Blood Infection by Mycobacterium Chelonae in a Uremic Diabetes Patient

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This regards a rare case of blood infection with a nontuberculous mycobacterium, Mycobacterium chelonae. A 50-year-old woman with uremic diabetes presented symptoms of aversion to cold, trembling and high fever at two months after an implant surgery of arteriovenous fistula. Multiple blood cultures all indicated positive results of bacterial infections. After subculture, a Kinyoun-stained smear revealed that the infected bacteria are acid-fast mycobacteria. Results of polymerase chain reaction coupled restriction fragment length polymorphism analysis concluded the M. chelonae infection. Since M. chelonae is fast growing and usually has multiple drug resistance, laboratories in hospitals should establish and provide rapid diagnostic methods for such nontuberculous mycobacterium infections.

Key words: Mycobacterium chelonae, Blood Infection, uremic diabetes patient, PCR-RFLP

Introduction

Mycobacterium chelonae is a fast growing species of saprogenic mycobacterium widely seen in water and soil [1, 2]. It is also one of the most common opportunistic infectious pathogens within hospitals and has the potential to cause various disease symptoms clinically [3-7]. Cuticles and soft tissues are the most likely locations to identify M. chelonae infections but rare blood infection reported [8, 9]. Furthermore, the most common NTM isolated in Shanghai were M. chelonae (26.7%), followed by M. fortuitum (15.4%) and M. terrae (6.9%) [10]. In Taiwan, an increase tendency to isolate M. chelonae too, but after M. avium-intracellulare complex and M. abscessus [11]. Since this bacterium possesses drug resistance against many antibiotics, medication treatments should be prescribed according to the result of the drug sensitivity test [12]. These bacteremia, therefore, need to be timely and accurately diagnosed to avoid prolongation of diseases and permanent damages to patients.

Case report

A 50-year-old woman, diagnosed with diabetes 10 years ago, showed some diabetic mellitus (DM) complications in the past few years, including DM-induced cardiovascular disorder, DM retinopathy and nephropathy. She was treated and monitored in the nephrology department at Chang Gung Memorial Hospital. Her blood creatinine reached 2.4mg/dl at the time with noticeable albuminuria. Her renal function was deteriorated during the course of monitoring treatment. She received naive arteriovenous fistula surgery in order to perform hemodialysis on November 24, 2006. In February 2007, the patient started to experience uremic symptoms such as nausea, vomiting and loss of appetite, and she started to receive regular hemodialysis treatment 3 times a week. The arteriovenous fistula in the patient’s body was obstructed and didn’t function normally due to repeated use. To perform hemodialysis successfully, she received arteriovenous graft (AVG) creation in her right forearm on March 13, 2007.
Two months after the AVG creation, the patient felt intermittent chill with fever when she received hemodialysis. On June 25, she was admitted to the emergency department because of high fever (over 40°C), chill and diarrhea with tiny blood. On the day of her arrival, various examinations and tests including CBC, biochemistry, urine analysis, and blood and urine cultures were performed. The CBC report revealed that Hb was 9.7g/L and white cell count was 9.7*10^6/cmm, neutrophils 86%. The results of biochemical tests were C-reactive protein 24.9mg/L, sodium 130 meg/L and potassium 5.5 mg/L. Result of urine strip test showed leukocyte esterase moderate, and examination of urinary sediments revealed WBC 45 cell/HPF. This patient, initially diagnosed with urinary tract infection according to test results, was treated with empiric Ceftriaxone (Rocephin). The patient was admitted again on June 27 due to persistent fever and she was treated with Ciprofloxacin. After one week of her hospitalization, the infected bacteria in blood cultures displayed faint Gram-positive reactions. According to these results, the patient was mistakenly diagnosed as infections with Gram-negative bacilli (Fig. 1), since the precise bacterial strain had not yet identified. Patient was continued prescribing with 500mg (Q8H) Aztreonam. We arranged an abdominal CT scan and whole body gallium scan for her but no definite infection source could be found. Persistent fever with chill was still noted during and after her dialysis process. On July 11, a double lumen catheter insertion was performed within her right internal jugular vein to avoid hemodialysis through the AVG in her right forearm. On July 16, results of blood cultures identified that the patient was infected with \textit{M. chelonae}. Result of antibiotic susceptibility test indicated these infected \textit{M. chelonae} were only sensitive to Amikacin and Imipenem. Her treatment was changed to a combination of i.v. Amikacin 350mg (QW135), Imipenem (Tienam) 250mg orally twice a day and Clarithromycin 500mg orally once a day. Nevertheless, patient’s conditions persisted for 3 days without a hint of improvement, AVG infection was highly suspected and the cardiovascular surgeon was consulted. No local infection sign at the site of AVG implanted was found, so the cardiovascular surgeon suggested that we continued the antibiotic treatment. However, the patient’s condition remained the same. Her fever persisted and associated delirium was noted on July 23. Patient showed consciousness disturbance while she continued to have a high fever. The cardiovascular surgeon was consulted again and her AVG was removed, and she continually received the treatment of antibiotics. Her consciousness recovered gradually although intermittent fever was still noted, but no more chills was found. On August 1, we removed the double lumen catheter and persisted with the antibiotic treatment. One week later, the fever and chill subsided. In order to perform the hemodialysis, a new double lumen catheter was inserted into her left internal jugular vein on August 7. At this time, no more fever or chill was noted. Amikacin treatment was stopped on August 9, followed by the termination of Imipenem treatment on August 13, but the oral Clarithromycin treatment continued. Patient’s condition was now stabilized and she was discharged on August 16.

