IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 1 Ser. 14 (January. 2019), PP 09-13
www.iosrjournals.org

Role of Atypical Mycobacteria in Port Site Infection after Laproscopic Surgery.

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Abstract: *Atypical mycobacterial infections at the laparoscopic port site are a frequent problem encountered in patients undergoing laparoscopic surgery. In this study we concentrate on the clinical diagnosis, management and prevention of this problem. In this series we assess 21 patients presenting with port hole infections after laparoscopic surgery and were treated with oral clarithromycin. Eight patients who had persistent nodules were given injections of amikacin directly into the infection foci along with standard oral therapy. Most of the patients treated with standard oral therapy for 28 days showed recovery. The patients with persistent nodules 4 weeks after completion of therapy were treated with injections of amikacin directly into the nodule which lead to resolution of symptoms. For prevention of infection, proper sterilization and storage of instruments is recommended. Laparoscopic port hole infections is a preventable problem and can also be treated by nonsurgical method.*

Keywords: *Laparoscopy, Atypical mycobacteria, Aminoglycosides, Sterilization, Disinfection-port hole infection.*

Date of Submission: 11-01-2019 Date of acceptance: 27-01-2019

I. Introduction

Atypical mycobacteria have been known to colonize tap water, natural waters, and soil and thus can easily contaminate solutions and disinfectants used in hospital settings. These infections have thus been a source of significant morbidity for patients recovering from laparoscopic surgeries [1]. Erroneous sterilization of laparoscopic instruments is almost always responsible for such outbreaks and makes it a problem mainly affecting developing countries, such as India. Thus proper sterilization of such instruments is essential to prevent the occurrence of post laparoscopic wound infections with atypical mycobacteria [2].

There has been much controversy surrounding the proper line of treatment for port hole infections with atypical mycobacteria. These microorganisms show limited response to first line anti-tuberculosis drugs. Thus, the standard treatment consist of combinations of second line anti-tubercular drugs including macrolides such as clarithromycin, quinolones such as ciprofloxacin, tetracyclines such as doxycycline, and aminoglycosides such as amikacin. [3]. Once there is manifestation of clinical symptoms, the standard treatment consists of a 28 day regimen of oral clarithromycin and ciprofloxacin or amikacin. However, local administration of aminoglcyosides has been shown to be highly efficacious in the treatment of particularly stubborn nodules and sinuses that persist after completion of oral therapy [4]. Here we report a series of 19 cases of *M.chelonae-fortuitum* infections at the port site of laparoscopic surgeries. 17 patients responded to standard oral chemotherapy while 7 patients with serious infection were administered aminoglycoside injections directly into the wound sites for five days in addition to oral combination therapy with a clarithromycin and ciprofloxacin which resulted in the bursting of the nodules within 7 days with resolution of symptoms.

II. Materials and Methods

Case Series

21 patients (male = 5 and female = 16, median age = 40.5 years) who had all undergone laparoscopic cholecystectomy, presented with symptoms typical of port hole infections approximately 3–4 weeks after surgery. At the time of discharge none of the patients showed any signs of surgical wound infections. The first stage of infection was typified by rounded erythematous swellings at the port sites with mild to moderate pain along with tenderness. This was followed by the second stage of infection in which there was further swelling and caseating lesion with discharge of sterile pus. None of the patients complained of febrile illness and there were no other signs of systemic infection. Blood tests done on the patients revealed an increased CRP due to inflammation but both white blood cell and differential count were normal thus confirming absence of systemic infection. Unlike standard bacterial infection, the culture of the pus collected from the nodules was found to be negative for acid fast bacilli, gram positive and gram negative bacteria (Table 1).

Table 1

Table showing patient data (n = 21)

No of cases	n
Male	5
Female	16
Type of surgery	
Lap cholecystectomy	21
Lap appendicectomy	0
Diagnostic laparascopy	0
Treatment	
Aminoglycoside injection	7
Oral chemotherapy (28 days)	19
Oral chemotherapy (3 months)	2
Conservative	19
Operative	0

Treatment

All the 21 patients in our case series, 19 showed good response to oral combination therapy with clarithromycin and ciprofloxacin (500 mg each, twice daily) for a period of 28 days. 2 patients with stubborn infection were continued on this therapy for 3 months after which symptoms resolved. A total of 7 patients with persistent local nodules were administered 500 mg amikacin injections directly into the nodules daily for a period of five days. This resulted in the bursting of the nodules with resolution of symptoms within 7 days, without sinus formation.

III. Discussion

Infections at the port sites of laparoscopic surgery can be of two types. The first type occurs immediately within a week of surgery. It is caused by gram negative or positive bacteria derived from infection acquired during surgery from the infected gall bladder or from the skin or the surgical procedure itself and can be treated by common antibiotics and local wound dressing. The second type is caused by atypical mycobacteria which includes the group of mycobacterial species that is not part of the *M. tuberculosis* complex, and has an incubation period of 3 to 4 weeks and do not respond to common antibiotics [5]. This second type of infection is the focus of our study.

