CASE REPORT

Mycobacterium Chelonae Developing Multidrug Resistance

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SUMMARY

Mycobacterium chelonae is a rapidly growing mycobacterium which is known to respond well to standard antibiotic treatment regimen. There are no specific guidelines for treatment. Antibiotics are chosen based on the bacterial sensitivity. Here we present a 47-year-old man with hip replacement who developed bright red papular generalised skin lesions and bilateral hip abscess. On workup, it was confirmed that *M. chelonae* was the causative organism. He was given 8 weeks of antibiotics; however, there was worsening of the hip abscess on interval imaging. The progression was most likely due to *M. chelonae* developing antibiotic resistance. Physicians should be aware of the rising resistance of this organism, and guide antibiotic therapy based on bacterial sensitivity to yield better outcomes.

BACKGROUND

Mycobacterium chelonae is a rapidly growing non-tuberculous mycobacteria (RGM). *M. chelonae* is a non-chromogen and is delineated on the basis of microbiological, clinical and epidemiological characteristics: (1) *M. tuberculosis* complex, (2) *M. leprae*, (3) slowly growing non-tuberculous mycobacteria (*M. avium* complex, *M. kansasii*, *M. marinum*, *M. xenopi*, *M. simiae*, *M. malmoense* and *M. ulcerans*) and (4) RGM (*M. abscessus*, *M. fortuitum* and *M. chelonae*). *M. fortuitum* is the most common of the RGM encountered in clinical practice or in the clinical microbiology laboratory. While *M. fortuitum* causes human infection primarily by direct inoculation, *M. chelonae* causes human infection in immunosuppressed patients. RGM are resistant to all of the antituberculosis drugs (rifampin, ethambutol and isoniazid). It was first isolated by Freidmann in 1903 from lung tissues of sea turtles (*Chelona corticata*). *M. chelonae* is ubiquitous and has been found in soil, water and aquatic animals.¹ The prevalence is highest in southern states of Florida, Georgia, Louisiana and Texas.² It is a non-motile, non-spore-forming, Gram-positive, acid-fast, fast-growing *Bacillus* that grows at a temperature of 28°C–33°C, unlike other mycobacteria which grow at 35°C–37°C, forming colonies in subcultures in ~15 days.² It is known to infect skin and soft tissues causing cellulitis and abscess mainly in extremities; it can occur in the setting of sclerotherapy, liposuction,³ facelift,⁴ acupuncture tattoos^{5,6} and other cutaneous procedures.^{1,5–11} They can progress to form pustules, haemorrhagic

crusts or even an abscess. The sweet syndrome can be a presenting feature of *M. chelonae* infection. Skin lesions may also mimic lupus vasculitis.² Umbilicated papules and pustules involving the face and upper trunk may be present as well. Disseminated cutaneous infections are common in immunosuppressed patients.^{1,12–15} It also infects the eye¹¹ and causes pulmonary infections commonly in cystic fibrosis, bacteraemia, osteomyelitis, cervical lymphadenitis in children and intra-abdominal abscesses.^{9–11} It is also known to cause catheter-related infections, along with infection of implants and transplants.^{16,17}

CASE PRESENTATION

A 47-year-old man presented with diffuse skin lesions. He was a current smoker and a former heroin user on a methadone programme. His medical history was significant for severe bilateral avascular necrosis for which he underwent bilateral hip arthroplasty 10 years prior to this presentation. A few years following the procedure, he developed bright red papular skin lesions. The skin lesions initially appeared on the right thigh and slowly involved the trunk, abdomen and upper and lower extremities. Heat shock protein 65 (hsp65) PCR-restriction analysis (PRA) of the biopsy sample revealed *M. chelonae* as the causative organism. During the hospital stay, he complained of severe pain in the hips, so MRI of the hips was performed which showed bilateral hip abscesses. Arthrocentesis was performed, and the fluid was sent for PRA which also grew *M. chelonae*. Long-term antibiotic treatment was then recommended for the patient; however, he left against medical advice. A year later, he presented with worsening skin lesions and worsening hip pain; his review of systems was positive for severe low back pain and fatigue. His vitals were within normal limits. Physical examination showed umbilicated pustules on the trunk, abdomen (figure 1) and upper (figure 2) and lower extremities. He had reduced active and passive range of motion in bilateral hips. MRI of the hips redemonstrated the hip abscess. High-performance liquid chromatography (HPLC) of aspirate showed *M. chelonae*-abscess complex. PRA was performed at an outside facility which showed *M. chelonae*.

TREATMENT

He was started on intravenous amikacin 20 mg/kg/dose thrice a week, oral azithromycin 250 mg and

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Figure 1 Skin lesions on the abdomen.

intravenous tigecycline 50mg every 12hours. He completed 8 weeks of the antibiotic treatment. Pretreatment and post-treatment antibiotic sensitivity can be found in tables 1 and 2, respectively.

OUTCOME AND FOLLOW-UP

After 7 weeks of antibiotic treatment, MRI of the bilateral hips was performed which reported enlargement of the abscesses in comparison with prior MRI at presentation. Infectious disease specialty recommended bilateral hip explant since the patient had failed antibiotic treatment. However, the patient declined the procedure. He is currently on hospice care, receiving palliative care (pain management) and not receiving any medical treatment. His skin lesions have worsened and his mobility has decreased.

