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ORIGINAL ARTICLE

Non tuberculous mycobacteria in surgical wounds- a rising cause of concern?

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Abstract

Introduction The non-tuberculous mycobacteria (NTM) have emerged as important opportunistic pathogens in the recent years. The NTM are rapid growing mycobacteria (RGM), which include *Mycobacterium fortuitum* and *M. chelonae* and are grouped as *M. fortuitum-chelonae* complex. Non-healing postoperative wound infections that do not respond to antibiotics used for pyogenic infections and having sterile routine aerobic cultures should raise a suspicion of NTM.

Patients and methods All patients with post operative wound infection over a five year period were included in the study. All wound infections were evaluated with wound culture and sensitivity and treated with appropriate antibiotics. All infections with underlying mesh were initially managed with dressings/debridement, long term antibiotics. Explantation of the mesh was to be used as a last resort.

Results We analyzed the records of patients with post operative wound infections who had wound cultures taken and found that 16 of our patients had initial sterile cultures. In all these cases, wound infection manifested itself as discharging sinuses between 2–3 weeks after surgery. Of these seven patients grew NTM on their repeat cultures. The commonest organism isolated was *M. fortuitum* (57%). The commonest antibiotic used for treatment was Tab Clarithromycin and the mean duration of treatment was 6 to 9 months. No patients required debridement or removal of mesh.

Discussion NTM infections in post operative wound though rare should be suspected in all post operative wound infections which occurs late, lack local and systemic signs of pyogenic infections and have sterile cultures. High index of suspicion for NTM infection will allow identification and treatment of these patients with long-term antimicrobial therapy alone without the need for surgical explantation of the mesh.

Keywords Non tubercular mycobacterium · Atypical mycobacterium · Post operative wound infection · SSI · Rapid growers · *M. fortuitum-chelonae* complex · *Mycobacterium fortuitum* · *Mycobacterium chelonae*

Introduction

Members of the genus *Mycobacterium* are ever expanding and presently stand at 95 species [1]. While tuberculosis, leprosy and paratuberculosis (Johne's disease) are specific diseases caused by *Mycobacterium tuberculosis*, *M. leprae* and *M. paratuberculosis*, respectively, other members are usually saprophytes but can be opportunistic pathogens, and are referred to as atypical mycobacteria or non-tuberculous mycobacteria (NTM) [1–5]. NTM are rapid growing mycobacteria (RGM), widely distributed in nature and

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have been isolated from natural water, tap water, soil, etc [4]. NTM have been isolated from various sites *viz*., cutaneous and soft tissue infections, after skin injury following inoculation or minor trauma and after surgical procedures including plastic surgery procedures like rhinoplasty and median sternotomy [6–11]. They are known to cause systemic infection in patients suffering from acquired immune deficiency syndromes (AIDS) and in other immunocompromized individuals while in immunocompetent hosts the infections are of localized nature such as cutaneous and soft tissue infections [12, 13].

There have been occasional case reports of post operative wound infection due to NTM like *M. fortuitum*, *M. chelonae*, *M. avium*, *M. scrofulaceum*, from different parts of India [14–18]. We analyzed our Center's data to report on the occurrence of non-tuberculous mycobacteria, in post-operative wounds after commonly performed general surgical procedures like mesh hernioplasty for inguinal hernia.

Material and methods

All patients with post operative surgical site infection (SSI) over a five year period from Jan 2004 to April 2009 were included in the study. All wound infections were evaluated with pus culture from wound and treated with appropriate antibiotics. A series of 16 samples of pus were collected from the wound without touching the margins of the wound as much as possible. The pus was sent for Mycobacterial and fungal culture and plated on LJ medium and SDA plain and with Chloramphenicol. NTM isolates when recovered from culture were subjected to antimycobacterial sensitivity. All infections with underlying mesh were initially managed with dressings/debridement and long term antibiotics; explantation of the mesh was reserved as a last resort.

Results

We analyzed the record of 230 patients with post operative surgical site infection over 05 years who had pus culture from wound taken and found that 16 of our patients had initial sterile cultures. All 16 patients had more or less similar clinical features: delayed onset of wound infection (10 days to 3 week after surgery), appearance of minimal erythema and oedema followed by breakdown of wound with suppuration and/or discharging sinuses (Fig. 1) absence of systemic symptoms/illness and lack of response to antibiotics used for pyogenic infections (Table 1). We suspected and asked for NTM and fungal cultures in these patients. Of the 16 pus/discharge samples examined microbiologically, 7 revealed growth of rapidly growing *Mycobacterium* spp. within 5–8 days of incubation i.e *M. fortuitum* in 04 cases and *M. chelonae* in 03 cases. All of these 7 samples revealed the presence of acid-fast bacilli

