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Case Report

A case of *Ureaplasma parvum* meningitis in an adult after transphenoidal ablation of craniopharyngioma

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ABSTRACT

We report the case of a *Ureaplasma parvum* meningitis in an immunocompetent patient, 17 days after surgical ablation of a craniopharyngioma. Presence of *U. parvum* in the cerebrospinal fluid was assessed by 16S rDNA sequencing and *U. parvum* specific PCR. This article details a surprising complication in an adult of a transphenoidal surgery for ablation of a craniopharyngioma. This is the first case, to our knowledge, of *U. parvum* meningitis in an adult patient.

Introduction

Ureaplasma species, including human pathogens *Ureaplasma urealyticum* and *Ureaplasma parvum*, are small spherical-shaped bacteria, lacking cell-wall, colonizers of the genito-urinary tract (Waites and Bébéar, 2019). In adults, these bacteria are mostly responsible for uro-genital infections (Waites and Bébéar, 2019). Infections outside the genital tract are unusual in adults, and few cases have been reported, especially in immunocompromised patients: intrarenal abscesses (Eilers et al., 2007), aortic graft infections (Levi et al., 1995), mediastinitis, pleuritis and pericarditis (García-de-la-Fuente et al., 2008) or sternal wound infections (Walkty et al., 2009). Here, we report meningitis due to *U. parvum* in an adult after endoscopic endonasal transphenoidal surgery for ablation of a craniopharyngioma.

Case report

A 29-year-old man was admitted to our hospital for a second transphenoidal ablation of an intra- and supra-sellar craniopharyngioma, 16 months after the first surgery. No other specificity was noticed in his past medical history, except zoster and appendectomy 3 years before. Sixteen days after the surgery, the patient presented to the emergency ward for fever, severe headaches, photophobia and meningeal irritation, without alteration of consciousness. A cerebral computed tomography scan identified no abscess, no bleeding and no cerebral herniation. The blood cultures, collected on admission, remained sterile after 5 days. Meropenem (2 g iv every 8 h) and linezolid (600 mg iv twice a day) were introduced. Blood analysis revealed leucocytosis (13.57×10^9/L), and raised C-reactive protein (79 mg/L) with normal level of procalcitonin (0.04 ng/mL). Cerebral spinal fluid (CSF) analysis showed leucocytosis (1450/μL with 58% of neutrophils), elevated protein level (2.13 g/L), and reduced glucose (1.9 mmol/L). No microorganism was detected on Gram staining. Standard culture methods, carried out on sheep blood and chocolate agar plates in an air atmosphere with 5% CO_2 as well as on Brain-Heart enrichment broth, remained negative. Regarding the antibiotherapy, for de-escalation purposes, meropenem was replaced by ceftriaxone (2 g iv twice a day) at day 4. Severe headaches persisted and 5 days after his admission, the patient presented a recurrence of meningeal syndrome. A new CSF was collected, which showed 3240 nucleated cells/μL (43% of neutrophils), protein at 2.48 g/L and glucose at 0.7 mmol/L. Antibiotic treatment was modified for ceftriaxone (2 g iv twice a day), vancomycin (3 g iv per 24 h) and levofloxacin (500 mg iv twice a day). Again, bacteriological cultures remained sterile. Analysis by 16S rDNA sequencing was performed on this second

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CSF. The 842 bp sequencing product was compared with sequences deposited in the GenBank database and results revealed 99.8% identity with *U. parvum* isolates, and 98.7–99.8% identity with *U. urealyticum* isolates. This result was confirmed by PCR analysis for *U. urealyticum* and *U. parvum* by the French National Reference Center for bacterial STIs, which identified *U. parvum* in the CSF sample (Yi et al., 2005). Levofloxacin (1 g daily PO) was maintained for 3 weeks. The patient's condition continued favorably.

