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Case Report

Sequential *Mycoplasma pneumoniae* pneumonia and *Chromobacterium violaceum* skin abscess in a pediatric patient

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Abstract

Mycoplasma pneumoniae is a common atypical respiratory pathogen causing community-acquired pneumonia in children. Co-infection with other respiratory viruses is common in pediatric patients but super-infection with bacteria other than *Streptococcus pneumoniae* and *Haemophilus influenzae* is rare. The first case of *Chromobacterium violaceum* infection incubated during and manifested after pneumonia caused by *Mycoplasma pneumoniae* in a 12-month old girl without any known history of immunodeficiency is here reported. The patient developed fever with redness and swelling over the middle phalanx of the right hand index finger which progressed to the formation of skin abscess. Following a course of intravenous meropenem and surgical drainage of the skin abscess, the patient fully recovered and was discharged.

Key words: *Chromobacterium violaceum*; *Mycoplasma pneumoniae*; abscess; pediatrics

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Introduction

Mycoplasma pneumoniae is a common atypical respiratory pathogen and is responsible for 20% to 40% of community-acquired pneumonia (CAP) cases in children and adults [1,2]. It accounts for up to 11% of the upper and lower respiratory tract infection (RTI) cases in children ≤ 14 years old, and around 21% and 6% in children aged ≥5 and ≤1 respectively [3]. Extra-pulmonary manifestations have been shown occurring in up to 25% of *Mycoplasma pneumoniae* infected patients, more commonly in pediatric patients [4]. Co-infection with other respiratory viruses is common and occurs in up to 15% of *Mycoplasma pneumoniae* infected pediatric patients [2,3]. Co-infection or super-infection with bacteria other than *Streptococcus pneumoniae* and *Haemophilus influenzae* has been rarely reported [5,6]. Human infections caused by *Chromobacterium violaceum* have been considered as rare but with a high case-fatality rate as concluded from several case reports [7].

Chromobacterium violaceum belongs to the ß-Proteobacteria class under the family Neisseriaceae, and is a facultative anaerobe. It is a large gram-negative bacillus sized 0.5 – 1 µm in length and 2 - 3µm in width, and motile with a polar flagellum and one or two lateral flagella. It is a free-living organism, ubiquitously and saprophytically inhabiting in the soil and water in tropical and sub-tropical regions. Isolates from natural habitats are capable of adapting and surviving in diverse adverse environments and ecosystems [8-11]. *Chromobacterium violaceum* was first described as a potential pathogen in water buffalos in the Philippines by Wooley in 1905 and in humans in Malaysia by Lesslar in 1927 [10,12]. Several cases of *Chromobacterium violaceum* human infections have since been reported despite of the bacterium being considered as of low infectivity and usually not as a human pathogen [9,10]. The type III secretory system (TTSS) components of *Chromobacterium violaceum* encoded by open reading frames (ORFs), as revealed by

complete genome sequencing, allow secretions of effector molecules into the host cells leading to cytoskeletal rearrangement, and have been found to differ from those TTSS in other gram-negative pathogenic bacteria. The lack of ORFs responsible for invasions such as invI and invH, and the secretion of tyrosin phosphatase SptP in *Chromobacterium violaceum* may explain its opportunistic pathogenicity [9,13].

The first case of *Chromobacterium violaceum* skin abscess developed after *Mycoplasma pneumoniae* pneumonia in a pediatric patient without any known history of immunodeficiency is here reported.

