# The Mysterious, Threat We Will Confront Mycobacterium Chelonae

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## Abstract:

**Background:** Surgical wound infection is an internationally recognized complication which is expected to get cured in few days time. Lack of antibiotic policies added to the existing chaos in free market policies is expected to end up with mysterious resistant organisms soon in future.

**Objectives:** To report our experience with 52 key hole protracted surgical wound infections in 23 patients.

**Patients and methods:** Demographic data of patients who suffered post operative subcutaneous wound nodules following minimal access surgery, duration of the disease and its clinical manifestations as well as results of investigations were collected and analysed.

**Results:** Two males and 21 females, age range 27-65 (median 42) years had 32 key-hole wound nodules and 20 persistent discharging wounds that had appeared in an average but latent period of nine weeks (range three weeks to sixmonths after surgery). Only two cultures were positive for Mycobacterium chelonae.

**Conclusion:** Mycobacterium chelonae should be suspected in protracted surgical wounds and treated promptly with meticulous frequent dressings, wound excision and clarithromycin plus ceftazidime.

Key words: surgical wounds, subcutaneous, mycobacterium, catalase, resistant organisms.

Mycobacterium is one of the oldest microorganism and one of the best-studied bacteria. The genus mycobacterium compromises the acid-fast bacilli due to their impermeability by certain dyes and stains[1]. The name mycobacterium, meaning fungus-like bacterium, is derived from the mould like appearance of *M tuberculosis* when growing in liquid media. On the basis of growth rate, catalase and niacin production, and pigmentation in light or dark, mycobacteria are classified into members of the *Mycobacterium tuberculosis* complex (*M tuberculosis, M bovis, M africanum, M microtii*) and Mycobacterium Other Than Tuberculosis (MOTT). Gene probe technology now facilitates this distinction[1,2].

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**Objectives:** To report our experience with 52 keyhole protracted surgical wound infections in 23 patients.

**Patients and Methods:** Data of patients operated in three different health facilities from June 2007 through November 2007 who presented to us with post operative subcutaneous wound nodules, and/or delayed wound discharge 3 weeks or more after the primary surgery were interviewed for the symptoms related to the keyhole surgical wounds that forced these patients to come back for further advise and treatment. The physique of the patients, presence of keyhole wound discharge or nodule, consistency of the nodules, type of antibiotics used, results of wound swap culture, histopathology of wound excision, duration of the disease and response to antibiotics were collected and analysed.

**Results:**

From June 2007- November 2007, 23 patients came back looking for medical advice for problems that developed in the surgical

pore wounds of the operation they have had. They were two males and 21 females. Age range was 27-65 (median 42) years. Their average body weight was <35 except five ladies who had body mass index >35 each. 16 patients had laparoscopic cholecystectomy (LC) for chronic calcular cholecystitis. Five cases had LC for acute cholecystitis, one mucocele of gallbladder and one open surgery for acute appendicitis. LC was performed via four conventional pores. All patients were discharged 24 hours following surgery. All patients except that who had appendicectomy (medical doctor) reported in follow up one week after their discharge with nice healed wound, no pain, local tenderness or fever. All patients admitted that they had recovered nicely, were satisfied with the result of surgery and had resumed their routine life activities few days after discharge. The medical doctor resumed his work but called five weeks after surgery describing presence of painful nodules at the vicinity of his appendicectomy wound.

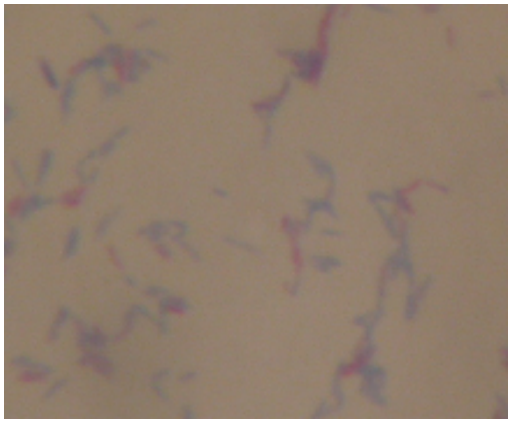
In an average of a few weeks to six months patients started to come back for medical advice because of low grade fever in five, generalized weakness, malaise with either painful nodules sour on touch in eight or protracted wound discharge in 10 patients. The average latent period was nine weeks (range three weeks to six months).

**Initial management:** Swabs were taken from five wounds for culture and sensitivity then wounds were kept on daily dressing with normal saline, diluted Betadine –saline solution (1:10 V/V) and/or ciprofloxacin tabs 500mg bid. 12 wounds healed in an average period of three weeks. Of these four wounds broke spontaneously with little discharge causing patient discomfort. All nodules regressed on treatment except 11 nodules in the five ladies with > 35 each were excised and sent for histopathology.

