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***Mycoplasma hominis* deep wound infection after neuromuscular scoliosis surgery: the use of real-time polymerase chain reaction (PCR)**

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Abstract *Mycoplasma hominis* is a commensal of the genitourinary tract. It mostly causes infections to associated structures of this system; however, occasionally it is a pathogen in nongenitourinary tract infections. Since, *M. hominis* strains require special growth conditions and cannot be Gram stained, they may be missed or delay diagnosis. This report describes a deep wound infection caused by *M. hominis* after neuromuscular scoliosis surgery; *M. hominis* was recovered by real-time polymerase chain reaction (PCR). An awareness of the role of *M. hominis* as an extragenital pathogen in musculoskeletal infections, especially in neuromuscular scoliosis, being a high-risk group for postoperative wound infection, it is

necessary to identify this pathogen. Real-time PCR for postoperative deep wound infection, in patients with a history of genitourinary infections, decreases the delay in diagnosis and treatment. In these cases rapid real-time PCR on deep cultures should be considered.

Keywords *Mycoplasma hominis* · Wound infection · Neuromuscular scoliosis · PCR

Introduction

Deep wound infections complicating spinal surgery are sources of major morbidity in neuromuscular scoliotic patients. *Enterobacter*, *Enterococcus*, *Escherichia coli*, *Proteus* and *Staphylococci* account for the majority of postoperative spinal wound infections in these patients [28]. Increasingly, previously uncommon pathogens are being identified in surgical infections. These organisms may be difficult to identify and/or resistant to most of the broad-spectrum antibiotics used for preoperative prophylaxis and for the treatment of postoperative wound infections. Among these pathogens, *Mycoplasma hominis* has been recognized as a cause of postoperative wound infections [25, 27, 31]. *M. hominis* is a commensal

bacterium in humans and is distinguished phenotypically from other bacteria by the minute size and lack of a cell wall. As a result, *M. hominis* cannot be Gram stained and is resistant to penicillin and other antibiotics that interfere with the cell wall metabolism. In addition, it is a fastidious slow-growing organism, which may not be readily identified by using routine culture protocols. Early diagnosis, however, is of utmost importance for adequate institution of appropriate antimicrobial therapy.

To our knowledge, only two cases of postoperative spinal wound infections due to *M. hominis* have previously been reported [18]. We describe a case report of a *M. hominis* postoperative deep wound infection in a patient with a progressive myelomeningocele scoliosis

who underwent posterior scoliosis surgery with bone allograft. Real-time polymerase chain reaction (PCR) provided a fast and secure diagnosis, which prevented further complications.

Case presentation

An 11-year-old girl with a complete paraplegia at level L2–L3 caused by a myelomeningocele was admitted to our hospital for surgical correction of a progressive right convex scoliosis. Preoperative physical examination revealed a flexible right convex thoracic scoliosis with a left convex thoracolumbar curve. The unsupported sitting anteroposterior radiograph showed a right convex thoracic scoliosis of 55° and a left convex thoracolumbar curve of 42° with no pelvic obliquity. Her medical history revealed a shunted hydrocephalus with an Arnold Chiari type II malformation, chronic urinary tract infections, and an auto-augmentation of the bladder.

The patient was treated with single stage scoliosis correction involving posterior instrumentation (Xia™ spinal system, Stryker Spine, Cestas, France) from T3 to L5. The spondylodesis was completed by applying allograft bone chips (Netherlands Bone Bank Foundation, Leiden, The Netherlands) over the laminae in the thoracolumbar region. In addition, Collagraft® (Neu-coll, Campbell, CA, USA), a synthetic bone graft substitute composed of collagen and a composite mineral (hydroxyapatite and tricalcium phosphate), was applied posterolateral in the lumbosacral region.

Prophylactic antibiotics, cefazolin (cefalosporin, Ke-fzol®) 1,000 mg IV, were administered at the induction of anaesthesia, and as a second and third dose 8 and 16 h postoperatively, respectively [6]. Because of a chronic urinary tract infection including a positive culture with *E. coli*, cefradin (cefalosporin, Velosef®) 500 mg orally was continued for 9 days at 8-h intervals.

The postoperative course was uneventful. At day 8 the patient was discharged. At discharge the wound produced negligible clear fluid at the distal end without any signs of infection. However, at day 18 postoperatively, the patient developed fever (39°C) and was re-admitted to our centre. On physical examination, an enlarged distal wound dehiscence was seen with increased fluid production. Infection parameters showed an increased C-reactive protein (CRP) (120 mg/l; normal <10 mg/l) and white blood cell (WBC) count ($10.9 \text{ cells} \times 10^9/\text{l}$; normal $4\text{--}10 \text{ cells} \times 10^9/\text{l}$). A surgical intervention was performed including a thorough debridement of necrotic tissue and removal of the bone grafts. The instrumentation was left in place. According to the established guidelines, cultures were taken of various deep areas by fluid aspiration and from the applied bone graft [15, 28, 32]. After extensively irrigating with pulsatile lavage, the wound was closed

leaving gentamicin collagen fleeces (Septocoll®, Bio-med, Darmstadt, Germany) over the instrumentation. Adjuvant therapy with gentamicin (aminoglycoside, Garamycinl®) 210 mg IV and flucloxacillin (isoxazol-ylpenicillin, Floxapen®) 2,000 mg IV were initiated immediately after obtaining appropriate intraoperative cultures, and was continued postoperatively at 6-h intervals.