Discussion

We report here *U. parvum* meningitis after a transphenoidal surgery for ablation of a craniopharyngioma. Ureaplasmas are commensals of the genito-urinary tract, and mostly known as urogenital pathogens, associated with non-gonococcal urethritis and adverse pregnancy outcomes such as premature-rupture of membranes or preterm birth (Waites and Bébéar, 2019). They can also cause infections in neonates, such as bacteraemia, pneumonia or meningitis (Waites and Bébéar, 2019). Meningitis in newborns are usually associated with the transmission of *Ureaplasma* either *in utero* or vertically at birth (Waites and Bébéar, 2019). Extragenital infections are rare in adults, even if cases of sternal wound infections, mediastinitis, aortic graft infections, arthritis or renal abscesses have been reported, especially in immunocompromised patients (Waites and Bébéar, 2019). Recently, a study established a model of *Ureaplasma* meningitis using human brain microvascular endothelial cells originating from adult human brain cortex (Silwedel et al., 2018). A pro-inflammatory capacity of *Ureaplasma* was reported in these cells, enhancing the expression of atypical chemokine receptor 3 (AKCR3), suggesting a role in blood-brain barrier breakdown (Silwedel et al., 2018). This observation partly enlightened the pathophysiological mechanism of *Ureaplasma* meningitis. To our knowledge, only one *Ureaplasma* meningitis has been described, but with *U. urealyticum* species (Geissdörfer et al., 2008). The infection occurred a few weeks after kidney transplantation and organ rejection. Authors suggested that the hematoma, which developed after the explantation of the kidney graft, had been infected with *U. urealyticum*. Then, meningitis could have occurred by haematogenous spread (Geissdörfer et al., 2008). Here conversely, the infection appeared 16 days after a neurosurgery. This context seems atypical for the development of *Ureaplasma* infection, as no description of *Ureaplasma* meningitis has been made in this context. However, some post-operative *Ureaplasma* infections have already been depicted (Table 1). Indeed, a patient developed a sternal wound infection ten days after coronary artery bypass grafting (Walkty et al., 2009). A man also developed mediastinitis, pleuritis and pericarditis due to *Mycoplasma hominis* and *U. urealyticum* a few days after aortic valve and superior third ascending aorta replacement (García-de-la-Fuente et al., 2008). Another patient

Table 1
Characteristics of 11 adult patients with non uro-genital post-operative *Ureaplasma* infections.

Year	Age, sex	Underlying conditions	Surgery	Specimen	Clinical features	Species	Identification method	Treatment	Reference
2018	29, M	Craniopharyngioma	Ablation of craniopharyngioma	CSF	Meningitis	*U. parvum*	16S rDNA sequencing and PCR	Levofloxacin (1 g daily)	This study
2017	31, F	Polymyositis	Lung transplantation	Bronchoalveolar lavage fluid	Sepsis	*U. parvum*	PCR and culture	Azithromycin Doxycycline	Fernandez et al. (2017)
2013	20	Burkitt lymphoma	Mastoidectomy	Abscess fluid	Brain abscess	*U. urealyticum*	16S rDNA sequencing and culture	Doxycycline (400 mg daily) Clarithromycin (1 g daily)	Deetjen et al. (2014)
2010	41, M	*Staphylococcus epidermidis* endocarditis	Aortic valve replacement	Wound sample	Sternal wound infection	*U. urealyticum*	16S rDNA sequencing	Clarithromycin (1 g daily)	Lucke et al. (2010)
2009	66, M	Ischemic heart disease, hyperlipidemia, hypertension, type 2 diabetes	Three-vessel coronary artery by-pass grafting	Wound sample	Sternal wound infection	*U. parvum*	PCR	Ciprofloxacin (1 g daily)	Walkty et al. (2009)
2008	66, M	Hypertension, chronic obstructive pulmonary disease	Aortic valve and superior third ascending aorta replacement)	Wound sample, mediastinal exudate, pleural fluid, pericardial fluid	Mediastinitis, pleuritis, pericarditis	*M. hominis*, *U. urealyticum*	Culture and 16S rDNA sequencing	Doxycycline (500 mg daily) Clindamycin (500 mg daily)	García-de-la-Fuente et al. (2008)
2007	54, M	Non Hodgkin Lymphoma	Total hip prosthesis implantation and resection of abdominal aortic aneurysm	Aorta tissue and specimens from the hip	Arthritis and disseminated infection	*M. hominis*, *U. parvum*	In-house multiplex real-time PCR	Moxifloxacin	MacKenzie et al. (2010)
2007	38, M	Interstitial nephritis and terminal kidney insufficiency	Kidney transplantation	CSF	Meningitis	*U. urealyticum*	16S rDNA sequencing and culture	Doxycyline Moxifloxacin	Geissdörfer et al. (2008)
2006	19, F	Nephronophthisis	Kidney transplantation	Abscess fluid	Intrarenal abscesses	*U. urealyticum*	16S rDNA sequencing and culture	Levofloxacin	Eilers et al. (2007)
1995	64, M	None	Aortobiiliac graft for a ruptured infrarenal aortic aneurysm and bilateral transmetatarsal amputation	Graft	Fever	*U. urealyticum*	Culture	Erythromycin	Levi et al. (1995)
1995	63, M	Hypertension, type 2 diabetes, ischemic heart disease	Coronary bypass	Wound sample	Sternal wound infection	*U. urealyticum*	Culture	Clindamycin Gentamicin Doxycycline	Pigrau et al. (1995)

