

Nontuberculous Mycobacterial Infection After Cholecystectomy: A Case Series and Literature Review

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Abstract

Nontuberculous mycobacteria (NTM) are ubiquitous micro-organisms that can cause skin, soft tissue, and respiratory infections. Some of these bacteria are resistant to the commonly used disinfectants in hospitals and lead to wound infections after surgery. The diagnosis of NTM infections requires a high index of clinical suspicion as their clinical presentation often overlaps with other bacterial infections. Moreover, the isolation of NTM from clinical samples is difficult and time-consuming. Also, there is a lack of standardized treatment protocols for NTM infections. We report four cases of delayed wound infections after cholecystectomy probably due to NTM which were successfully treated by a combination of clarithromycin, ciprofloxacin, and amikacin.

Categories: Family/General Practice, General Surgery, Infectious Disease

Keywords: disinfection, cholecystectomy, clarithromycin, atypical mycobacteria, wound infection

Introduction

The two most common species of the genus *Mycobacterium* responsible for human infections are *Mycobacterium tuberculosis* and *Mycobacterium leprae*. The remaining species of *Mycobacterium* are collectively called nontuberculous mycobacteria (NTM). NTM are one of the environmental pathogens which have the potential to cause infection in humans. Currently, there are more than 125 recognized species of NTM, out of which at least 42 species are related to human diseases [1]. NTM have varying degrees of virulence. These are environmental organisms that get colonized in tap water, natural waters, and soil. They can contaminate solutions used as disinfectants in hospitals [2]. NTM most often lead to lung infections but they also cause skin/soft tissue, lymphatic, and disseminated infections. Immunocompromised individuals are at high risk of NTM infections [1]. The use of contaminated disinfectants for the sterilization of laparoscopic instruments can lead to outbreaks in hospitals [3,4]. NTM infections show a wide range of clinical symptoms such as infected wounds, pus discharging sinuses, swollen lymph nodes, nosocomial infections, and lung disease [5,6]. We report four cases of port site NTM infections in immunocompetent individuals following cholecystectomy performed at other hospitals and treated successfully by a combination of antibiotics.

Case Presentation

Case 1

A 36-year-old female underwent laparoscopic cholecystectomy (LC) for symptomatic gallstone disease at another hospital. After three weeks, there was a pus discharging sinus close to the epigastric port. The patient underwent multiple sessions of incision and drainage of the pus by the primary surgeon along with oral antibiotics. However, the wound failed to heal and the patient visited our outpatient department. On examination, there was a 2 x 2 cm non-healing tender epigastric wound with minimal pus discharge (Figure 1).

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FIGURE 1: A nodular lesion (white arrow) near the epigastric port with a thin layer of crust over it.

The wound swab was a Gram stain, Ziehl Neelsen (ZN) stain did not identify any organism, and the bacterial culture was sterile. Based on the clinical history and examination, NTM infection was suspected. The patient was not willing to NTM culture due to the high cost. Based on the previous studies [2,5], empirical treatment with oral ciprofloxacin (20mg/kg/d in two doses) and clarithromycin (20mg/kg/d in two doses) was initiated along with daily dressing and topical antibiotics. The patient responded to the treatment and there was a reduction in pus discharge. After one month of oral therapy, once daily amikacin injection (10mg/kg/d) was administered to accelerate wound healing for the next two months. Pus discharge stopped in three months and the wound healed completely in six months. Oral antibiotics were prescribed for an additional one month to prevent a recurrence. On the last follow-up at one year after starting oral antibiotics, the patient is symptom-free (Table 1).

	Case 1	Case 2	Case 3	Case 4
Age (years)	36 years	55 years	34 years	58 years
Sex	Female	Female	Female	Female
Surgery	Laparoscopic cholecystectomy	Laparoscopic cholecystectomy	Open cholecystectomy	Laparoscopic cholecystectomy
Duration of onset pus discharge from date of surgery	3 weeks	3 months	1 month	1 month
Treatment given	Clarithromycin, ciprofloxacin, and amikacin	Clarithromycin and ciprofloxacin	Clarithromycin and ciprofloxacin	Clarithromycin, ciprofloxacin, and amikacin
Time required for healing of wounds/nodules	6 months	3 months	4 months	10 months
Duration of therapy	7 months	4 months	6 months	10 months
Recurrence	No	No	No	The patient is currently on antibiotics

TABLE 1: Summary of the clinical course of the study patients.