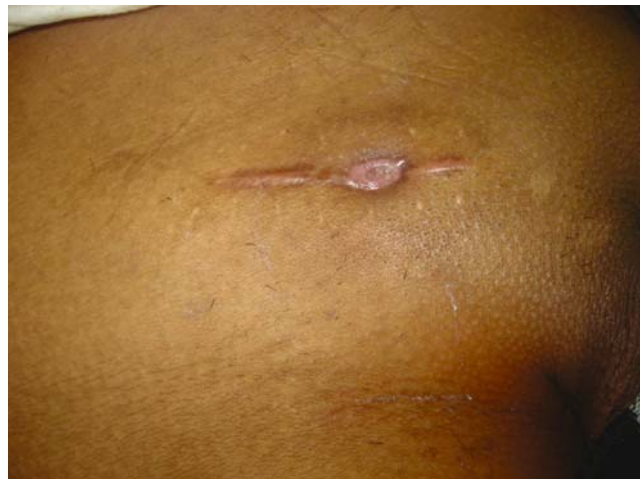

Fig. 1 A chronically discharging sinus on a inguinal hernia surgery scar. Note absence of any signs of inflammation

(AFB) on examination of smear prepared directly from specimens and also yielded the growth of *Mycobacterium* on LJ medium. All these isolates were rapidly growing, nonpigmented, and thus belonged to Runyon group IV. Further, they were positive to nitrate reduction, tolerant to NaCl, grew on MacConkey's agar and three and seven day Aryl sulphatase test positive. Based on the results of these key tests, all isolates were identified as *M. fortuitum-chelonae* complex. The remaining nine negative cases had received prior treatment with one or other fluoroquinolones which are known drugs for treatment of mycobacterial infections. Three of the 16 specimens also revealed growth of coagulase-negative staphylococci which were possibly skin commensals. No anaerobic bacteria or fungi could be isolated from any of the samples examined.

For the seven NTM isolates antibiotic sensitivity was noted for one of the following antimicrobials Ciprofloxacin, Clarithromycin, Tobramycin and Amikacin. The commonest antibiotics used for treatment by us were Clarithromycin 500mg bd and/or Ciprofloxacin 500mg bd. The duration of treatment was at least 6–9 months. The treatment continued till 3 months after cessation of discharge from surgical site. None of the patients required debridement or explantation of mesh. None of the patients developed any recurrent symptoms/discharging sinuses at an average follow up of 2 years.

Discussion

Though nontubercular mycobacteria infections cause little mortality they can cause morbidity, especially when they are not diagnosed and therefore not treated effectively. Investigators have defined 30 facultative saprophytes and entities that are acid-fast mycobacteria but do not cause tuberculosis or leprosy. These atypical mycobacteria or NTM exist in almost all habitats. Atypical mycobacteria though

Table 1 Distribution of surgical technique, isolated mycobacteria and treatment with final outcome

Case no	Procedure	Initial antibiotic	Repeat culture (when isolated post op)	Treatment (duration)	Final outcome (no recurrence at)
1	MH for IH	Cefotaxime (3)	*M. fortuitum* (at 3 weeks)	Clarithromycin (6)	4 years
2.	MH for IH	Cefotaxime (3)	*M. fortuitum* (at 4 weeks)	Clarithromycin (9)	3 years
3.	MH for IH	Cefotaxime (3)	*M. chelonae* (at 4 weeks)	Clarithromycin (9) Ciprofloxacin (9)	2 years
4.	MH for IH	Cefotaxime (3)	*M. fortuitum* (at 4 weeks)	Clarithromycin (6)	2 years
5.	MH for IH	Cefotaxime (3)	*M. chelonae* (at 4 weeks)	Clarithromycin (6)	2 years
6.	MH for IH	Cefotaxime (3)	*M. chelonae* (at 4 weeks)	Clarithromycin (9) Ciprofloxacin (9)	2 years
7.	Laparotomy & resection & anastomosis	Inj ciprofloxacin inj flagyl (3 days)	*M. fortuitum* (at 6 weeks)	Clarithromycin (6) Ciprofloxacin (6)	2 years

MH for IH- Mesh hernioplasty for inguinal hernia

Cefotaxime (3) : Inj cefotaxime 1gm X 3 doses

Clarithromycin (6): Tab clarithromycin 500 mg bd for 6 months

Clarithromycin (9): Tab clarithromycin 500 mg bd for 9months

Ciprofloxacin (6): Tab ciprofloxacin 500 mg bd for 6 months

recognized soon after the discovery of *M. tuberculosis* in the 19th century, were not deemed significant pathogens until the acquired immune deficiency syndrome (AIDS) epidemic brought forth the drastic increase in opportunistic infections.

In 1996, Horsburgh [19] noted clinically important nontuberculous mycobacteria, including *M kansasii*, *M scrofulaceum*, *M szulgai*, *M intracellulare*, *M abscessus*, *M chelonae*, *M fortuitum* and *Mycobacterium smegmatis*.