Contrary to earlier belief, different studies have established the role of these microorganisms in causing specific diseases in both humans and animals [6]. It has been shown that endospores of atypical mycobacteria, particularly *M. chelonae* and *M. fortuitum*, both of which belong to the group of rapidly growing mycobacteria, widely colonize soil, and water. This mycobacterial complex primarily presents itself as localized cutaneous infection 3–4 weeks after surgery. There is, however, very little evidence of disseminated disease following infection with this complex except in immunocompromised hosts [7]. These bacteria have an affinity for the dermis and the subcutaneous area and protective factors within the peritoneum destroy the mycobacteria and prevent infection within the peritoneal cavity. In theory, these microorganisms can be isolated through culture of affected tissue but takes a long time to grow and is difficult to culture [8].

After laparoscopic procedures, the infection starts at the 10 mm port sites such as the epigastric or umbilical ports after which it spreads sequentially to the other ports. It is very important to make clinical diagnosis based on the signs, since culture of the pus collected from the port sites is negative for mycobacterial culture and AFB staining. The only method to obtain microbiological evidence is through tissue culture from the wall of the cavity, which is very difficult to obtain and takes 3 weeks to isolate from culture leading to delayed treatment, which makes clinical diagnosis the best option. The presentation can be described in a few stages. The first stage is characterized by tender nodules which appear 4 weeks after the laparoscopic surgery and projects out in the vicinity of the port site. During the second stage, the nodules get bigger in size, become more tender and inflamed and eventually form a sinus discharging white pus. In the third stage of infection, there is a reduction of pain following discharge of pus with necroses of overlying skin. In the fourth stage, the area develops into a chronic sinus discharging white fluid followed by the fifth stage where the area darkens with necrosed skin. If left untreated, the infection can continue for months and multiple nodules appear in different areas.

Infections with atypical mycobacteria have been primarily reported after laparoscopic procedures [9, 10]. This is because, unlike open surgery, the instruments used here have a layer of insulation that restricts the

use of the autoclave in the sterilization process. Also, proper mechanical cleaning of the instruments is not done, which leaves the deposit of blood and charred tissue that collects in the joints of the instruments during surgery. Contaminated instruments deposit the endospores on to the subcutaneous tissue during the surgical process, which then germinate following which clinical symptoms appear after an incubation period of 3 to 4 weeks. The current practice in India is to immerse instruments in 2–2.5% glutaraldehyde solution for 20 minutes which achieves disinfection but not sterilization; in gist it does not kill the mycobacterial spores thus causing infections. Furthermore, the source of infection is often the boiled tap water used for cleansing of the instruments after immersion in glutaraldehyde. There are several options available for attaining proper sterilization of the laparoscopic instruments which is discussed as follows.

Instruments that enter sterile tissue, such as laparoscopes and hand instruments, are critical devices for which sterilization is an absolute requirement. High level disinfection that kills all microorganisms except bacterial endospores, is appropriate for only semi-critical devices, such as endoscopes which are used for GI endoscopy, and touch only the mucosa [11]. The use of disposable laparoscopic instruments is the gold standard for prevention of infection. However, they are hardly used in India, where reusable instruments are used for laparoscopic surgeries. Reusable instruments have multiple joints where dirt, grime and blood clots collect during surgery. Poor mechanical cleansing of these instruments allows bacteria to accumulate. Unlike other surgical instruments, laparoscopic instruments cannot be sterilized by autoclaving, as the high temperatures involved destroy the insulation on them. Thus, the standard sterilization procedure has been a 20 minute exposure to 2.0–2.5% glutaraldehyde. At the current exposure time, these solutions act as high level disinfectants and not sterilants thus allowing bacterial endospores to survive [12]. Current guidelines on infection control recommend a minimum exposure time of 8–12 hours to achieve the desired level of sporicidal activity of these germicides and the use of higher concentrations (3.4%) of glutaraldehyde disinfectants. Furthermore, proper disposal of glutaraldehyde based disinfectants is not followed. These chemical can be used for maximum of a 100 cycles or a period of 14 days (2.5% glutaraldehyde) or 28 days (3.4% glutaraldehyde), but often no count of cycles are kept in some hospitals and thus the chemicals often do not have the right potency to achieve the desired level of sterilization. Finally, the practice of rinsing the instruments with boiled tap water to rinse off the glutaraldehyde, further limits the efficacy of use of this system of sterilization as it causes the re-introduction of mycobacterial spores on the instruments that are then deposited at the ports [13]. Apart from tap water, the sharing of instruments between gynaecological and urological practice, has been observed as another source of infection. However, there is little scientific evidence for this as mycobacterial spores are generally not found within the body, although there is a possibility of acquiring spores on hysteroscopes during use in the non-sterile zone.