Intraoperative cultures from both the fluid aspiration and the bone graft yielded *Mycoplasma* after 4 days incubation. Real-time PCR on the peri-operative biopsy material was only positive for *Mycoplasma* and the species was identified by 16S DNA amplification as *M. hominis* (Fig. 1). Separately a Collagraft® sample of the same batch was tested for *Mycoplasma*, however, the culture as well as real-time PCR remained negative. Gentamicin and flucloxacillin were stopped, and doxycycline (tetracycline, Vibra-S®) 100 mg was administered orally at 12-h intervals and continued for 3 weeks. The patient was discharged 5 days after surgery.

Wound healing and temperature were monitored at regular intervals at the outpatient clinic. After 3 months, the infection parameters were normalized and the wound was healed (Fig. 2). Four years after surgery there were no signs of infection. Radiographs at final follow-up demonstrated no instrumentation failure and no loss of correction of the scoliotic deformity (Fig. 3).

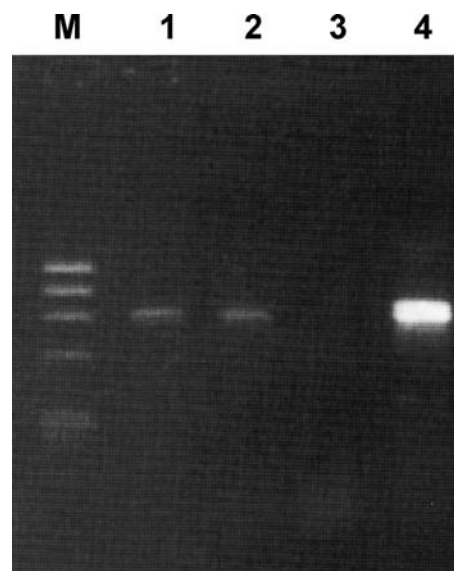


Fig. 1 Agarose gel analysis of duplo PCR amplification of *Mycoplasma* DNA. M Molecular weight marker, Lanes 1 and 2 positive PCR amplification of clinical sample, lane 3 negative control, lane 4 positive control. Subsequent sequencing results revealed *M. hominis*

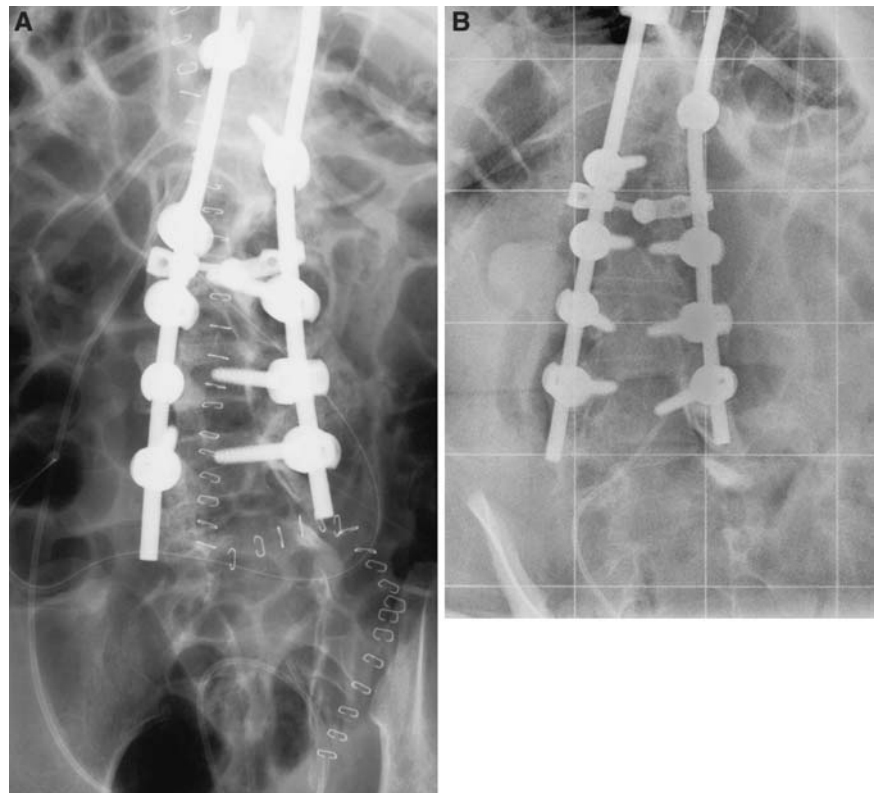


Fig. 2 Clinical appearance 3 months after surgical intervention for deep wound infection, located at the distal end of the wound