\textbf{Fig. 1.} The colonies smeared from a BP show very faint stained Gram positive bacilli (a, 1000x amplification) and acid-fast smear signals by Kinyoun stain (b, 1000x amplification).
Discussion

*M. chelonae* is a non-pigmented rapidly growing mycobacterium [5] and colonies can be seen on solid media in merely 3 to 5 days. Although there are many types of media suitable for culturing mycobacteria, the Lowenstein-Jensen medium and the first-generation Middlebrook 7H11 are most widely utilized [6]. It is believed that non-pigmented, rapidly growing mycobacteria can also be cultured on a common medium, such as BP, with no difference of growth in comparison with cultured on previous media [13]. Bacteremia is an acute infection that may lead to septic shock. In order to reduce the mortality rate of patients, it is necessary to identify the pathogen and confirm the source of infection as soon as possible. The results of blood cultures are the most important evidences for early diagnosis of bacteremia. In this case report, blood culture was first carried out. Once positive reaction identified, subcultures were carried out using EMB agar and chocolate plates (Fig. 2). Although only tiny apparent colonies were observed on day 3, there were singular colonies distinct in shape observed on day 5. Since the increases of patients suffer impaired immune functions, there are more cases of opportunistic infections due to rapidly growing non-tuberculous mycobacteria. Because there is a large chance of rapidly growing non-tuberculous mycobacteria existing in an ordinary blood culture, therefore, all microbiological laboratories in hospitals should establish methods for rapid diagnosis of non-tuberculous mycobacteria in hospitals as soon as possible.

![Fig. 2. Colony morphologies of M. chelonae grown on a BP for 5 days (a), on a EMB agar plate for 5 days (b) and on a chocolate plate for 3 days (c).](image)

Non-tuberculous mycobacteria demonstrate a diversity of shapes on Gram-stained smears [14]. They can be Gram-positive or neutral, long or short, slightly bent or in a shape similar to a cue. They must be identified using an acid-fast stain but not the Gram stain, which may result to a wrong judgment [15]. Generally, they can be confirmed after mycobacterium culturing tests. However, conventional tests take a very long time. Some molecular biotechnology methods, such as PCR-RFLP, are ideal for the rapid identification of pathogens in blood. In addition, utilizing PCR-RFLP, it is possible to identify species of mycobacteria and distinguish *M. avium* from *M. intracellulare* [16], and *M. abscessus* from *M. chelonae* [17]. These bacteria are difficult to be distinguished using conventional methods.

Most catheter infections are caused by staphylococcus and enterococcus [18]. There are reports indicating that *M. chelonae* can also cause catheter infections, such as Port-A-Cath infection [1, 5, 19]. Unlike previous cases, the case we reported here is the blood infection of *M. chelonae* because we identified *M. chelonae* in blood cultures. *M. chelonae* is resistant to common anti-tuberculosis drugs [18]. Therefore, an effective treatment must be decided according to results of drug-resistance tests. Furthermore, the patient demonstrated continuous bacterial infections, which resulted in the continuous fever even after correct antibiotics were administered. In patients with catheters implanted, bacteria may move to the catheters and form films on catheters’ walls [20]. This phenomenon makes the infectious bacteria hard to treat. Therefore, it is necessary to remove all catheters in patient first although there is no sign of infection at the locus of catheter implantation, and then a new catheter is implanted at a proper stage of treatment.
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References


糖尿病尿毒症病患由龜分枝桿菌引起之血行感染

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龜分枝桿菌(Mycobacterium chelonae)的血行感染比較罕見，本案例為一位五十歲女性病患有糖尿病併尿毒症，在接受人工動靜脈廔管植入術兩個月後出現畏寒、顫抖及高燒症狀，多次血液培養呈現陽性反應，經由次培養後，菌落塗片Kinyoun染色顯示有抗酸性桿菌，使用聚合酶鏈鎖反應合併核酸限制酶截切多型性分析法鑑定結果為龜分枝桿菌感染。龜分枝桿菌為快速生長菌且對許多抗生素具有抗藥性，醫院臨床微生物實驗室應建立並提供快速診斷方法以因應這種非結核分枝桿菌的感染。

關鍵詞：龜分枝桿菌，血行感染，糖尿病尿毒症病患，聚合酶鏈鎖反應合併核酸限制酶截切多型性分析