CASE REPORT

Mycobacterium fortuitum as a cause of acute CNS infection in an immune-competent girl undergoing repeated VP shunt surgeries

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SUMMARY

We present the case of a 14-year-old immune-competent girl with ventriculoperitoneal shunt who was repeatedly hospitalised with meningeal signs despite repeated shunt revision surgeries. Eventually *Mycobacterium fortuitum* was isolated and the patient improved after specific treatment. *M. fortuitum* is a rapidly growing, non-tuberculous mycobacterium (NTM). NTMs are associated with postsurgical, post-trauma and device-related infections. Most of the present-day surgical equipment, catheters, prostheses and indwelling devices comprised silicone, stainless steel, polyvinyl chloride and polycarbonate, on which NTMs have the tendency to form biofilms. Central nervous system infection caused by NTM carries a high mortality rate (ranging from 35% to 70%), especially in immune-compromised patients. Indwelling device removal along with prolonged treatment with a combination regimen is recommended in such cases.

BACKGROUND

Ventriculoperitoneal (VP) shunt-associated central nervous system (CNS) infections are known iatrogenic infections; however, rapidly growing mycobacteria are neither mentioned as offending organisms nor any recommended treatment protocols given in the present Infectious Diseases Socciety of America (IDSA) guidelines for healthcare-associated ventriculitis and meningitis and management of VP infections in adults. Non-tuberculous mycobacterium (NTM) may be a rare cause of VP shunt-associated infections but should always be considered as a differential diagnosis. A high index of suspicion based on clinical presentation is essential to diagnose such rare pathogens.

CASE PRESENTATION

A 14-year-old girl presented with high-grade fever and altered sensorium in the emergency department of our institute. Her Glasgow Coma Scale score was 7 (eye response 3, verbal response 1, motor response 3). Her history revealed that she had an episode of headache and convulsions in February 2014, which was ascribed to posterior fossa glioma with bilateral ventricular dilation. Neurosurgical procedure involving excision of the glioma with bilateral VP shunt implant was considered but could not be performed due to proximity of the glioma to the vital areas of the brain. VP shunt was placed to relieve the ventricular obstruction. The patient was doing well following the procedure.

In October 2017, the patient complained of right lower abdominal pain, diagnosed as acute appendicitis, and appendicectomy was performed in a peripheral hospital. Immediate postoperative period was uneventful, but after 20 days she presented with convulsions and altered sensorium. CT scan of the brain revealed dilated ventricles for which revision shunt surgery was performed. However, she again started to have headache and convulsions in December 2017. CT revealed bilateral dilated ventricles for which repeat shunt surgery was performed. An ultrasound of the abdomen revealed cystic space-occupying lesion in the epigastrium engulfing the peritoneal ends of both shunts. An exploratory laparotomy was performed and 150 cc of fluid was drained around the shunt ends. Postoperatively the patient's fever persisted and she started having seizures. An ultrasound of the abdomen again revealed fluid collection at the peritoneal ends of the shunt (200 cc). Repeat aspirations were performed but the symptoms continued. A presumptive diagnosis of tuberculosis was made, and the patient started on antitubercular treatment. The patient was now referred to our institute. Cerebrospinal fluid was sent for Ziehl-Neelsen staining, Gene-Xpert MTB/RIF assay (Cepheid), mycobacterial culture (mycobacterial growth indicator tube [MGIT 960], Becton and Dickinson Diagnostics), fungal culture and bacterial culture (table 1).

DIFFERENTIAL DIAGNOSIS

- Bacterial meningitis (coagulase-negative *Staphylococcus*, *Staphylococcus aureus*, *Enterococcus* spp, *Streptococcus* spp and *Propionibacterium acnes*).
- Fungal meningitis (*Cryptococcus neoformans*).
- Tubercular meningitis.

TREATMENT

- VP shunt removal and excision of the mass associated with the peritoneal ends of the shunt was performed.
- Linezolid 10 mg/kg two times per day.
- Ofloxacin 20 mg/kg once a day.
- Clofazimine 5 mg/kg once a day.
- Clarithromycin 15 mg/kg two times per day.
- The patient has been on medication for the last 3 months.