CSF: Cerebrospinal Fluid.

developed *U. urealyticum* sternal wound infection 13 days after bioprosthetic aortic valve replacement (Lucke et al., 2010). A 64-year old man underwent an *U. urealyticum* aortic graft infection two months after the operation of a ruptured infrarenal aortic aneurysm (Levi et al., 1995). For all these post-operative infections, a likely explanation could be ureaplasmal haematogenous spread following urinary catheterization. Here, this case should raise alarm about potential consequences of these urogenital commensals as a possible source of post-operative infections.

Invasive *Ureaplasma* infections in adults are often reported in immunocompromised hosts, especially with hypogammaglobulinemia (Arber et al., 2007; Cordtz and Jensen, 2006; Deetjen et al., 2014). Another meningitis due to *U. urealyticum* has been reported in immunosuppression context, with organ transplantation (Geissdörfer et al., 2008). An *U. urealyticum* brain abscess was reported in a patient treated for a Burkitt's lymphoma by several cycles of combination chemotherapy (Deetjen et al., 2014). Conversely, extragenital adult infections outside of immunosuppression context are rare. However, some *Ureaplasma* infections have been reported in immunocompetent adults: post-operative mediastinitis, pleuritis and pericarditis (García-de-la-Fuente et al., 2008), or some post-operative sternal wound infections (Walkty et al., 2009; Lucke et al., 2010) have been described out of any immunosuppression context. As in these descriptions, no immunodeficiency has been noticed in our case. Therefore, *Ureaplasma* infections should possibly be investigated, especially in a post-operative context, not only in immunocompromised hosts, but also in immunocompetent patients.

Ureaplasma infection was documented here by 16S rDNA sequencing, and no culture was performed. Such molecular methods are helpful in the diagnosis of post-operative *Ureaplasma* infections. Indeed, *Ureaplasma* culture requires specific and selective media such as Shepard medium (Waites and Bébéar, 2019). However, these tests are not currently performed on post-operative samples such as CSF. In our case, the diagnosis was made with molecular methods. Other *Ureaplasma* infections diagnosed in an unexpected way by 16S rDNA sequencing have been described: *U. urealyticum* in peri-operative samples for a sternal wound infection, *U. urealyticum* in post-mastoidectomy brain abscess, or *U. urealyticum* in CSF (Geissdörfer et al., 2008; Lucke et al., 2010; Deetjen et al., 2014). Here, 16S rDNA sequencing appeared as a reliable method for the detection of such fastidious, unexpected pathogens in post-operative meningitis.

This case reports a rare description of *U. parvum* meningitis after ablation of craniopharyngioma, in an immunocompetent patient. This suggests the importance of *Ureaplasma* diagnosis in post-operative context, and the usefulness of molecular methods for the diagnosis of such unexpected infections. Indeed, the paucity of Ureaplasma reported meningitis may be also due to the hurdle of *Ureaplasma* diagnosis in CSF samples. This case should alert the surgeons about such potential infections both in immunocompromised and also in immunocompetent patients in a post-operative context.

Conflict of Interest/Funding

None.

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