Four clinical syndromes are noted: pulmonary disease, lymphadenitis, skin or soft tissue disease, and disseminated disease in AIDS. All 4 clinical syndromes seem to be increasing in frequency, particularly in immunosuppressed hosts. Disease in patients due to NTM, who are immuno-competent usually consists of localized skin and soft tissue infections.

NTM are important human pathogens and have been reported from postsurgical wound infections in many countries including India, [4–6, 21–23]. Breast implant infection with *M. fortuitum* group was reported by Vinh et al. [20]; it required removal of the implant and a prolonged course of antibiotics. After the infection resolved, a new implant was successfully placed. Infections with NTM following trauma have also been reported.

In our study all sixteen cases with post operative surgical site infection (SSI) had a sterile aerobic and anaerobic cultures in spite of stopping antibiotics for a week or so prior to collection of the specimen. Typically, wound infections due to atypical mycobacteria do not occur as an immediate post-operative complication [21, 22]. There is apparent immediate post-operative healing and gradually over a variable period of time, the scar breaks down to a persistent non-healing superficial wound with discharging sinuses, as also seen in our study where all these patients had presented with discharge between 10 days to three weeks post op. Such wounds do not respond to antibiotics used for acute infection and persist for a prolonged period of time. The wounds were painless and patients were afebrile with no other systemic illness. A chronic non-healing wound may therefore present a confusing picture and in such cases mycobacterial infection should always be ruled out by appropriate investigations specially AFB culture. We had 7 cases which were culture positive for NTM. Rapid growing mycobacteria are usually resistant to rifampicin and isoniazid (INH) whereas these are sensitive to drugs like new generation macrolides, cephalosporins and sulphones. Clarithromycin and a combination of Amikacin and Doxycycline have been observed to be effective against *M. fortuitum-chelonei* infections [1]. In our study we used Tab Clarithromycin in the dosage of 500mg twice a day.

Water, soil, animals and marine life have been mentioned as sources of *M. fortuitum-chelonae* complex [4]. As the sample collection with stringent criteria is still not routinely followed in most parts of India and there is a tendency to ignore such isolates as contaminants, it would therefore be difficult to comment on the exact magnitude of the problem. As 80 per cent of the specimens yield AFB in culture as against 40 per cent positive in the ZN stained direct smears,

this indicates a possibility of missing a mycobacterial infection if only direct smears are taken for diagnosis [24]. In contrast, LJ medium culture method for rapidly growing mycobacterium (RGM) has been found to be a much more sensitive system as all direct smear positive specimens are also found to be positive in LJ medium [24]. In a hospital in Taiwan, 12 cockroaches (*Periplaneta americana*) were found to be infected with NTM [25]. Because cockroach infestation commonly occurs in the hospital environment, cockroaches might be implicated as a cause of hospital-acquired infections due to NTM. Further studies to reveal the sources of infection will also be helpful in the epidemiologic control of such infections. The optimal culture for NTM isolation should be performed at multiple temperatures 25°C, 37°C, and 42°C to ensure that the cultures grow all possible pathogens. The development of DNA fingerprinting technology, especially pulsed-field gel electrophoresis, has been suggested as a diagnostic tool. Polymerase chain reaction has been used to aid in diagnosing these conditions [26]. In our study we isolated *M. fortuitum* in 04 cases and *M. chelonae* in 03 cases.

Infections with NTM can be treated with a variety of antibiotics. Some infections can be resistant, and proper antimycobacterial sensitivity patterns must be obtained. The recommended treatment of NTM causing SSI is usually drugs from macrolide, fluoroquinolone and aminoglycoside groups. The specific drugs which have shown efficacy against NTM are Clarithromycin, Azithromycin, Ciprofloxacin, Levofloxacin, Amikacin and Tobramycin [27, 28]. One should start one of these medications on clinical suspicion and while awaiting culture reports and add on the specific antimicrobial based on the culture and sensitivity report. We treated our patients with Clarithromycin and / or Ciprofloxacin and treatment continued for 3 months after cessation of discharge from site. Most of our patients required 6 to 9 months of treatment.

Conclusion

Nontubercular mycobacteria are unique not only in their in vitro cultivation characteristics, but also in clinical presentations. Predominant presentation includes post operative, post injection or post trauma wound infections and catheter associated sepsis. Three species are responsible for the vast majority of diseases due to NTM: *M fortuitum*, *M chelonae* and *M abscessus*. Though suggestive clinical features, poor response to antibacterial treatment and repeated isolation of the organisms from the clinical specimens can help in establishing correct diagnosis, many such epidemic and sporadic cases in India probably remain unreported for a variety of reasons. Our findings suggest we need to have a high index of suspicion for NTM infections in our daily surgical practice. Appropriate treatment of these NTM infections will avoid the need for surgical explantation. of the mesh.

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