The result of 11 wound cultures was Klepsiella spp. in five, Staph. Aureus in three and no growth in another three wounds discharge cultures. Histopathology reported features of non-specific infection with non-casiating granuloma seen in five out of nine wound excisional biopsies. However, the result of the wound culture of the appendicectomy wound in Rhyadh, KSA revealed Mycobacterium chelonae and the minimum inhibitory test was done in Mayo's clinic showed that M chelonae is sensitive to clarithromycin and Amikacin. After this result two weeks and 2 months respectively wound cultures in Fedail Hospital Microbiology Laboratory, Khartoum, Sudan was successful in isolating M chelonae in culture colonies (Fig 1 & Fig 2a and b).

Fig 1: LJ culture showing cream-colour colonies of M chelonae

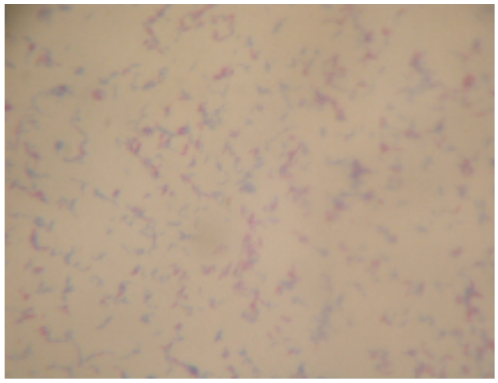

Fig 2 a: High power microscopic appearance of M chelonae with ZN stain



Literature was reviewed and accordingly treatment was instituted with Clarithromycin 500mg tablets bid in 16 patients for six weeks and Clarithromycin in the same dose combined with ceftazidime one gram i.v daily for three weeks in another seven patients. This later regimens combined with wound

excision resulted in complete cure. During wound excision the nodule was found in all cases of wound excision to be confined to the subcutaneous fat and adherent to the apponeurosis of the external oblique muscle.

Fig 2 b: Low power microscopic appearance of M chelonae with ZN stain



**Discussion:**

Increased attention to mycobacteriology in the first half of 20th century, led to recognition of a number of clinical mycobacterial isolates that had colonial characteristic different from *M tuberculosis*. In the 1950 Ernest Runyon and Timpe provided convincing evidence for the role of these mycobacteria in human disease and classified these mycobacteria based on growth rate and pigment production on solid media into four broad groups: Group I (photochromogenics), Group II (scotochromogenics), Group III (nonchromogenics) and Group IV (rapid growers)[2,3].

Mycobacterium Other Than Tuberculosis (MOTT) is free-living organisms with no significant person to person spread but is resistant to anti-tuberculous drugs. Medical important Runyon group IV (rapidly growing mycobacteria) includes *Mycobacterium fortuitum*, *M. chelonae/abscessus*, *M. mucogenicum* and M. *smegmatis* groups[2,3]. *M fortuitum* and *M chelonae* are major pathogen in the latter group. They were recovered readily from soil, dust and water. They have been isolated from tap water, municipal water supplies, and moist area in the hospital, reagents and wash solutions used in the hospitals etc. The source of surgical contamination has often been obscure[4].

Advances in the knowledge of genetics, cell structure and phenotypic properties of old and newly discovered strains of mycobacteria have advanced the knowledge beyond the neat packing of species under classic Runyon system of classification[5]. Woods and Washington have suggested a clinically oriented classification of mycobacteria. Nevertheless, the traditionally trained mycobacteriologist will continue classifying MOTT into four Runyon group[5].

*M chelonae* is one of the group of the rapidly growing mycobacteria classified as Runyon Group IV that can cause various clinical syndromes, including lung disease, local cutaneous disease, osteomyelitis, joint infections, and ocular disease such as; keratitis or corneal ulcers. With the exception of lung disease, these syndromes commonly develop after trauma. *M chelonae* is a rare cause of isolated lymphadenitis and endocarditis. Disseminated disease, usually with disseminated skin and soft tissue lesions, occurs almost exclusively in cases suffering from immuno-suppression, especially AIDS[2]. Soft-tissue infections caused by *M. chelonae* typically manifest initially as slightly tender nodules with scanty discharge and minimal surrounding cellulites; systemic manifestations often are absent. Therefore, the clinical presentation in our patients is in keeping with that described in the literature. The indolent course typical of these infections, together with a low index of suspicion and failure to request or perform the appropriate diagnostic tests (e.g., acid-fast staining), can make timely diagnosis of *M. chelonae* infections and treatment difficult[9]. This explains why we were able to suspect and isolate *M chelonae* very late after we got the diagnosis from Ryiadh, KSA. *M chelonae* is an extremely rare cause of infection among humans and is difficult to treat. This is why we opted to excise all wounds that did not respond adequately to treatment and regular dressings.

