Nontuberculous Mycobacterial Infection in Patients with Neurosurgical Hardware: Two Cases and A Review of the Literature

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Abstract
Central nervous system infections with nontuberculous mycobacteria (NTM) are rare but have been increasing in frequency. A small fraction of these infections are related to surgical hardware, with approximately 20 cases reported. Patients typically present with an indolent course but can rapidly deteriorate. We report two novel cases of NTM infection in ventriculoperitoneal shunts, and review the literature on treatment options, challenges and outcomes in these patients. Clinicians should consider NTM when dealing with unusual hardware infections as it is an emerging infectious disease with high potential for morbidity and mortality.

Categories: Infectious Disease, Neurosurgery
Keywords: nontuberculous mycobacteria, cns infection, ventriculoperitoneal shunt, review, case report

Introduction
Nontuberculous mycobacteria (NTM) defined as mycobacterial species other than Mycobacterium tuberculosis complex or Mycobacterium leprae. These organisms are ubiquitous and are found in water, dust and soil. Reports of infection with the organisms have been increasing worldwide, involving the lungs, skin, soft tissue and central nervous system [1]. Central nervous system (CNS) infections with NTM are rare but have high mortality.

Cerebral spinal fluid (CSF) infection from neurosurgical hardware is relatively common with rates ranging from 5% to 15% [2]. Most infections develop from colonization of skin flora [2]. We report two cases of NTM infection in neurosurgical patients related to ventriculoperitoneal (VP) shunt hardware, and review the literature, common presentations and current treatment strategies for CNS NTM infections related to neurosurgical hardware.

Case Presentation
Patient no. 1
A 24-year-old man with a history of posterior fossa tumor requiring VP shunting presented with worsening headaches, confusion and weight loss over several months. He had a history of vague pain along the shunt site, chest and abdomen as well as swallowing difficulties over several weeks. The patient had a history of multiple shunt revisions, the most recent of which approximately 10 months prior to our evaluation when he had undergone a proximal shunt revision for an obstructed ventricular catheter.

Patient Course
A CT of the head and abdomen revealed ventricles stable in size and a pseudocyst around his distal catheter (Figure 1).
He was immediately taken to the operating room for complete shunt externalization and placement of an external ventricular drain (EVD). He was started on broad-spectrum antibiotics (vancomycin, cefepime and metronidazole) and underwent percutaneous drainage of the pseudocyst in his abdomen. Cultures from both the percutaneous drainage and CSF were positive for acid-fast bacilli (AFB) and presumed NTM. His antibiotics were switched to azithromycin, amikacin and cefoxitin by postadmission day 4. He continued to decompensate requiring multiple EVD replacements due to loculated ventriculitis. AFB was identified as Mycobacterium abscesses. Intrathecal (IT) amikacin was started on postadmission day 9. This was delayed due to the inability to clamp the EVD and safely administer IT amikacin. During the course of treatment, he had significant QTC interval prolongation which necessitated holding IV azithromycin and starting linezolid with readministration of azithromycin via nasogastric tube to minimize the risk of QTC prolongation by avoiding high peaks. He remained critically ill on a ventilator and required 12 EVD replacements in attempts to clear his loculated hydrocephalus. A brain MRI with contrast showed severe ventriculitis and cerebral inflammation (Figure 2).

On postadmission day 30, he was transitioned to comfort care. He passed away on postadmission day 36.

Patient no. 2

A 71-year-old woman with normal pressure hydrocephalus status post placement of VP shunt approximately two years prior presented with recurrent and prolonged abdominal discomfort. She had a history of multiple abdominal surgeries including gastric lap band complicated by gastric perforation as well as cholecystectomy a year after her shunt was initially placed.

Patient Course

She was initially admitted with cellulitis and an abscess around an epigastric port site which crossed the VP shunt catheter. She underwent irrigation and drainage of the abscess as well as externalization of the VP shunt at her clavicle. Her hardware was removed completely, and she underwent an endoscopic third ventriculostomy. Abdominal wound catheter site culture grew Mycobacterium fortuitum. CSF remained negative on serial testing. She was treated with imipenem and doxycycline for five weeks, and then switched to oral azithromycin and doxycycline which was continued for three months. Doxycycline was changed to oral sulfamethoxazole-trimethoprim with azithromycin for another 1.5 months. She discontinued antibiotics at approximately six months due to nausea and intolerance. She continued to do well without any sign of infection.

