A Preterm Neonate with *Mycobacterium Fortuitum* Infection

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Abstract Late-onset neonatal sepsis causes significant morbidity and mortality. Coagulase negative Staphylococci and Gram-negative bacilli contributed most of the cases of late-onset neonatal sepsis. *Mycobacterium fortuitum*, which is a rapidly growing mycobacterium, has not been reported to cause late-onset neonatal sepsis. It is the first reported case of a preterm neonate with disseminated *mycobacterium fortuitum* infection. Long duration and combination antibiotics are required for treatment.

Key words Late-onset neonatal sepsis; *Mycobacterium fortuitum*; Neonate; Rapidly growing mycobacteria

Introduction

Late-onset neonatal infections which occur more than 48 hours after birth, are caused by organisms acquired from the postnatal environment, rather than transplacentally or from the birth canal.[1] The mortality rate was about 9%. The commonest organisms causing late-onset neonatal sepsis are Coagulase negative Staphylococci (CONS) (55%), Gram-negative bacilli (18%), *Staphylococcus aureus* (9%) and Candida species (7%).[1] Rapidly growing mycobacteria (RGM) are rare causes of late-onset neonatal sepsis. Only two case reports from English literature were described for *Mycobacterium chelonei* and *Mycobacterium abscessus* by Speert[2] and Di Pentima[3] respectively. *Mycobacterium fortuitum* (*M. fortuitum*), another RGM had not been reported as an organism responsible for the late-onset neonatal sepsis. This is the first reported case of premature

newborn suffering from *Mycobacterium fortuitum* septicaemia and the third case of RGM septicaemia.

Case Report

A female baby was born at 27 week gestation by vaginal breech delivery with birth weight of 0.91kg, being appropriate for gestational age. Mother was followed up at our hospital with uneventful antenatal course until the preterm labour. Maternal blood tests screening for hepatitis B virus (HBV), syphilis and human immunodeficiency virus (HIV) were negative. She was the first baby of a non-consanguineous couple. At delivery, she was intubated at labour ward because of poor respiratory effort. The Apgar score was 6 at the first minute and 8 at the fifth minute. She was transferred and managed at our neonatal intensive care unit (NICU). Mechanical ventilation was started and umbilical arterial and venous catheters (UAC and UVC) were inserted. Sepsis workup was performed and empirical intravenous antibiotics with penicillin G and aztreonam were started.

She had respiratory distress syndrome (RDS), and was given 4 doses of surfactant (Survanta) and mechanical ventilation (with the highest pressure up to 18/5 cmH$_2$O and oxygen concentration up to 40%). She had a large patent ductus arteriosus (PDA) noted since day 6 of life, with size

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up to 3.9 mm and left atrium to aorta ratio up to 2. The PDA failed to close after 2 courses of indomethacin and therefore was surgically ligated on day 40 of life. Trophic feeding was started on day 3 of life with expressed breast milk (EBM). Total parental nutrition (TPN) was given from day 2 to day 46 of life. The blood culture taken after birth and the serial C-reactive proteins (CRP) were normal, therefore penicillin G and aztreonam were stopped on day 5. She developed mild bile-stained gastric aspirate on day 6, together with thrombocytopenia (97 x 10^9/L) and neutropenia (1.4 x 10^9/L). The Abdominal X-ray showed thickened bowel wall at the left lower quadrant. Sepsis workup was repeated and she was empirically covered with cefotaxime, gentamicin and metronidazole for stage I necrotising enterocolitis (NEC). The serial CRPs were not raised and blood culture was negative and the antibiotics were given for 1 week. There was difficulty in setting a central venous catheter until day 18, when the UVC was changed to a peripheral long line over the right lower limb. There was no sign of exit site inflammation of the UVC and blood culture from the UVC was taken before withdrawal. She developed a kick of fever (up to 38.5°C) on day 24. Sepsis workup including lumbar puncture was performed and empirical treatment of cloxacillin and aztreonam were started. On the same day, report of blood culture taken from UVC (taken on day 18) grew

M. fortuitum. After discussion with our microbiologist, antibiotics were changed to amikacin and tienam (imipenem and cilastatin). Figure 1 outlined the sequence of events before the septicaemia. Peripheral blood culture taken on day 24 also grew *M. fortuitum*. In-vitro susceptibility test showed it to be sensitive to amikacin and clarithromycin, intermediately susceptible to cefoxitin and resistant to doxycycline. The white cell counts were normal (total white cell count 12.9 x 10^9/L, neutrophil 4.5 x 10^9/L, lymphocyte 5.4 x 10^9/L). The highest CRP was 20.1 mg per litre, which was normalised afterwards. The cerebrospinal fluid (CSF) culture was negative. The peripheral long line was removed. Amikacin and tienam were given for 4 weeks, followed by 4 weeks course of clarithromycin. The blood culture taken after the first dose of amikacin and tienam was negative. Multiple blood cultures were taken, with the last one taken after 3 month of age, all were reported no growth.

For other neonatal problems, she had bronchopulmonary dysplasia (BPD), total parental nutrition (TPN) related cholestasis and rickets of prematurity.