Case 2

A 55-year-old female underwent LC for symptomatic cholelithiasis at another hospital. Post-operative recovery was uneventful. After three months of surgery, the patient noticed pus discharge from the epigastric port site. She was treated by the primary surgeon with an incision and drainage of the pus. However, the wound failed to heal and pus discharge continued. On clinical examination at the time of the first consultation, there was a small non-healing wound in the epigastric region with minimal pus discharge. A wound swab was sent for aerobic bacterial culture which was sterile. NTM infection was suspected. NTM culture was not performed due to high cost and low yield. The patient was started on oral clarithromycin and ciprofloxacin for two weeks. At the first follow-up after two weeks, pus discharge was reduced. Hence, the patient was advised to continue the same antibiotics. Gradually, the wound healed completely over a period of three months (Figure 2). However, to prevent the recurrence, the oral antibiotics were continued for an additional one month. On the last follow-up after three months of stopping antibiotics, there was no evidence of recurrence.



FIGURE 2: The healed epigastric wound (white arrow) after three months of antibiotic therapy.

Case 3

A 55-year-old female underwent open cholecystectomy for acute calculous cholecystitis at another hospital and had an uneventful post-operative recovery. After one month of surgery, she developed a small nodule near the scar site. Subsequently, the nodule increased in size and there was pus discharge from the nodule. On physical examination, there was a small nodule of 1 cm just below the open cholecystectomy scar with surrounding redness and mild tenderness on palpation. A wound swab could not be sent for culture and sensitivity as there was no discharging sinus. The patient was not willing to surgical excision. Due to high

clinical suspicion of NTM infection, the patient was started on oral clarithromycin and ciprofloxacin. Gradually over a period of two months, the wound healed but the nodule persisted for the next two months. The patient was continued on the same antibiotics for six months which resulted in the complete resolution of the nodule. There was no recurrence at two months after stopping the antibiotics (Table 1).

Case 4

A 58-year-old female underwent LC for chronic calculous cholecystitis with uneventful post-operative recovery. One month after surgery patient noticed redness at the epigastric port site followed by pus discharge. The patient received oral antibiotics and daily dressing from the primary surgeon. But the epigastric wound started increasing in size. So, incision and drainage were performed by the primary surgeon. However, the wound failed to heal with the appearance of new lesions with pus discharge in the adjoining area. The patient visited our outpatient department for a second opinion. On physical examination, there was a non-healing wound with active pus discharge in the epigastric region with multiple satellite nodules. Pus was sent for Gram stain, ZN stain, aerobic bacterial, and NTM culture and sensitivity. Both the stains failed to identify any organism and the cultures were sterile. However, due to the strong suspicion of NTM, oral clarithromycin and ciprofloxacin were started along with the daily dressing. There was a slow response to oral antibiotics with persistent discharge. Hence, amikacin (500mg/d) was started once a day intramuscularly. There was a significant reduction in the pus discharge from the epigastric wound and complete healing of the epigastric wound over the next four months (Figure 3). The satellite nodules also significantly reduced in size. Currently, at the last follow-up at 10 months after starting oral antibiotics, there is a significant reduction in the size of the wounds with no pus discharge. However, oral antibiotics will be continued till the complete healing of all the wounds.

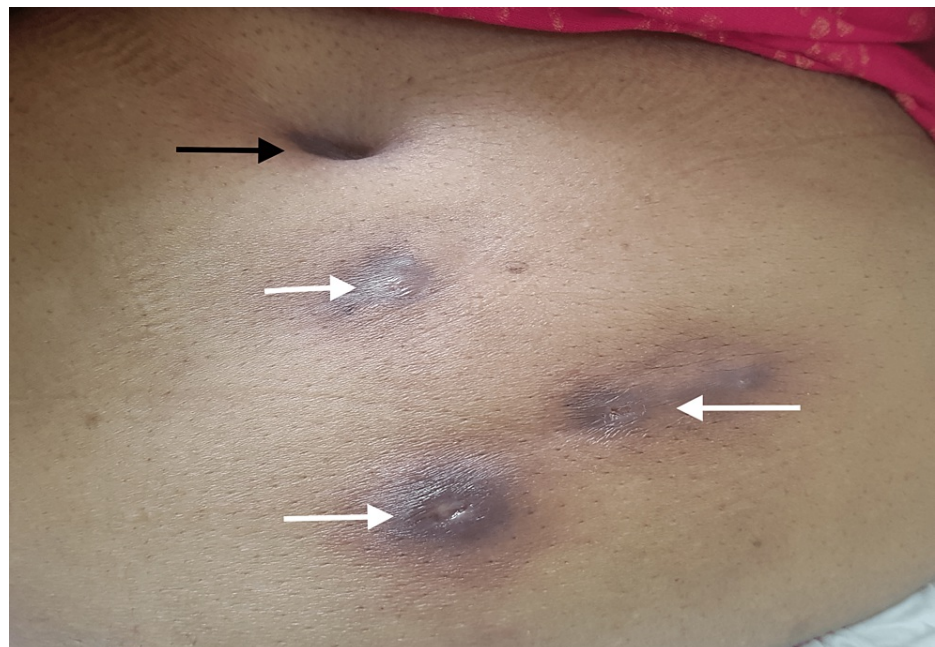


FIGURE 3: The healed depressed epigastric scar (black arrow) with the adjoining satellite nodules (white arrows) in the different stages of healing after 10 months of treatment with clarithromycin, ciprofloxacin, and amikacin.

