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# Doxycycline Failure in Lymphogranuloma venereum

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## Abstract

The number of Lymphogranuloma venereum (LGV) cases is currently reemerging in the homosexual community, particularly in HIV seropositive patients. The standard treatment for this infection caused by *Chlamydia trachomatis* L1, L2 and L3 serotypes is a 3 week doxycycline regime. We report the case of a male patient presenting with an LGV and rapidly cured by moxifloxacin after an initial clinical failure following an extended therapy with cyclines. This fluoroquinolone is known to be highly active in vitro on the LGV pathogenic agent. Thus, it could represent a useful alternative to doxycycline in case of failure.

## **Introduction**

Lymphogranuloma venereum (LGV) is a sexually transmitted infection (STI) caused by *Chlamydia trachomatis* L1, L2 and L3 serotypes. This infection is currently reemerging in Europe and is most often cured by an extended cycline antibiotic regimen. We report an original case of a successful fluoroquinolone treatment after an initial clinical failure following doxycycline therapy.

## **Clinical case**

A 27 year old man was admitted to our infectious diseases department for anal pain and large, inflammatory and painful inguinal lymphadenopathies which was persisting despite a 2 week doxycycline regime. This treatment had been prescribed by his general practitioner for a proctitis with a positive *Chlamydia trachomatis* testing on a superficial anal sample (Roche technique PCR).

He reported unprotected anal intercourse two weeks prior with an irregular partner. He had no fever, nor urethral or anal discharge. No STI history nor previous doxycycline treatment were reported. Clinical exam found bilateral lymphadenopathies, approximately 3 cm large, stretched and very tender without any cutaneous lesion on the lower limbs. Proctological examination using rectoscopy showed a 5 mm diameter racket-like shaped ulceration on the anal margin, without discharge. Blood tests showed a mild inflammatory syndrome with a 39 mg/l CRP and a normal full blood count. A lymph node aspiration revealed a macroscopically purulent liquid. The culture was sterile, as the patient had already been taking doxycycline for 10 days. PCR *Chlamydia trachomatis* testing (Cobas TaqMan Roche technique) was positive in this sample and in the anal ulceration biopsy. The molecular analysis conducted at the national Chlamydiae reference center confirmed the L2 serotype LGV. Culture on McCoy cells remained sterile. No other STI was found (HIV, HBV, HCV, syphilis, gonorrhoea). *C.trachomatis* serology was positive with 1/512 IgG and 1/256 IgA titers for a 1/8 positivity

threshold. Despite an extended 200 mg per day doxycycline regime for more than 3 weeks, the patient developed discharging inguinal sinuses requiring repeated drainage and the anal lesion was still observed on proctological examination. Following this clinical failure, doxycycline was replaced by a 400 mg daily moxifloxacin therapy allowing a spectacular recovery in 10 days. No relapse was observed after a 2 month follow up.

## **Discussion**

Lymphogranuloma venereum is a sexually transmitted infection caused by *Chlamydia trachomatis* L1, L2 and L3 serotypes. Recent outbreaks were reported in Europe and in the United-States, mainly in the HIV seropositive homosexual community. Clinical presentation includes a genital or rectal ulceration with inguinal lymphadenopathy. The diagnosis of *C. trachomatis* infection can be made by culture, antigen or nucleic acid detection (gene amplification) on a genital or lymph node sample [1]. A serology with high levels of antibodies can be helpful in case of suggestive clinical history [1].

Doxycycline remains the first line of LGV treatment at a bidaily 100 mg dose for 21 days. This lengthy treatment duration is suggested as published studies have shown persistent *Chlamydia* RNA in rectal samples after more than 2 weeks of doxycycline therapy in LGV patients while DNA was undetectable in less than 7 days in proctitis cases due to other *Chlamydia* serotypes [2]. Macrolides represent an alternative [1].

*C. trachomatis* is naturally sensitive to cyclines, macrolides and fluoroquinolones. However, the concept of *C. trachomatis* acquired resistance is not clear [3,4]. Some treatment failures related to less sensitive strains were reported in the literature without determining the genetic support [5,6]. In vitro, it is possible to obtain resistant mutants, particularly to fluoroquinolones. Currently, little is known about the epidemiology of *Chlamydia trachomatis* acquired resistance. In general practice, evaluation of *in vitro* sensitivity is not

routinely done due to some difficulties related to its compulsory intracellular feature, the lack of a standardized method and the poor reproducibility of the sensitivity tests [5]. It also depends on the availability of the strain. Unfortunately, in this case, cell culture remained negative. It could be possible to look for a resistance gene as TetM which is responsible for tetracycline resistance. However, in clinical specimens containing polymicrobial flora, the presence of antibiotic resistance genes does not prove that they are located on the *C.trachomatis* strain. In addition, it is always difficult to assign clinical failure to treatment failure due to possible reinfection [3]. Our patient was compliant with the antibiotic therapy. Moreover, his painful symptomatology made him unfit for new anal intercourse which could have explained the lack of recovery after more than three weeks of doxycycline therapy. Thus, a fluoroquinolone like moxifloxacin was chosen, due to its good intrinsic activity on *C. trachomatis* and to its possible use in genital infections. No study has shown its efficacy in LGV treatment [1]. *In vitro*, Bébéar et al showed that moxifloxacin is the most active molecule against *Chlamydia trachomatis* with a MIC 90 higher than doxycycline, macrolides and other fluoroquinolones [7]. In our patient, the spectacular regression of symptoms with this new fluoroquinolone seems to support the hypothesis of a good *in vivo* activity also. To our knowledge, no cyclines' treatment failure was reported in LGV. In these situations, new fluoroquinolones such as moxifloxacin could represent a useful alternative.

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