There is a further cause for concern in the use of glutaraldehyde based disinfectants in hospital settings. A recent study has shown that atypical mycobacteria such as *M. chelonae* and *M. smegmatis* are showing increased resistance to these chemicals due to defects in porin expression in the bacterial cell walls [14]. Porins are cell wall proteins found in *Mycobacteria* and have been known to create channels that allow the passage of small hydrophilic molecules, such as antibiotic drugs, through the highly hydrophobic mycobacterial cell wall [15]. Mutations leading to defects in porin expression prevent the delivery of antibiotics such as β-lactams, fluoroquinolones and chloramphenicols into the mycobacterial cell thus conferring drug resistance [16]. Thus, it has been suspected that increased exposure to glutaraldehyde based disinfectants will select for drug resistant atypical mycobacterial strains thus making treatment more difficult.

In light of the current evidence and guidelines on hospital infection control, it is recommended that several steps be utilized to ensure proper sterilization of laparoscopic instruments and other invasive surgical devices.

Firstly, the instruments should be thoroughly mechanically cleansed after each use, with complete dismantling of parts to ensure removal of all organic soil [17]. This is best achieved by using an ultrasonic technology which is available in some hospitals. , Secondly, it is necessary to limit glutaraldehyde disinfectants and replace it with ethylene oxide gas sterilization, as this has been shown to be highly effective in reducing atypical mycobacterial infections following laparoscopy [18]. When liquid chemical sterilants are used, higher concentrations (3.4%) must be used and the exposure time should be increased to 8–12 hours to activate sporicidal activity. Furthermore, the water used to rinse the instruments should be autoclaved to prevent recontamination with spores post sterilization. Conventional autoclave can be used for sterilization of the metallic cannula of the ports.

The use of advanced sterilization systems such as STERRAD, which uses gas plasma technology to kill spores at low temperatures, or the use of ethylene oxide gas is strongly recommended for sterilization of insulated laparoscopic instruments. Another option is to keep instruments for 24 hours in a formalin gas chamber. However, the instruments must be thoroughly cleansed and dried for this process to be effective, as the presence of dirt and moisture prevents the penetration of formalin gas, thus giving the same disastrous results. Finally, the use of disposable laparoscopic instruments, as is done in Western countries, is strongly advocated.

Once clinical diagnosis of atypical mycobacterial infection of laparoscopic port sites is made, treatment with a combination of second line anti-tuberculosis drugs is started. Of the different antimicrobial drugs used, aminoglycosides have been highly effective in the treatment of atypical mycobacterial infections of laparoscopic wounds. The course of antibiotic treatment for these organisms is often prolonged, with courses known to last for up to 6 months. In some cases surgical excision of the wound may be necessary followed by prolonged antimicrobial therapy [19]. However, this process of surgical wound debridement is generally not desired as it leaves a nasty wound and poses the risk of bacteria spreading into non-invaded zones. This method should only be reserved for critical cases, where there is gross tissue destruction with necrosis of skin, and not for all cases.

In our case series, five patients were treated by directly injecting amikacin into the nodule for a period of five days along with the standard oral drug regimen. The symptoms resolved within 7 days following completion of treatment with no accompanying sinus formation. Since, *M.chelonae-fortuitum* infections of laparoscopic wounds are local infections, this treatment protocol produces a local concentration of the aminoglycoside much higher than the MIC of atypical mycobacteria for aminoglycosides thus leading to faster resolution of symptoms. It was further observed that patients with lower BMI showed better response to therapy. However, a larger case series is needed to further establish the efficacy of this antimicrobial treatment.Go to:

IV. Conclusion

Port hole infection is a problem faced by laparoscopic surgeons in developing countries which is preventable through proper sterilization of instruments and early clinical diagnosis and treatment.

Presentation

- 3-4 weeks after surgery
- First stage: erythematous nodule in or around the port site with tenderness and mild to moderate pain
- Second stage: Caseating lesion with discharge of sterile pus
- No signs of systemic infection

Diagnosis

- Clinical diagnosis based on signs of presentation is the best option
- Microbiological evidence can be obtained from tissue culture of the wall of the cavity: takes time and delays treatment
- Culture of pus is usually negative for acid fast bacilli, gram positive and negative bacteria

Causative Organisms

- Atypical Mycobacteria:
  M. chelonae
  M. fortuitum

Prevention

- Good mechanical cleansing of instruments to remove organic soil
- Exposure to 2-2.5% glutaraldehyde for 8-12 hours to kill endospores and use of higher concentration of glutaraldehyde
- Use of autoclaved water to rinse off the glutaraldehyde
- Use of alternative systems of sterilization such as ETO gas, STERRADS etc.
- Use of formalin chamber
- Use of disposable laparoscopic instruments

Treatment

- Oral treatment with clarithromycin and ciprofloxacin (500mg each, twice daily) for 28 days to 3 months
- For persistent local nodules, direct injection of amikacin into the nodules for five days (500mg, twice daily).

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Dr Apurva Agarwal. "Role of Atypical Mycobacteria in Port Site Infection after Laproscopic Surgery." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 1, 2019, pp 09-13.