Editorial

Mycoplasma genitalium in medical practice: silent as Chlamydia, but with greater potential for aggressiveness

Mycoplasmas belong to the *Mollicutes* classification. The first species was discovered in 1898 by Nocaard & Roux in a case of pneumonia. In this classification four species have a higher impact on a bovine pneumonia case. The *Ureaplasma* genus focusing on the *Urealiticum* and *Parvum* species may be related with problems during pregnancy or even with perinatal impact⁽¹⁾, whereas the *Mycoplasmas* genus represented by the *hominis* and the *genitalium* species are more related to disturbances in the genitals, but can also have an impact on pregnancy⁽¹⁾. Among these, *Mycoplasma genitalium* (MG) stands out regarding its pathogenicity, especially the growing resistance to antibiotics as shown in recent studies^(2,3).

In terms of pathogenicity, *Chlamydia trachomatis* (CT) can be compared with MG. It was first described in 1907, in Berlin, by the zoologist and microbiologist Stanislaus von Prowazek, who defined the existence of inclusion corpuscles of *Chlamydia* in trachoma cases.

After their discovery, both MG and CT were studied as to their pathogenicity mechanisms; however, most studies have been accentuating the *Chlamydia* bacterium. However, several factors have led to an increasing concern regarding MG, requiring more studies.

At first, MG differs from CT in its microbiological structure, since it does not show a cytoplasmic membrane⁽⁴⁾, which allows the resistance to all antimicrobial agents that have their action mechanism addressed to that organelle. But the pathogenicity mechanisms are similar to this bacterium: both attach closely to the cells so that these can be included through receivers⁽⁴⁾. In addition to their very small size (the MG is the smallest existing bacterium), it requires intracellular parasites⁽⁴⁾.

MG is different than the *Ureaplasma* and the *Mycoplasma hominis* species, which can compose the vaginal microbiome⁽⁵⁾. However, a study showed the presence of MG not associated with the pathogenicity⁽⁶⁾.

The prevalence of CT is around 10% in the young population, whereas MG has been reported in about 1 to 2% of the women⁽⁷⁾. Despite this difference, MG has been shown to be increasing; a review of the literature pointed to progressively higher rates by comparing more recent studies⁽⁸⁾. While Manhart et al.⁽⁹⁾ reported 7% of MG prevalence in the symptoms of cervicitis in 2003, Gaydos et al.⁽¹⁰⁾, also evaluating cervicitis, found this microorganism in 19.3% of the cases in 2009.

It is important to note that a large group of entities can be associated with both CT and MG, which can include cystitis, cervicitis, changes to the vaginal environment, and even pelvic inflammatory disease, with consequent implication on fertility⁽¹¹⁾. These situations are fundamentally important to conduct our diagnostic "clues" towards these agents.

Regarding the diagnosis of both CT and MG, if we wait for signs and symptoms we will miss the diagnoses in about 70 to 80% of the time, since both behave so insidiously; they are known as "silent epidemic" agents. It would be ideal for us to base the laboratory diagnosis on molecular biology testing⁽¹²⁾. These diagnostic methods are sensitive, and in case of CT they should be used for tracking, especially among teenagers, as it is not usually applied in case of MG. MG should be considered in cases of chronic cystitis, cervicitis or pelvic process, even when the first suspicion leads to CT and this agent's treatment.

As far as treatment is concerned, studies show the difference between MG and CT. MG has been categorically more and more resistant to numerous agents that act on $CT^{(3)}$. In general terms it is possible to state that doxycycline provides 60% of resistance and, therefore, proved to be an ineffective drug to treat $MG^{(12)}$. Long clinical signs or symptoms that lead us to think of MG as the agent involved involve azithromycin as the first treatment option⁽¹⁰⁾. However, studies refer to 30% of resistance to this drug⁽²⁾, and it seems that increasing the time of administration of a single dose of 1 g (used for treating cervicitis by CT) to 5 or even 7 days does not reduce such resistance⁽¹³⁾. Moxifloxacin has been used in case of resistance to azithromycin, although a resistance of more than 5% to moxifloxacin has already been mentioned⁽¹⁴⁾.

In conclusion, we have observed that MG is an emerging pathogen, affecting the reproductive health. It is difficult to be clinically diagnosed and has growing resistance to antibiotics, which makes it more aggressive than CT. Therefore, it should get more attention from the community that works with both male and female genital tract infections.

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REFERENCES

- 1. Taylor-Robinson D. Infections due to species of Mycoplasma and Ureaplasma: an update. Clin Infect Dis. 1996;23:671-82.
- Bissessor M, Tabrizi SN, Twin J, Abdo H, Fairley CK, Chen MY, et al. Macrolide resistance and azithromycin failure in a Mycoplasma genitalium-infected cohort and response of azithromycin failures to alternative antibiotic regimens. Clin Infect Dis. 2015;60:1228-36.
- Manhart LE, Gillespie CW, Lowens MS, Khosropour CM, Colombara DV, Golden MR, et al. Standard treatment regimens for nongonococcal urethritis have similar but declining cure rates: a randomized controlled trial. Clin Infect Dis. 2013;56:934-42.
- Razil S, Yogev D, Naot Y. Molecular biology and pathogenicity of mycoplasmas. Microbiol Mol Biol Rev. 1998;62:1094-156.

- Chaban B, Links MG, Jayaprakash TP, Wagner EC, Bourque DK, Lohn Z, et al. Characterization of the vaginal microbiota of healthy Canadian women through the menstrual cycle. Microbiome. 2014;2:23.
- Falk L, Fredlund H, Jensen J. Signs and symptoms of urethritis and cervicitis among women with or without Mycoplasma genitalium or Chlamydia trachomatis infection. Sex Transm Infect. 2005;81(1):73-8.
- Sonnenberg P, Ison CA, Clifton S, Field N, Tanton C, Soldan K, et al. Epidemiology of Mycoplasma genitalium in British men and women aged 16–44 years: evidence from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). Int J Epidemiol. 2015;44(6):1982-94.
- Sethi S, Singh G, Samanta P, Sharma M. Mycoplasma genitalium: an emerging sexually transmitted pathogen. Indian J Med Res. 2012 Dec;136(6):942-55.
- Manhart LE, Critchlow CW, Holmes KK, Dutro SM, Eschenbach DA, Stevens CE, et al. Mucopurulent cervicitis and Mycoplasma genitalium. J Infect Dis. 2003;187(4):650-7.

- Gaydos C, Maldeis NE, Hardick A, Hardick J, Quinn TC. Mycoplasma genitalium as a contributor to the multiple etiologies of cervicitis in women attending sexually transmitted disease clinics. Sex Transm Dis. 2009;36:598-606.
- Lis R, Rowhani-Rahbar A, Manhart LE. Mycoplasma genitalium infection and female reproductive tract disease: a meta-analysis. Clin Infect Dis. 2015 Aug 1;61(3):418-26.
- Jensen JS, Cusini M, Gomberg M, Moi H. 2016 European guideline on Mycoplasma genitalium infections. J Eur Acad Dermatol Venereol. 2016;30:1650-6.
- 13. Horner P, Blee K, Adams E. Time to manage Mycoplasma genitalium as an STI: but not with azithromycin 1 g! Curr Opin Infect Dis. 2014;27:68-74.
- 14. Couldwell DL, Tagg KA, Jeoffreys NJ, Gilbert GL. Failure of moxifloxacin treatment in Mycoplasma genitalium infections due to macrolide and fluoroquinolone resistance. Int J STD AIDS. 2013;24:822-8.