She was discharged home at three and half months of age. Subsequent follow-up at our neonatal clinic showed normal growth and development (adjusted for her prematurity). The body weight was at 90th percentile, height and head circumference at 75th percentile. The brainstem auditory evoked potential (BAEP) showed normal hearing
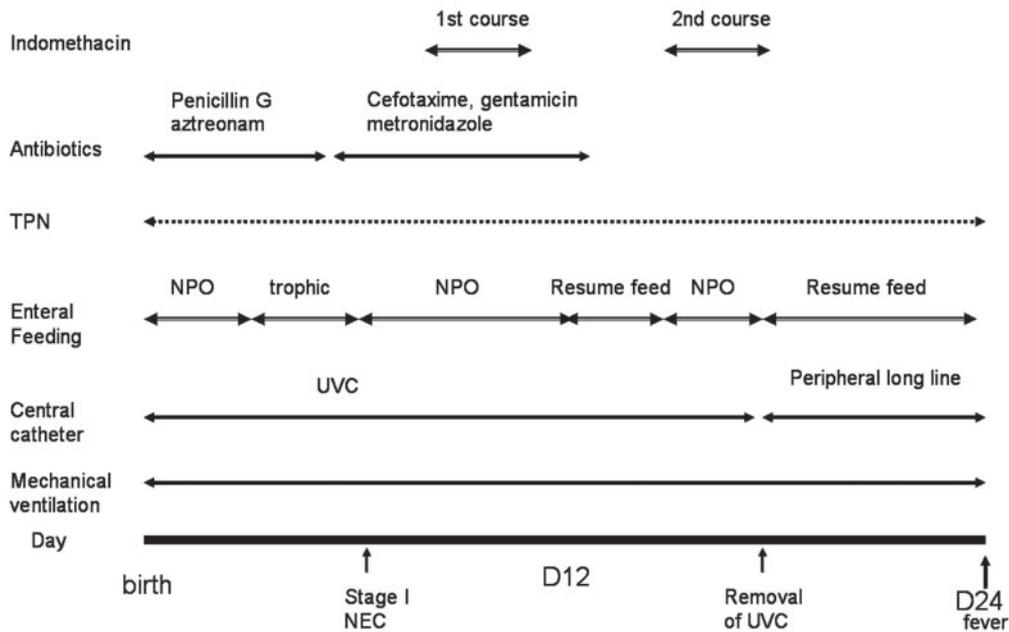
Figure 1   Sequence of the events before the septicaemia

threshold. Retinopathy of prematurity (ROP) screening by ophthalmologist was normal. The ultrasonogram of brain by radiologist was normal. She does not have significant infection episodes since discharge from hospital.

Discussion

Mycobacterium fortuitum (*M. fortuitum*) belongs to a group of rapidly growing mycobacteria (RGM, Runyon class IV). RGM can have sufficient growth in 3 to 7 days and allow identification. They generally grow on routine culture but specific culture (e.g. Lowenstein-Jensen agar) is preferred. RGM are saprophytes and they are normally found in soil, water and dust.[4] They can survive in high temperatures and are resistant to many chemical disinfectants.[4,5] There are about 40 recognised species among the RGM but *M. fortuitum*, *M. chelonae* and *M. abscessus* cause most of the human infections. A variety of diseases ranging from soft tissue abscess (especially after trauma and surgery), lymphadenitis, corneal infections, pulmonary and disseminated diseases have been reported. The incubation period is variable and there is no reported human to human transmission. Risk factors for disseminated disease include immunocompromised states such as congenital immune deficiency,[6,7] HIV infection,[8] malignancy, transplantation, immunosuppressive therapy[9-11] and indwelling catheters[12] or implants.

Compared with the two reported cases of neonatal rapidly growing mycobacteria (RGM) septicaemia,[2,3] our patient shared similar risk factors of being extreme prematurity, very low birth weight, with long duration of mechanical ventilation, presence of central venous catheter and PDA requiring surgical ligation. For the response to treatment, the blood culture of our patient became sterile about one day after start of antibiotics compared to 11 days of the two reports. The patient with *M. abscessus* septicaemia[3] and our patient had appropriate growth and development after the treatment.

As regards to paediatric patients with disseminated disease of *M. fortuitum*, it has been reported in an 11-month old infant with clear cell sarcoma of the kidney[11] and a 4 year-old boy with Wilms' tumor.[9] They both had central venous catheters and were on combination chemotherapy. It has also been reported in 2 teenagers with sickle cell anaemia,[10] who had central venous catheters and were on hydroxyurea. Tsolia et al reported a two-year old boy with complete interferon-γ receptor 1 (IFNγR1) deficiency who got uncontrollable disseminated *M. fortuitum-M. peregrinum* complex infection.[6]

Paone et al reported a four month-old infant suffering from *M. fortuitum* necrotising pneumonia.[13] He required right pneumonectomy because combination antibiotics failed to control the infection.

It is necessary to differentiate colonisation from genuine infection, especially if the RGM is obtained from non-sterile sites.[4,5] Pseudo-outbreaks have been reported of *M. fortuitum* isolated from respiratory tract specimens due to contaminated ice machines.[14]

As regards to treatment of RGM (or *M. Fortuitum*), anti-tuberculous drugs are not effective. *M. fortuitum* is usually susceptible to amikacin, cefoxitin, imipenem, ciprofloxacin, sulfonamides and clarithromycin.[12] Currently there are no controlled trials of treatment of RGM infections; consultation with a microbiologist is advised. Combination antibiotic therapy is recommended to prevent emergence of drug resistance. In-vitro susceptibility testing is important for the choice of antibiotics, as there is strain to strain variation in antibiotic susceptibility. Long duration of antibiotics is suggested, preferably at least 4 to 6 weeks. Removal of the foreign body or catheter is usually required.[12]

In conclusion, our patient had a rare infection of *M. fortuitum*, which was successfully treated with satisfactory growth and neurodevelopment. An increased awareness is required especially when the patient is immunocompromised, has a central venous catheter and the infection cannot be controlled with conventional antibiotics.

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