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Table 1 Relevant investigations

Haematological parameters	Biochemical parameters	Microbiology	Radiology
Haemoglobin: 6.9 gm/l White cell count: 14×10^9/L Platelet count: 350×10^3/µL	*CSF chemistry* Glucose: 40 mg/dL. Protein: 50 mg/dL. RBC: 50 cells/mm^3. LFT within limits. KFT normal limits.	*Ziehl-Neelsen staining CSF*: long, slender acid-fast bacilli seen (3+). Gene-Xpert: negative. MGIT: growth seen in 5 days. TbcID: negative. LJ media: growth seen in 5 days. MacConkey's agar: growth seen in 5 days. Catalase: positive. Nitrate: positive. Niacin: negative. Identification: *Mycobacterium fortuitum*. MALDI-TOF: *M. fortuitum.* Bacterial culture: negative. Fungal culture: negative.	CT scan: bilateral ventriculomegaly. Abdominal ultrasound: cystic space-occupying lesion engulfing the peritoneal end of both shunts.

CSF, cerebrospinal fluid; LJ, Lowenstein-Jensen media; MALDI-TOF, matrix-assisted laser desorption and ionisation-time of flight; MGIT, mycobacterium growth indicator tube; LFT, liver function test ; KFT, kidney function test; TbcID,tuberculosis complex identification test.

Table 2 World reports of rapidly growing mycobacteria isolated from the central nervous system after insertion of VP shunt

Authors	Country	Age/Sex	Underlying disease	Mode of acquisition	*Mycobacterium* spp	Treatment	Duration of therapy	Outcome
Chan *et al*[6]	Hong Kong	60 years/female	Cerebral haemorrhage	VA shunt	*M. fortuitum*	Intravenous amikacin, ofloxacin	2.5 months	Alive
Midani and Rathore[5]	USA	13 years/female	Spina bifida	VP shunt	*M. fortuitum*	Intravenous amikacin, cotrimoxazole	7.5 months	Alive
Viswanathan *et al*[7]	India	60 years/male	Traumatic brain injury	Ventriculoarterial shunt	*M. fortuitum*	Intravenous kanamycin, ciprofloxacin	6 months	Alive
Cadena *et al*[4]	USA	14 years/male	Congenital hydrocephalus	VP shunt	*M. fortuitum*	Intravenous meropenem, oral cotrimoxazole, oral moxifloxacin		Alive
Baidya *et al*[3]	India	59 years/male	Tubercular meningitis/hydrocephalus	VP shunt	*M. abscessus*	Intravenous amikacin, clarithromycin, meropenem, shunt removal	1 week	Died
Montero *et al*[2]	USA	30 years/male	Hydrocephalus	VP shunt	*M. abscessus*	Intravenous azithromycin, imipenem, amikacin, shunt removal	2 years	Alive
Present case	India	14 years/female	Glioma/Hydrocephalus	VP shunt	*M. fortuitum*	Intravenous linezolid, ofloxacin, clofazimine, clarithromycin	Continuing	Alive

VA, ventriculoatrial; VP, ventriculoperitoneal.

OUTCOME AND FOLLOW-UP

- The patient was shifted out of intensive care unit.
- Improvement in Glasgow Coma Scale score: 11 (eye opening response 4, best verbal response 3, motor response 4).

DISCUSSION

Talati *et al*[1] reported 19 cases of primary and secondary CNS infections, with 14 cases caused by *Mycobacterium fortuitum*, with subacute meningitis as the most common clinical presentation and with symptom duration ranging from 3 days to 5 months. Other isolated reports of CNS infections after VP shunt insertions are summarised in table 2. Two cases of VP shunt infection have been reported due to *M. abscessus*: a 30-year-old man with hydrocephalus[2] and a 59-year-old man also with hydrocephalus[3] (our previous report). Postinsertion of VP shunt, the patients presented with meningeal signs and symptoms, and the duration of onset of symptoms varied from 8 days to months, and in two cases 16 and 30 years.[4–7] Other reports of cases of CNS infections due to *M. fortuitum* associated with intrathecal pump infections, epidural catheter, balloon mitral valvotomy, chronic suppurative otitis media, mastoiditis, sacral trauma and meningioma resection have been published.[8–10] A study conducted by Muthusami *et al*[11] observed that *M. fortuitum* was the offending organism in 20 patients who underwent surgical procedures and later on presented with recurrent abscesses or chronic discharging sinuses. It is presumed that the organism was introduced through contaminated instruments used during surgery or the use of unsterile water for final rinse of surgical equipment.

