Title: *Mycoplasma hominis* parapharyngeal abscess following acute Epstein Barr virus infection in a previously immunocompetent adult

Running Title: *Mycoplasma hominis* parapharyngeal abscess

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Abstract

*Mycoplasma hominis* most frequently causes disease of the genitourinary tract.

Extragenital infections are uncommon, with almost all occurring in the immunosuppressed or those predisposed due to trauma or surgery. We present the case of a previously well man, who developed a *M. hominis* parapharyngeal abscess following acute Epstein Barr virus infection.
A previously healthy twenty-year-old man was referred to a tertiary care hospital for management of a parapharyngeal abscess complicating acute Epstein Barr virus (EBV) infection. Two weeks previously he was admitted to a rural hospital with dehydration, associated with a five-day history of sore throat, fever and progressive dysphagia. He was treated with intravenous fluids and benzylpenicillin 1.2g six hourly. Acute EBV infection was diagnosed on the basis of a positive monospot test, positive EBV VCA IgG and IgM, and negative EBNA IgG. Intravenous dexamethasone 8mg daily was commenced with improvement of the symptoms. The man was discharged from hospital after seven days. On the day of discharge he noted a painful papular rash, which evolved rapidly over the subsequent three days into pustules and vesicles, covering the forehead, nose and left cheek. He was readmitted to hospital and treated for three days with intravenous acyclovir 600mg three times daily and cephazolin 1g twice daily. Direct immunofluorescence of a skin scraping confirmed type 1 herpes simplex virus. During this time he complained of persistent dysphagia. A CT scan of the neck demonstrated a 3cm hypodense mass in the post styloid parapharyngeal space with mild peripheral contrast enhancement and fat stranding consistent with a parapharyngeal abscess. He was transferred to a tertiary care hospital, and treated with intravenous flucloxacillin 1g four times daily, ceftriaxone 1g twice daily and metronidazole 500mg twice daily. Serology for human immunodeficiency virus was negative. When a CT scan performed one week later (Figure 1) failed to demonstrate improvement, the collection was surgically drained.
The operative findings were of a 2ml collection with a large amount of associated soft tissue swelling. Gram stain of the abscess fluid showed moderate numbers of polymorphic cells, but no bacteria. After 72 hours incubation there was a heavy growth of small colonies on horse blood agar incubated aerobically in 5% CO$_2$ and on anaerobic agar. Gram-stain of the colonies failed to demonstrate any organisms, and a provisional diagnosis of *Mycoplasma sp.* was made. This was supported by electron microscopy (Figure 2). A 1282 base-pair fragment of the organism was amplified by PCR using eubacterial domain specific broad range PCR primers for the 16S rRNA gene. The sequence of the PCR product showed 100% homology to the 16S rRNA gene of *Mycoplasma hominis* (Genbank, accession number AF443616.3) by a BLAST search (www.ncbi.nlm.nih.gov/BLAST). Susceptibility testing was performed by Etest (AB Biodisk, Solna Sweden) on Mueller Hinton agar with sheep blood using a 0.5 McFarland inoculum, incubated anaerobically at 35°C and read at 48 hours. The isolate was regarded sensitive to clindamycin (MIC $<$0.016ug/ml) and ciprofloxacin (MIC 0.125ug/ml), but resistant to tetracycline (MIC $>$256ug/ml) and erythromycin (MIC $>$256ug/ml). The man was discharged two days post-surgery on oral amoxycillin-clavulanate 875/125mg twice daily. This was changed to clindamycin 450mg three times daily 2 days later, once *Mycoplasma sp.* was suspected. The dysphagia completely resolved within 2 weeks, and he remained asymptomatic four months later.
Mycoplasma hominis is a common commensal of the genitourinary tract. [13]

Colonisation of the oral or respiratory tracts by *M. hominis* occurs in only 3% of healthy adults [11, 15], although was found in 20% of children undergoing tonsillectomy for recurrent adenotonsillitis. [6] The first reported case of *M. hominis* infection was from a Bartholins abscess in 1937. [2] It has subsequently been implicated in causing pyelonephritis, pelvic inflammatory disease, post-partum fever, caesarean wound infection, prematurity and respiratory illness in the newborn. [13, 19] Less commonly, *M. hominis* causes extragenital infections. There have been 25 reported cases of *M. hominis* infection involving the lower respiratory tract [3-5, 7, 9, 10, 13, 14, 18] but none involving the upper respiratory tract or oral cavity. In all but two cases, there was a history of organ transplantation, trauma or tracheal intubation. Pharyngitis due to *M. hominis* has been induced experimentally following oropharyngeal and nasopharyngeal inoculation [16], however natural infection has not been reported.

