A case of an *Ureaplasma* infection causing significant soft tissue destruction to the vagina, perineum and abdominal wall in a patient with hypogammaglobulinemia

Debbie Hunt, Shomari Dotun Lee Zack-Williams, Janet Purcell, John Cheesbrough, Jeyramam Srinivasan

**ABSTRACT**

**Introduction:** *Ureaplasma* species make up part of the normal genital flora and rarely penetrate the submucosa, except in the case of immunosuppression/instrumentation. However, so far in literature, there is no cases of Ureaplasma causing significant tissue loss. We present a case of significant tissue destruction of the abdominal wall and perineum caused by Ureaplasma.

**Case Report:** A 23-year-old female with B lymphocyte deficiency presented with a urinary tract infection (UTI) which quickly progressed into recurrent abscesses and then widespread infection of the pubic region and genitalia, requiring multiple surgical debridement. This leads to a significant soft tissue defect producing complex reconstructive challenges. A distally based rectus abdominis turn down flap and skin graft was used to reconstruct the pubic defect. However, despite the flap being viable and no outward evidence of infection, the healthy tissue did not heal. In addition, the surgical wound used to raise the flap broke down and the anterior rectus sheath disintegrated. Despite multiple wound swabs and cultures the cause could not be isolated. Numerous broad spectrum antibiotics were trialed, yet the wound persisted for over a year, with recurrent admissions and operations. Finally, specific viral transport medium and PCR identified *Ureaplasma* and after starting doxycycline, the patient drastically improved within weeks.

**Conclusion:** It is important to suspect mycoplasma when the clinical picture indicates infection, but the infectious agent cannot be isolated on standard culturing methods. Involving support from microbiologists early would be helpful in such cases.
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Keywords: Abdominal wall, Destruction to the vagina, Hypogammaglobulinemia, Perineum

**How to cite this article**

Hunt D, Zack-Williams SDL, Purcell J, Cheesbrough J, Srinivasan J. A case of an *Ureaplasma* infection causing significant soft tissue destruction to the vagina, perineum and abdominal wall in a patient with hypogammaglobulinemia. Int J Case Rep Imag 2016;7(4):267–271.

Article ID: Z01201604CR10634DH

doi:10.5348/ijcri-201646-CR-10634

**INTRODUCTION**

*Ureaplasma* species make up part of the normal genital flora and rarely penetrate the submucosa, except
in the case of immunosuppression/instrumentation. However, so far in literature, there are no cases of Ureaplasma causing significant tissue loss. We present a case of significant tissue destruction of the abdominal wall and perineum caused by Ureaplasma.

CASE REPORT

A 22-year-old female with agammaglobulinemia due to absent B lymphocytes had been receiving regular immunoglobulin replacement therapy since childhood. She maintained good health until early 2012, when, aged 20, she developed cystitis and a vaginal discharge. An initial diagnosis of urinary tract infection was made which failed to respond to antibiotics. Pelvic inflammatory disease (PID) was then suspected and in March 2012 she had a laparotomy at which multiple intra-abdominal abscesses were found. These failed to yield any growth on routine culture. Her symptoms improved following surgery and antibiotics. However, her vaginal discharge and abdominal pain returned and she received several further courses of antibiotics for PID over the next 15 months. In May 2013, she developed a swelling of the left vulva, initially felt to be a Bartholin’s abscess which spontaneously discharged. Anaerobes were isolated on culture and metronidazole given. Failure to improve resulted in an admission for drainage in July, at which time enterococci were isolated from pus. By this time the vulva was ulcerated. A diagnosis of genital herpes was made and aciclovir given but this was not confirmed by polymerase chain reaction (PCR). By November 2013, she had a large vulvar ulcer with widespread soft tissue infection of the pubic and genital region requiring multiple wound debridements and packing under general anesthetic due to the severe pain. Magnetic resonance imaging showed two abscesses deep to the left vulva/labia which required further drainage. Biopsy of the ulcer margin showed chronic inflammation with no evidence of malignancy or vasculitis. Mycobacterial culture was negative and PCR was negative for HSV 1 and 2. HIV and syphilis were not detected by PCR in plasma. A Plastic surgery opinion was sought for the resultant complex wound management and the patient transferred to the regional centre.

Reconstructive surgery

The degree of soft tissue loss involving vagina and perineum in such a young lady required multi-disciplinary input from plastic surgery, urology, immunology, microbiology and caring nursing support. In addition, the patient was malnourished after prolonged hospitalization and frequent visits to theatre. These nutritional and psychological aspects were further handicap to the reconstructive efforts, and treatment as a whole (Figure 1).

The aim of the reconstructive surgery at this stage was to provide a healed wound first in order to turn the tide of ongoing catabolism in this individual. A distally based rectus abdominis flap and skin graft was used for reconstruction of the pubic defect and vaginal roof (Figure 2). Despite the flap being viable, the healthy tissue did not show any healing with the vaginal vault tissue. In addition, the abdominal wound used to harvest the rectus abdominis flap also started to break down showing further loss of healing between abdominal skin flap and the rectus sheath. In fact, the entire anterior rectus sheath completely disintegrated exposing the inlay prolene mesh, despite the administration of Tazocin and later meropenem and clindamycin (Figure 3).