Although *M. chelonae* was identified as the cause of approximately 10% of nosocomial outbreaks attributed to rapidly growing mycobacteria[4, 5]. This probably explains our first reported epidemic in Sudan. To our best of knowledge this is the first time for *M. chelonae* to be isolated and reported in Sudan. *M. chelonae,* resist the activity of disinfectants and biocides such as organomercurials, chlorine, and alkaline glutaraldehyde. Reports from India[10] showed an outbreak associated with the water used to rinse endoscopes for laparoscopic surgery, resulting in 35 patients related infection caused by *M chelonae*. Up-to-date no human-to-human transmission has been documented[5, 10]. Data from US Centers for Disease Control and Prevention (CDC) in between 1993-1996 showed, 0.93-2.64 cases per million populations for *M chelonae* related infection[11].

*M chelonae* can be suspected if growth of an acid-fast organism is observed after two to four days of incubation. The colonies of this bacterium appear smooth and hemispherical, usually with a butyrous or waxy consistency. Colonies are typically nonchromogenic but may appear off-white or faintly cream-color. To separate *M fortiutum* and *M chelonae*, *M chelonae* does not reduce nitrates, incapable assimilating iron from ferric ammonium citrate, resistant to ciprofloxacin and pipemidic acid, but sensitive to polymyxin B; *M fortiutum* has the opposite reactions[1,2,12]. Adequate and proper specimen collection together with notifying the microbiologist will enhance isolation and identification of the microorganism. In cases of cutaneous infection biopsy or aspiration materials are better than swab. Erythrocyte sedimentation rate or C-reactive protein may be helpful to differentiate colonizer and pathogen, but these are nonspecific tests and the results must be carefully evaluated within the clinical context of the patient[9,13]. Histological findings may reveal presence of acute inflammatory cells, microabscesses, granulomatous inflammation, or granulomas (with or without caseation). These findings may be mixed. However, special tissue stains for AFB may reveal organisms[2,14].

These organisms are difficult to treat once true infection is diagnosed and documented. This explains why the disease was took long time to be eradicated in our patients. Most information regarding treatment of *M chelonae* infection is derived from case reviews and expert opinion. Definitive statements regarding diagnosis and treatment are often lacking[9]. Tobramycin, clarithromycin, imipenem, and amikacin are drugs of choice for treatment infections related to the *M chelonae*. The treatment of localized infections due to *M. chelonae* is currently managed by using the newer macrolide clarithromycin as the cornerstone of therapy. However, more serious disease should be treated, for at least the first two weeks, with clarithromycin in combination with one of the injectable agents. This is why we opted to add ceftazideme to clarithromycin in our patients. For serious disseminated infections involving *M. chelonae,* the injectable agents as tobramycin plus imipenem have been used for the first two to six weeks in combination with clarithromycin to avoid or minimize the development of drug resistance to the macrolide. Relapses may occur especially with those immunocompromised cases. We didn't use tobramycin for fear of drug toxicity particularly in prolonged usage of drugs. On the other hand, newer oral agents such as gatifloxacin and/or linezolid are promising for use in combination with clarithromycin. However, there is little experience with these newer agents

The lesson of this paper is that postoperative patients who show poor healing of the surgical site or indwelling infection not responsive to empiric antibiotics and regular dressings should have careful screening for *M. chelonae.* Also, patients with erythema, tenderness, and chronic discharge of the surgical incision that does not result in positive routine cultures should be cultured specifically for *M. chelonae* and wound tissues should be sent for histopathological

investigation. Performed Zeihl-Neelsen (ZN) stain may show acid fast bacilli. Materials should be cultured on Lowenstein-Jensen (LJ) medium and incubated at 35°C. Culture on LJ medium showed non pigmented colonies after 4th day of incubation, which is presumptively identified as a rapidly growing non-tuberculosis mycobacterium as shown in Fig 1. For further identification, various biochemical tests can be done to identify the species of rapid Growing Mycobacterium. The definite identification of the organism as *M chelonae* was based on various test such as; growth at 25°C and 37°C not at 42° C, arylsulphatase, urease, 68°C catalase test, negative nitrate reduction test and tolerance to 5% NaCl.

To our knowledge this is first report on *M Chelonae* related wound infection reported in Sudan. To identify possible source of microorganism environmental, disinfectant and water sampling should be carried out. We recommend that physician to think possibility of *M chelonae* related wound infection especially when they face poor healing chronic surgical site which is not responding to broad spectrum of antibiotics.

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