Isolation of *Mycoplasma sp.* in the laboratory may be difficult, as the organism is slow growing, produces small translucent colonies that may be missed unless examined under a stereomicroscope, produces little turbidity in broth culture and may be overgrown by other bacteria. *Mycoplasma sp.* are also inhibited by sodium polyanethol sulfonate in blood culture media. Although this can be overcome by the addition of gelatin, automated detection systems fail to detect the growth of *Mycoplasma sp.* [8, 21] In addition, most *Mycoplasma sp.* do not grow on standard bacteriologic media, requiring specialised media (eg SP4, Shepard’s 10B broth), which may not be available in all
Mycoplasma sp. infections, particularly extragenital infections, are under-diagnosed. *M. hominis* is one species which may grow on routine bacteriologic media, such as blood agar [22] however this is not always reliable. *Mycoplasma sp.* are facultative anaerobes, growing best either anaerobically or in room air supplemented with 5-10% carbon dioxide. Growth of *M. hominis* usually appears within 2-4 days, typically appearing as pinpoint translucent colonies with a fried egg appearance. [22] The inability of these organisms to take up Gram stain allows for a presumptive diagnosis of *Mycoplasma/Ureaplasma sp.* Species identification may be suggested by the colony morphology, rate of growth, site of origin and biochemical properties. *M. hominis* is unable to produce acid from glucose but hydrolyses arginine. Molecular techniques, such as 16s rRNA gene sequencing, however may be a more accurate and practical method of species identification. There are no universally accepted standards for *Mycoplasma sp.* susceptibility testing or specific MIC breakpoints. *Mycoplasma sp.* are innately resistant to penicillins, cephalosporins, rifampicin, sulphonamides and trimethoprim. [12, 20] *M. hominis* is also resistant to macrolides, but sensitive to clindamycin. Tetracycline susceptibility is variable, with resistance associated with the tet M gene increasing in certain locations. [11, 13] Drainage of collections and debridement of tissue, in the absence of specific anti-mycoplasma antibiotics, has been associated with cure. [10, 13, 16]

This is the first reported case of upper respiratory tract infection with *M. hominis*, and is
particularly notable in that it occurred in a young adult with no prior history of immunosuppression, urinary tract manipulation, surgery or trauma. The *M. hominis* abscess complicated acute EBV pharyngitis, suggesting that the localised inflammation induced by the EBV infection may have facilitated secondary infection by *M. hominis*. The use of cell wall active antibiotics, by inhibiting normal flora, and the immunosuppressive effect of dexamethasone, may have also contributed to the infection. The reactivation of herpes simplex virus infection is consistent with a transient deficiency in cell-mediated immunity. We cannot entirely dismiss the possibility that other oral-type bacteria were contributing to the infection, being inhibited in culture by the antibiotics, The early institution of intravenous benzylpenicillin following onset of symptoms of EBV infection, and the absence of organisms seen on Gram stain of the abscess fluid despite moderate numbers of polymorphic cells, are against other bacteria being involved. It is also difficult to determine whether clinical response was due solely to surgical drainage of the collection or a combination of surgery and antibiotics.
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Figure 1: CT scan image of the neck approximately three weeks following the onset of the illness demonstrating a 3cm hypodense mass in the right post styloid parapharyngeal space with mild peripheral contrast enhancement and fat stranding consistent with a parapharyngeal abscess (arrow). There is deviation of the airway to the left.

Figure 2: Transmission electron micrograph of the cultured organism from solid media demonstrating multiple polymorphic bacteria lacking a true cell wall, typical of *Mycoplasma/Ureaplasma* species (arrows).
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Conflicts of Interest

The authors declare that they have no conflict of interest.