Discussion

NTM infections are more frequent in immunocompromised patients. However, outbreaks of NTM-associated skin/soft tissue infections in immunocompetent patients have been reported after laparoscopic surgeries [3,4]. Port-site NTM infections occur due to direct or indirect contamination at the time of surgery by the laparoscopic or open instruments. Deficiencies in the sterilization process, reuse of disposable devices without appropriate sterilization, and disinfection of reusable laparoscopes with 2% glutaraldehyde as a substitute for sterilization are responsible for most outbreaks of NTM infections [2,5]. The most frequent NTM species responsible for skin/soft tissue infections are *M. abscessus*, *M. fortuitum*, *M. marinum*, *M. ulcerans*, and *M. chelonae* [1,3,4,6]. In most of the previously reported series, females are more commonly affected as seen in the present series [2,6]. The exact reason for female preponderance is not known but it may be because laparoscopic procedures such as cholecystectomy, hysterectomy, and myomectomy are more frequently performed in females.

The port-site NTM infections usually manifest as nodule formation, pus pockets, non-healing wounds, and subcutaneous nodules. Classically, the symptoms of NTM infection occur three to four weeks after the surgery, unlike wound infections due to other aerobic bacteria. Chaudhuri et al. have described five clinical stages of port-site NTM infections [2]. In the first stage, there is the formation of small tender nodules at or near the port sites (Figure 1) which gradually enlarge in size and later burst open to form discharging sinuses. In the last stage, multiple nodules appear in different areas as seen in one of our patients (Figure 3). As there is no pus discharge in the initial stages, diagnosis of NTM infection is often delayed. Moreover, most of the patients are being treated with incisions and drainage along with common antibiotics. Also, the routine pus cultures are often sterile. Hence, high clinical suspicion is required for timely diagnosis in order to reduce the morbidity and duration of therapy in such patients. The epigastric and umbilical ports are the most common port sites to be affected after laparoscopic cholecystectomy similar to that observed in this series [2].

The definitive diagnosis of NTM infections can be made by ZN staining of the pus, wound swab, or aspirate fluid. The sample should be simultaneously sent for NTM culture. The culture can be performed in solid egg-based (Lowenstein-Jensen) or agar-based or liquid medium (Middlebrook). The bacterial growth will appear in two to five days of incubation for rapid growers while it may take two to eight weeks for slow growers [5]. Pan-mycobacterial polymerase chain reaction (PCR) test can also be used for diagnosis. However, these tests are costly (USD 100-150 in India) and cannot be afforded by all patients. Also, these tests are often negative despite the high clinical suspicion of NTM infection as seen in the present series. Hence, treatment should be started in such patients without delay. If surgical excision of the port site is performed, then the tissue must be sent for histopathology and culture.

NTM are resistant to many antimicrobials. Hence, culture and sensitivity must be obtained whenever possible. There are no guidelines on the most appropriate empirical treatment for NTM as the drug sensitivity depends upon Mycobacterial species. However, some NTM species show limited sensitivity to the standard first-line antitubercular drugs [1,7]. The current American Thoracic Society and Infectious Diseases Society of America guidelines recommend combination therapy with two or more drugs from different classes based on drug sensitivity results to prevent the development of resistance [1]. The most commonly prescribed combination for port-site NTM infections in literature has been macrolide (clarithromycin or azithromycin) along with fluoroquinolone (ciprofloxacin, ofloxacin, or levofloxacin) or amikacin [1,2,5,6,8]. Most patients prefer to take oral drugs. Amikacin is administered by intravenous or intramuscular route. Hence, we used amikacin only when patients showed slow or no response to oral drugs for up to three months. Other drugs found to be effective in NTM infections are cefoxitin, imipenem, doxycycline, cotrimoxazole, and linezolid [1,5,8]. The minimum recommended duration of therapy is four months [1]. However, a longer duration of drug therapy may be required till the complete healing of the wounds followed by additional therapy for one to two months to prevent recurrence as seen in the present case. Surgical debridement may be required to obtain tissue for culture/histology and in cases not responding to drug therapy.

Conclusions

Port-site NTM infections are most commonly seen in females after laparoscopic procedures. NTM infections should be suspected if the wound complications occur three to four weeks after surgery. Pus or tissue sample should be sent for ZN staining, PCR, and NTM culture. The most effective empirical treatment has been a macrolide in combination with fluoroquinolone or amikacin for four to six months. Most of the port-site NTM infections can be prevented by appropriate sterilization of the laparoscopic instruments.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived 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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