicto de interés.

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Azithromycin and moxifloxacin resistance-associated mutations in *Mycoplasma genitalium*, in the Region of Murcia, by a commercial PCR assay

Detección mediante PCR de mutaciones asociadas a resistencia a azitromicina y moxifloxacino en Mycoplasma genitalium *en la Región de Murcia*

Dear Editor:

Mycoplasma genitalium (MG) is an extremely slow-growing and fastidious organism to culture, and it was not until the first polymerase chain reaction (PCR) was developed that its role as a pathogen in human disease was established. This sexually transmitted infection (STI) is a well-recognized cause of non-gonococcal urethritis (NGU).[1,2]

European treatment guidelines recommend azithromycin for the treatment of uncomplicated MG infection and moxifloxacin for uncomplicated macrolide-resistant MG infection.[2]

The rapid emergence and spread of antimicrobial resistance in MG is a growing concern. Antimicrobial resistance rapidly spread to Europe, where the reported azithromycin resistance rate ranges from 20.1% to 35.6%, and mutations associated with fluoroquinolone resistance were found in 1.9–3.7% of MG infections.[3,4]

The established gold standard method for detection of mutations associated with antimicrobial resistance is Sanger sequencing of resistance-determining regions in the 23S rRNA and the *parC* genes. However, few commercial assays are available for this pur-

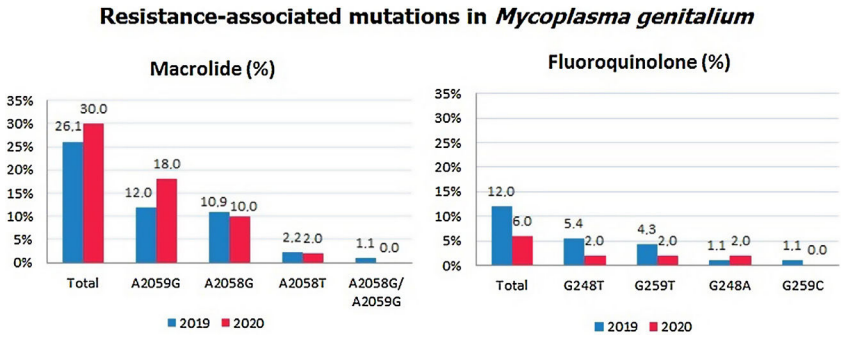

Fig. 1. Prevalence of single-nucleotide mutations detected in *Mycoplasma genitalium* by year.

pose. In this context, specimens from male and female patients with a suspected diagnosis of a STI from April 2019 to March 2021 were analyzed using a commercial real-time PCR assay for detection of mutations associated with azithromycin and moxifloxacin resistance, in order to determine the resistance rates for these antimicrobials and their evolution throughout the study period.

A total of 142/3633 (3.9%) patients who tested positive for MG were included in the study. The first sample from the first episode was taken for each patient. The assay used to diagnose the MG infection was the RT-PCR Allplex™ STI Essential Assay (Seegene®, Seoul, South Korea). Specimens positive in this assay were subsequently tested by the RT-PCR Allplex™ MG & MoxiR Assay (Seegene®) and RT-PCR Allplex™ MG & AziR Assay (Seegene®) for azithromycin, as well as moxifloxacin resistance-associated mutations. The biological specimens were endocervical and urethral swabs that were transported in DeltaSwabs Amies (Deltalab S.L., Barcelona, Spain) and first-void urine samples in a sterile sample container.

MG was detected in 76 (53.5%) male and 66 (46.5%) female patients. Resistance-associated mutations against macrolides were detected in 39/142 (27.46%) strains and against fluoroquinolones in 14/142 (9.86%) strains. The median age was 29 (IQR 25–37.25; 17–58) years, and the prevalence was significantly higher in male patients (44.7% vs. 13.2%, $p = 0.049$).

The percentage of SNPs detected in the 23S rRNA was 26.1% in 2019 and 30% in 2020, while the percentage of SNPs detected in the *parC* gene was 12% in 2019 and 6% in 2020. Detailed information about these detected mutations by year is shown in Fig. 1.

Throughout the study period, we found a slight increase of 3.9% in the resistance rate to azithromycin. The prevalence of mutations associated with fluoroquinolone resistance alone decreased from 12% in 2019 to 6% in 2020. Both evolutions between these 2 years, were not statistically significant.

The most frequent SNP detected was A2059G (37.7%), while A2058G (28.3%) was in second position.[5] Dual mutations conferring resistance to both antimicrobials were found in a total of nine (17%) mutant strains: four A2059G/G248T, three A2058G/G259T and two A2059G/G248A. The presence of dual mutations could increase treatment failure, which was similarly concluded in a study where patients were followed up closely to observe the implication of the presence of dual markers after monotherapy.[6]

Treatment failure in MG infection is associated with recurrent or persistent NGU.[7] Commercial PCR assays for the detection of these mutations allow for the resistance-guided treatment of MG infections, improving cure rates and preventing the spread of resistant strains. Furthermore, the fact that the study can be made with the same DNA extraction is an advantage over other commercial assays.

The main limitations of this study were the lack of a complete clinical history and the number of patients lost to follow-up, which would allow for an analysis of antibiotic failure. However, there is enough data available to support that the presence of these mutations causes treatment failure.[3,7,8]

Finally, the high macrolide resistance rates and the increase of resistance-associated mutations during the study period and, in addition, the established fluoroquinolone resistance rate, which was similar to that from other studies, supports the necessity of analyzing the presence of mutations to perform targeted treatment.

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Case-fatality rates and risk of death from COVID-19 and influenza A/H3N2 in Brazil: A nationwide ecological study

Tasas de letalidad y riesgo de muerte por COVID-19 e influenza A/H3N2 en Brasil: un estudio ecológico a nivel nacional

Brazil is one of the countries with the highest incidence and mortality rates from COVID-19 worldwide. In 2022, the country faced a third wave of the disease associated with community transmission of the Omicron variant. During the first 10 epidemiological weeks (January 2–March 12, 2022), 7,058,717 cases and 35,840 deaths from COVID-19 were recorded. In addition, Brazil has faced an out-of-season outbreak of influenza A virus (A/Darwin/6/2021(H3N2)), first detected in Rio de Janeiro in November 2021, and widely spread in the country in the first weeks of 2022. In most Brazilian states, the flu season usually occurs from May to July, starting in the Northeast region and spreading to the South.[1] The simultaneous transmission of COVID-19 and influenza in 2022 resulted in a significant increase in demand for hospital beds, but the country's case-fatality rates associated with the most severe forms of these diseases during this period are unknown.

In this nationwide ecological study, we estimated the case-fatality rates and risk of death from COVID-19 and influenza A/H3N2. Brazil has a geographic area of ~8.5 million square kilometers and a population of *circa* 213 million people. In addition, the country comprises 26 states and one federal administrative district and is divided into five regions: North (seven states), Northeast (nine states), Midwest (three states and one federal district), Southeast (four states), and South (three states). The human deve-