Discussion
NTM is a rare cause of infection in patients with neurosurgical hardware. We present two cases of serious hardware infection with NTM. These types of infections are rare, with only 19 cases reported (Table 1) [3-18]. Most cases involved infections with subgroups within the Mycobacterium fortuitum (48% of cases) and Mycobacterium abscessus (43% of cases). None of the patients were immunocompromised. The age range was 2 to 71 years, with a median age of 45 years. The majority of neurosurgical hardware involved was shunt catheters (70% of cases). Interestingly, 43% (9/21) of patients in the series and 64% (9/14) of patients with shunt hardware had symptoms of distal infection with peritonitis, pseudocyst or abscess formation. The majority of patients (86%; 18/21) had a positive CSF culture. The majority of device-related NTM infections are caused by Mycobacterium abscessus and Mycobacterium fortuitum, such as in our patients, whereas disseminated disease most commonly caused by Mycobacterium avium complex. Even with rapid hardware explantation and high-dose antibiotic therapy, mortality was 19% (4/21).

| Author/year        | Age/sex | Organism                | Hardware | + CSF | Treatment                                      | Prognosis           |
|--------------------|---------|-------------------------|----------|-------|-----------------------------------------------|---------------------|
| Current study      | 25M     | Mycobacterium abscessus | VP shunt, pseudocyst | Yes   | Azithromycin, amikacin, cefoxitin, IT amikacin | Death, 1 month      |
|                    | 71F     | Mycobacterium fortuitum | VP shunt, pseudocyst | No    | Imipenem, doxycycline (5 weeks), azithromycin, bacitracin | Stable, 8 months t/u |
| Zakrzewski et al., 2019 [3] | 26F | Mycobacterium fortuitum | LP shunt | Yes   | Amikacin, imipenem, moxifloxacin, TMP/SMX | Stable, 1 year t/u  |
| Xess et al., 2019 [4] | 14F | Mycobacterium fortuitum | VP shunt, pseudocyst | Yes   | Linezolid, ofloxacin, clofazimine, clarithromycin | Stable, 3 months    |
| Giovannenze et al., 2018 [5] | 46M | Mycobacterium abscessus | PEEK implant | No    | Amikacin, imipenem, linezolid (6 weeks) | Stable 12 months t/u |
| Moritz et al., 2017 [6] | 62M | Mycobacterium goodii | DBS electrode | No    | TMP/SMX, doxycycline (6 months) | Stable, 12 months t/u |
| Baidya et al., 2016 [7] | 59M | Mycobacterium abscessus | VP shunt | Yes   | Amikacin, clarithromycin, meropenem | Death, 1 month      |
| Levy et al., 2018 [8] | 67F | Mycobacterium abscessus | VP shunt, distal tubing in abdomen | Yes   | Meropenem, amikacin, azithromycin | Death, 1 month      |
| Montero et al., 2015 [9] | 30M | Mycobacterium abscessus | VP shunt, signs of peritonitis | Yes   | Amikacin, imipenem, azithromycin, IT amikacin | Stable, 4 years t/u  |
| Cadena et al., 2014 [10] | 14M | Mycobacterium fortuitum | VP shunt, abd pseudocyst | Yes   | Meropenem, TMP-SMX, moxifloxacin (9 months) | Stable, 2 years t/u  |
| Lee et al., 2012 [11] | 49M | Mycobacterium abscessus | Ommaya | Yes   | Amikacin, clarithromycin, imipenem, minocycline, minofloxacin | Stable, 1 year t/u  |
|                    | 19F     | Mycobacterium abscessus | EVD    | Yes   | Amikacin, clarithromycin, imipenem, levofloxacin, moxifloxacin | Stable, 1 year t/u  |
|                    | 28F     | Mycobacterium abscessus | Ommaya | Yes   | Amikacin, cefoxitin, clarithromycin, linezolid, meropenem, moxifloxacin, tigecycline, TMP/SMX | Stable, 2 years t/u  |
| Aliabadi et al., 2008 [12] | 60M | Mycobacterium fortuitum | Baclofen pump | Yes   | Amikacin, cipatro, clarithromycin, TMP/SMX (19 months) | Stable, 4 years t/u  |
| Uche et al., 2008 [13] | 60F | Mycobacterium goodii | VP shunt | Yes   | Imipenem, moxifloxacin | Stable, 3 months    |
| Viswananathan et al., 2004 [14] | 60F | Mycobacterium fortuitum | VP shunt, abdominal abscess | Yes   | Kanamycin, ciprofloxacin | Stable, 6 months    |
| Quinn et al., 2002 [15] | 12M | Mycobacterium fortuitum | VP shunt, peritonitis | Yes   | Amikacin, cefoxitin, clarithromycin, TMP/SMX | Stable, 14 months    |
TABLE 1: Overview of reported nontuberculous mycobacterial infections in patients with neurosurgical hardware