Our patient was asymptomatic for 3 years after the VP shunt procedure, but after undergoing appendicectomy the patient's condition worsened with meningeal signs, for which two consecutive surgeries of VP shunt revision and exploratory laparotomy were performed. It is possible that during one of these procedures the offending organism was introduced. The present case describes temporal association of CNS infection with emergency abdominal surgery or shunt revision surgery, hence suggests possible ways of inoculation of organism and VP shunt infection even after 3 years of insertion.

According to the IDSA guidelines for healthcare-associated ventriculitis and meningitis, there are four mechanisms through which CSF shunts can get infected: (1) colonisation of the shunt at the time of surgery, (2) retrograde infection from the distal end of the shunt (peritoneal end), (3) through the skin and (4) haematogenous seeding.[12]

NTMs form biofilms on the material used for manufacturing indwelling devices. Among the NTMs, *M. fortuitum* is a good biofilm assembler and is known to cover the entire surface of the stainless steel, polyvinyl chloride and polycarbonate with thin growth.[13 14] *M. fortuitum* has the propensity to colonise foreign bodies in devices such as central venous catheters, prostheses, heart valves and shunts. It is capable of forming biofilms

Table 3 Sterilisation procedures for instruments used in hospitals

Instruments used in hospitals	Sterilisation/High-level disinfection
► Ventriculoperitoneal shunt. ► Ventriculoarterial shunt. ► Dental implants.	► Removal of implants.
► Cardiac/Urinary catheters. ► Implants. ► Ultrasound probes in sterile body cavities.	► Initial manual cleaning with a detergent (soak for 30 min)/enzyme. ► Rinse with sterile water. ► Blow completely dry with compressed air. ► Repackage in sealed envelope. ► Sterilise with ethylene oxide. ► Aerate catheters for at least 14 days at room temperature.
► Laproscopes. ► Arthroscopes. ► Cystoscopes.	► Initial manual cleaning with detergent/enzyme. Or automated washer/disinfector containing peracetic acid as liquid disinfectant.Soak in 2% glutaraldehyde for 15–20 min. Or orthophthaldehyde (low vapour pressure). Or gas plasma technology.Use of *sterile water* for terminal rinsing.
► Gastrointestinal endoscopes. ► Bronchoscopes. ► Nasopharyngoscopes.	► Clean mechanically internal and external surfaces with detergent/enzymes. ► Soak in 2% glutaraldehyde for 15–20 min. Or orthophthaldehyde for 12 min. Or 2% glutaraldehyde at 25°C×45 min. Or ethylene oxide sterilisation.Rinse with sterile water. ► Dry and rinse the insertion tube and inner channels with alcohol and dry with forced air after disinfection.

on surfaces and air–liquid interface. Short-chain mycolic acid in the cell wall contributes to hydrophobic extracellular matrix, which provides a permeability barrier to antibiotics and disinfectants favouring the survival of NTM.

Indwelling devices are critical items that enter the sterile space and vascular system. Sterilisation of these critical items is recommended by treatment with different chemical sterilising agents, but most importantly meticulous cleaning must precede any high-level disinfection or sterilisation process. After high-level disinfection, items must be rinsed and flushed using sterile water to prevent contamination with organisms in tap water, such as NTM, *Legionella* or Gram-negative bacilli such as *Pseudomonas*, followed by an alcohol rinse and forced air-drying (table 3).[15]

Learning points

- Non-tuberculous mycobacterium (NTM), especially rapidly growing mycobacteria such as*Mycobacterium fortuitum*, has the ability to colonise and form biofilms on central venous catheters, prostheses, heart valves and shunts.
- NTMs can be introduced into the body during surgery or during procedures through improperly disinfected laparoscopes, arthroscopes and cystoscopes (source: use of tap water during final rinse of scopes).
- Sterilisation and high-level disinfection of critical items are essential.
- Removal of infected implants/indwelling devices in such cases is mandatory, along with a course of multidrug therapy, for a prolonged period of time.

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Contributors ABX: patient's medical history, details and follow up; sample processing, isolation of organism and identification; case report writing. KB: patient follow-up, reporting of the organism; planning of the study; analysis of the case and case report writing. US: conception and design of the study; analysis of the case, interpretation and case report writing. AP: medical history, follow-up of the patient.

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Reminder of important clinical lesson