Discussion

Mycoplasma hominis is a commensal bacterium in humans. The organism is commonly associated with infections of the genitourinary tract, particularly in females. Rates of colonization in the urogenital tract range from 21 to 54% among women and from 4 to 13% among men [20]. Reports on *M. hominis* infections outside the genitourinary tract are scarce. Most of them are case reports describing extragenital infections, such as septic arthritis [17, 21], septicemia [11, 12], prosthetic valve endocarditis [3, 10], postoperative wound infections [25, 31], peritonitis [13], neonatal encephalitis [30], meningitis [7, 9], brain abscess [33], thrombophlebitis [27], and mediastinitis [19]. Extragenital infections are mainly related to patients with immunosuppression [3, 7, 9, 17, 19, 21, 25, 27, 30, 33]. Osteomyelitis caused by *M. hominis* is predominantly reported in combination with hypogammaglobulinemia [5, 14, 16, 24]. In an extensive overview of nongenitourinary *M. hominis* infections, Madoff and Hooper [18] described only two cases of postoperative deep wound infections caused by *M. hominis* after orthopedic surgery. Both cases concerned with deep wound infections after scoliosis surgery, one of them with a history of pyelonephritis.

Fig. 3 AP radiographs of the lumbar spine at the site of the deep wound infection immediately after surgical intervention and debridement of necrotic tissue including removal of the bone grafts (a) and at 4 years of follow-up (b)



Postoperative deep wound infections after scoliosis surgery are more common in neuromuscular patients than in patients with idiopathic scoliosis [28]. Risk factors associated with increased postoperative wound infection rates include a generalized decline in the immune status of neuromuscular patients, poor personal hygiene, and soiling of the wound. Sponseller et al. [28] reported 25 patients (12%) with a deep wound infection out of a series of 210 surgically treated patients with neuromuscular scoliosis in a 10-year retrospective study. From these 25 patients, 16 had a scoliosis related to myelomeningocele. Two risk factors were found to be significant: the degree of cognitive impairment and use of bone allograft. Furthermore, 52% of the infections were polymicrobial, which could point to contamination during or after surgery. However, the authors did not report any case of *M. hominis* wound infections in their series.

Antibiotics are used routinely to prevent postoperative wound infection in patients undergoing spinal implant procedures. Currently, first or second-generation cephalosporin (e.g. cefazolin) are recommended as prophylaxis [6]. Prophylactic cefazolin was also routinely given in our case. Since, cephalosporins act on the cell wall of organisms in a manner similar to the penicillins, postoperative wound infection by *M. hominis* was not prevented. Antimicrobial treatment for *M. hominis* include protein-synthesis inhibitors such as tetracycline (e.g. doxycycline) [26] and doxycycline was administered accordingly. The postoperative deep wound infection resolved favorably after surgical debridement and appropriate antimicrobial treatment with doxycycline.

The source of *M. hominis* deep wound infection in our case is unclear. *M. hominis* is commonly associated with infections of the genitourinary tract [20] and patients with meningomyelocele are known to have a high incidence of urinary tract infections [8]. In addition, it has been shown that children with myelomeningocele have a high incidence of urological complications after surgical treatment of scoliosis [4]. Possibly, in our case

the *M. hominis* could have been present in the urinary tract infection and spread hematogenous or by contamination, either at the time of surgery or secondarily through the wound. Other possible sources are the materials that were used during surgery. Obviously, the instrumentation and the applied Collagraft®, were sterilized. In addition, cultures and PCR on the same batch of the Collagraft® were negative. Bone allograft, used to induce and facilitate spinal fusion, could also have been the source of the infection. The fact that the bone allograft was positive for *M. hominis*, proved that it was infected before retrieval, however, not that it was the source of the infection itself. Bone allograft has not been reported as a carrier of *M. hominis* in the literature, however, it must be noted that the standard screening at the Netherlands Bone Bank Foundation does not include screening on *M. hominis*. Unfortunately, no other specimen of the donor could be retrieved for testing. As a result, haematogenous spread or contamination from a colonized urogenital tract or contamination by the bone allograft as source of the infection could not be excluded.

In the presented case, cultures taken during the reintervention proved to be positive for *Mycoplasma*. However, the diagnosis of a *Mycoplasma* infection was delayed due to the fastidious nature of mycoplasmas. To identify the *Mycoplasma* species, which in our case was cultured, 16S DNA amplification was used. Because isolation of *M. hominis* is difficult, time consuming, and not routinely done, a rapid specimen processing is required. Real-time PCR on deep cultures could provide a rapid alternative with a higher sensitivity and specificity than culture for the detection of *M. hominis* [1, 2].

In conclusion, *M. hominis* infections should be considered in postoperative deep wound infection after neuromuscular spinal surgery, especially in patients with genitourinary tract comorbidity. Since, *M. hominis* is not covered by routine prophylactic and therapeutic antibiotics, rapid real-time PCR is advised in these patients to initiate appropriate antibiotic treatment.

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