| Author(s)       | Age | Gender | Organism                  | Type of Hardware | Result | Treatment                                                                 |
|-----------------|-----|--------|---------------------------|------------------|--------|---------------------------------------------------------------------------|
| Midani et al.,  | 13F | M      | Mycobacterium fortuitum   | VP shunt, retroperitoneal abscess | Yes    | Amikacin, TMP-SMX (6 months)                                             |
| 1999 [16]       |     |        |                           |                  |        |                                                                            |
| Madaras-Kelly   | 45F | M      | Mycobacterium fortuitum   | IT pain pump     | Yes    | IV imipenem, ciprofloxacin, doxycycline, clarithromycin, 10 months of oral abx | Stable, 10 months |
| et al., 1999    |     |        |                           |                  |        |                                                                            |
| Flor et al.,    | 2M  | M      | Mycobacterium gordonae    | VP shunt, peritonitis | Yes    | Isoniazid, ethambutol, streptomycin                                      | Stable, unknown f/u |
| 1996 [18]       |     |        |                           |                  |        |                                                                            |
| Chan et al.,    | 60F | F      | Mycobacterium fortuitum   | VA shunt         | Yes    | IT amikacin, amikacin, ofloxacin                                        | Stable, 1 year f/u |
| 1991 [19]       |     |        |                           |                  |        |                                                                            |

TABLE 1: Overview of reported nontuberculous mycobacterial infections in patients with neurosurgical hardware

VP, ventriculoperitoneal; P, lumbar-peritoneal; PEEK, polyetheretherketone; DBS, deep brain stimulation; EVD, external ventricular drain; IT, intrathecal; TMP/SMX, trimethoprim-sulfamethoxazole; f/u, follow-up.

The gold standard for diagnosis is AFB culture, which should be ordered based on clinical suspicion as it is often not routinely done. Our microbiology lab uses matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) technology to identify mycobacteria but the sensitivities take weeks to result at a reference lab.

Immediate surgical hardware removal must be performed. Antibiotic regimens follow American Thoracic Society guidelines on pulmonary NTM [5]. Treatments include parenteral therapy with amikacin and cefoxitin or imipenem with at least one oral agent for at least six months. If there is good clinical response, parenteral regimens are typically discontinued in four to six weeks [20]. Given its rarity, there is no single regimen established for the treatment of CNS infection but three to four drugs should be given until sensitivities become available. Mycobacterium abscessus complex comprises a group of multidrug-resistant NTM, and new treatment regimens are urgently needed [1].

The blood-brain barrier remains a unique problem. IT antibiotics with aminoglycosides may allow theoretically higher doses, and is a safe treatment option; however, there are no efficacy studies to date. Three cases from Table 1 utilized IT amikacin, of which CSF was effectively cleared in two.

Conclusions
CNS hardware-related NTM infections are rare but are becoming more prevalent. Aggressive treatment should be pursued with immediate hardware removal, parenteral and oral antibiotics as well as IT antibiotics in severe cases. Clinicians should be aware of these organisms in patients with indolent and unusual presentations.

Additional Information
Disclosures
Human subjects: Consent was obtained by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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