DISCUSSION

M. chelonae is known to cause disseminated cutaneous infections in immunosuppressed patients.¹ There are only a handful of cases with such presentation in immunocompetent patients.^{7 8 18} *M. chelonae* has a mycolic acid residue bilayer in the cell wall; thus, it is well-structured and relatively impermeable.¹⁹ The various other components of cell wall are glycolipid components, lipomannans or lipoarabinomannans and are known to be

Figure 2 Skin lesions on the forearm.

Table 1 Pretreatment antibiotic culture sensitivity

Antibiotic	Sensitivity
Amikacin	Sensitive
Linezolid	Sensitive
Clarithromycin	Sensitive
Tigecycline	Sensitive
Imipenem	Intermediate
Cefoxitin	Intermediate

different compared with other *Mycobacterium* species. A glutaraldehyde-resistant strain had reduced arabinogalactan making the cell wall increasingly hydrophobic, thus reducing the entry of glutaraldehyde molecules through the cell wall. Lipomannan component in its cell wall can cause secretion of interleukin 8 and tumour necrosis factor in THP-1 cell line. It is known to be dose dependent; however, it can be evaded by deacylation. Arabinan component of lipoarabinomannan prevents its recognition by lectins such as concanavalin A through steric hindrance with the binding sites.¹⁹ Its virulence and resistance are aided by the formation of biofilms as well. Various biofilm structures have been proposed. However, the greatest growth is provided by its stalk like a model with penetrates the microchannels which pierce the matrix.¹⁹ *mtrA* gene plays a great role in cross-species infection and invasion of cells at 37°C.⁸ It is essential to diagnose RGM species because of their resistance to antitubercular drugs and their variability in susceptibility to antibacterial drugs. Microscopy and culture are the mainstays in the identification of mycobacteria. Isolation of organism from blood, bone marrow or skin biopsy can be performed as well. Skin biopsy and cultures are mainly carried out in patients who are immunocompromised, who are not responding to antibiotics or in patients who had invasive procedures which led to infection. Mycobacterial species identification can be performed by commercial DNA probes, HPLC, molecular techniques such as PCR and restriction fragment length polymorphism.²⁰ HPLC cannot differentiate between *M. chelonae* and *M. abscess*.²⁰ Acridinium ester-labelled DNA probes specific for *M. chelonae* have not been approved yet. hsp65 PRA currently has been adopted widely for identification of Nontuberculous mycobacteria (NTM) which was the method used in this case. This system involves coupling of PCR of a heat shock protein and is followed by species-specific restriction fragment length identification.²¹ *M. chelonae* are mostly sensitive to macrolide and aminoglycosides; however, routine susceptibility testing should be performed with various antibiotics.²² Isolates of *M. chelonae* are susceptible or intermediate in susceptibility to tobramycin, clarithromycin, linezolid, imipenem, amikacin, clofazimine, doxycycline and ciprofloxacin.²² Tobramycin is supposedly more active than amikacin in vitro. Since *M. chelonae* isolates are uniformly resistant to cefoxitin, imipenem is preferred. Current literature supports combination therapy to avoid development of multidrug-resistant

Table 2 Post-treatment antibiotic culture sensitivity

Antibiotic	Sensitivity
Amikacin	Resistant
Linezolid	Sensitive
Clarithromycin	Resistant
Tigecycline	Intermediate
Imipenem	Intermediate
Cefoxitin	Resistant

strains and also recommends prolonged treatment period to prevent relapse.^{21 23–25} A minimum of 4 months of a combination drug therapy is necessary for serious skin, bone and soft tissue diseases. Six months of treatment is recommended for bone infections including osteomyelitis. Surgical removal of the infected foreign body or implanted device in conjunction with antibiotic therapy is recommended to optimise the therapeutic outcome.²⁶ Topical and oral agents are first line for corneal infections. However, surgery is the definitive mode of therapy.^{10 27} Patients who develop *M. chelonae* lung infections should be screened for cystic fibrosis; however, the optimal treatment is yet to be determined. During treatment of disseminated cutaneous *M. chelonae* infection, the emergence of resistance to clarithromycin was noted,²⁶ so it is used with a second agent such as linezolid²⁸ for a duration of 12 months with negative sputum culture.²² The GenoType Nontuberculous Mycobacteria - DR (NTM-DR) test is efficient in detecting mutations predictive of antimicrobial resistance in *M. avium* complex, *M. abscessus* and *M. chelonae*.²⁹ Interferon (IFN) gamma therapy has increased the success rate in the treatment of refractory disseminated *M. abscessus* infection; however, it has not been used in the management of *M. chelonae*.³⁰ Treatment has been known to increase the success rate.^{10 31} It has been hypothesised that a mutation in the IFN-gamma receptor gene increases susceptibility to IFN-gamma-based success on a case.^{6 32} In conclusion, there are no specific guidelines or randomised controlled trials comparing different therapeutic regimens for the treatment of *M. chelonae*. The decision on antibiotic treatment is based on identification of antimicrobial susceptibility through culture. Combination of antibiotics has been recommended to avoid resistance and to increase treatment success.

Learning points

- There are no specific guidelines or randomised controlled trials comparing different therapeutic regimens for treatment of *Mycobacterium chelonae*.
- The decision on antibiotic treatment is based on identification of antimicrobial susceptibility through culture.
- Combination of antibiotics has been recommended to avoid resistance and to increase treatment success.

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