Further surgical interventions were stopped at this stage and vacuum assisted dressing were applied to manage this total wound break down. Infection with Mycoplasma and/or Ureaplasma was suspected due to the background of hypogammaglobulinemia and lack of response to previous antibiotics. Doxycycline was commenced after collecting samples for Mycoplasma/ Ureaplasma culture and PCR in viral transport medium. A non-specific 16S eubacterial PCR was also requested. Ureaplasma urealyticum was confirmed by both methods and azithromycin and moxifloxacin added to optimize anti-Ureaplasma activity and reduce any risk of resistance emerging. The CRP fell rapidly and wound healing improved dramatically allowing the abdominal wall and the pubic/vaginal area showing satisfactory healing around the rectus muscle flap.

This patient was eventually discharged from the hospital with well healing perineal region and abdominal wall. She was able to pass urine per urethram despite a long period of catheterization and supra pubic urine diversion during multiple surgical procedures. Her nutritional status also improved dramatically leading to weight gain. She has resumed most of her social activities, studies, etc. Her ongoing concerns are related to the appearance of the vaginal introitus and her ability to have normal sexual relationship in future.

This young woman was posing many challenges – in identification of the cause and the management of the soft tissue defect. Conventional wound cultures did not reveal any definite pathogens and many courses of antibiotics with activity against this colonizing flora did not help in reversing the trend of continuing infection, delayed tissue healing and ongoing catabolic state for this individual. The need for a MDT approach was identified very early on from the Plastic surgery care and was instrumental in managing this difficult condition.

DISCUSSION

The family Mycoplasmataceae consists of two genera: Mycoplasma and Ureaplasma. They are the smallest free living organisms and are classified as bacteria since their cultivation does not require cells. They are the only prokaryotes that lack a cell wall— a feature that is largely responsible for their biologic properties, including lack of a Gram stain reaction and non-susceptibility to many
commonly prescribed antimicrobial agents, including beta-lactams. They are commonly associated with mucosae, residing extracellularly in the respiratory and urogenital tracts and rarely penetrate the submucosa. *Ureaplasma* sp. (*U. urealyticum* and *U. parvum*) along with *Mycoplasma hominis*, make up part of the normal genital flora of both men and women and at least one of these organisms is found in about 70% of sexually active humans [1–3].

Occasionally *U. urealyticum* has been shown to have a causal role in a spectrum of urogenital diseases in women including urinary calculus formation, nonspecific urethritis, pyelonephritis, bacterial vaginoses, pelvic inflammatory disease, infertility, chorioamnionitis, spontaneous abortion, prematurity and intrauterine growth retardation. Extranatal infection is rare and often in the context of underlying immunosuppression [4] or a prosthetic device. Site of infection may include; arthritis, meningitis, brain abscess, sternal wound infection, mediastinitis and aortic graft infection and an abscess in a transplanted kidney (Jof Infection Ref) [5–8]. However, their role in localized genital disease is still unclear given their low pathogenic potential and high background prevalence.

Despite the above, an extensive review of literature, has shown that were no cases of ureaplasma causing such significant tissue loss in adults. It is known however, to cause sepsis in neonates [9]. Reports have also shown that mycoplasma hominis, another commensal of the urogenital tract, can cause extensive and sometimes even life-threatening, slow healing infections [10]. However, there have been no reports specifically for *Ureaplasma urealyticum*.

**Treatment**

Doxycycline is the drug of choice in the treatment of ureaplasma. Azithromycin can also be used as can the fluoroquinolones, especially moxifloxacin [11]. Resistance has been reported to all these agents. This risk of this should be reduced with combination treatment. Sensitivity testing can be technically difficult and was not undertaken in our case. The prompt response to doxycycline monotherapy indicates that the isolate was sensitive in our case and the subsequent addition of other
agents aimed to reduce risk of late relapse rather than hasten clinical response penicillins are ineffective as *U. urealyticum* does not have a cell wall [12, 13].

The learning points from this case are two-fold. Firstly, it is imperative to involve the microbiology and immunology specialists early in cases when there is an underlying immune defect that might render the patient susceptible to infection with microbes not detected by routine culture. It is important for practitioners to bear in mind that samples from open skin sites will always grow microbes, and while some may be potential pathogens and reported with sensitivities, the same microbes often just represent colonizing flora. Suspicion that microbes isolated on culture may be irrelevant should be heightened when antibiotics with in vitro activity confer no clinical benefit. Good communication and teamwork are essential to manage the patient as effectively as possible. It is important both for doctors, and for microbiologists to suspect mycoplasma when the clinical picture indicates infection, and the infectious agent cannot be isolated on standard culturing methods [14].

Secondly, surgical attempts to debride and reconstruct the defect would not have been successful till the source of the infection has been identified and adequately treated. When a healthy muscle flap such as rectus abdominis was not healing as expected, the index of suspicion was raised and further attempts of reconstruction were with held till the wound healing was restored by appropriate antibiotics. With a collaborative working pattern among the varied specialties—surgical and medical teams—the situation was brought under control.

**CONCLUSION**

While rare, *Ureaplasma* can have potentially devastating consequences in the immunocompromised and therefore needs to be tested for early in a case of soft tissue infection resistant to standard treatment.

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**Author Contributions**

Debbie Hunt – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Shomari D Dotun Lee Zack-Williams – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Janet Purcell – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

John Cheesbrough – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Jeyramam Srinivasan – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

**Conflict of Interest**

Authors declare no conflict of interest.

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