Case Report

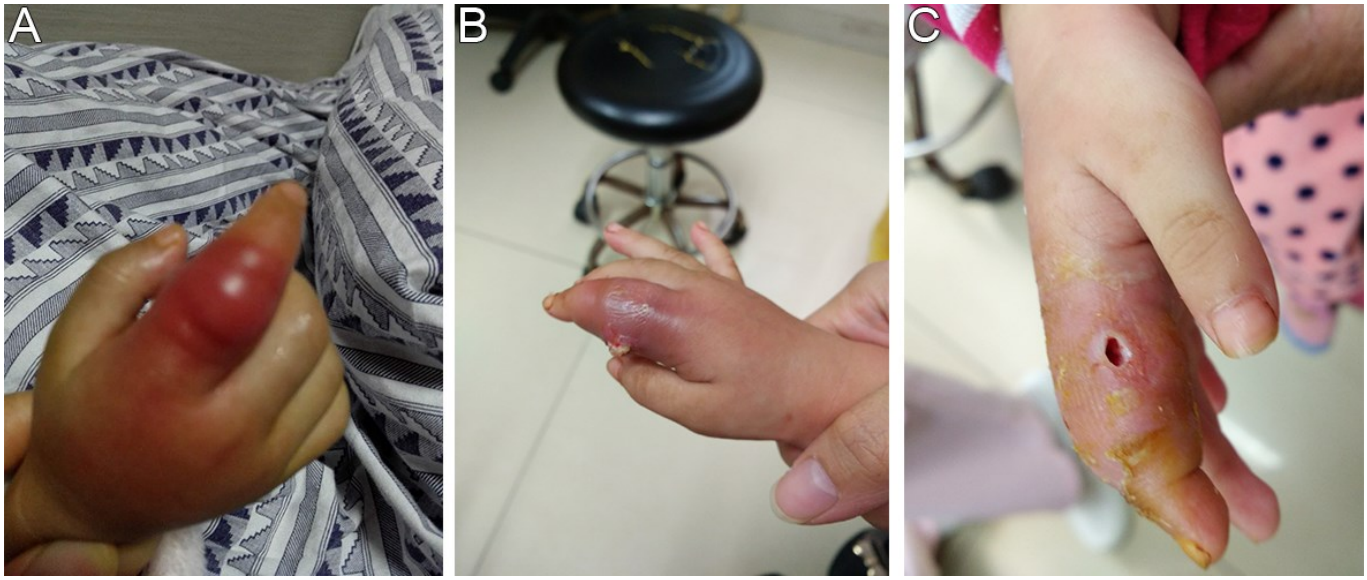
A 12-month old girl was admitted in November 2015 for recurrent fever without localized symptoms.

She presented in our hospital 3 days after discharge from another hospital where she had been hospitalized for community-acquired pneumonia due to *Mycoplasma pneumoniae,* presented with a 5-day history of on and off fever with peak temperature of 40°C, running nose, non-productive cough, and bronchopneumonia upon chest X-ray examination. Clinical improvement had been observed after initial empirical antibiotic treatment directed towards the most common respiratory pathogens involved in typical and atypical pneumonia. Her serum had been subsequently tested positive to *Mycoplasma pneumoniae* IgM antibodies, while nasopharyngeal aspirates and sputum samples were negative for respiratory viruses and bacterial pathogens, respectively.

At admission to our hospital, she had fever and non-productive cough, without dyspnea, and no skin rash or other obvious symptoms suggestive of extra-pulmonary manifestations of the recent *Mycoplasma pneumoniae* infection. The patient was hemodynamically stable and her physical examination was unremarkable, except signs of pharyngitis and enlarged tonsils. Laboratory tests showed white blood cell count of 40×10^9 cells/L with 76% neutrophils and 8% lymphocytes, hemoglobin 10.4g/dL, platelets 359×10^9/L, and C-reactive protein (CRP) at 195.5 mg/L. Her serum was still positive for *Mycoplasma pneumoniae* IgM antibodies and negative for *Legionella pneumophila* serogroups 1-7, *Chlamydia* and *Rickettsia* species, *Adenoviruses*, *Influenza viruses* A & B, *Respiratory syncytial virus* and *Parainfluenza viruses*. She was given a 3-day empirical cefoperazone-sulbactam treatment for the management of her non-responding pneumonia, however her fever persisted with elevated white blood cell count of 29×10^9 cells/L and CRP at 127 mg/L.

On day 6 after admission in our hospital, she developed redness and swelling over the middle phalanx of the right index finger and hand (Figure 1a and b). X-ray of the right hand showed soft tissue swelling of the index finger without bone erosion. The swelling progressed to abscess with pus discharge requiring surgical drainage which was performed on day 11 after admission. The pus was cultured on blood agar at 37°C with 5% CO2 and after 24 hours of incubation, a growth of round, smooth and convex colonies of 1 to 2mm diameter with ß-haemolysis was

Figure 1. A and **B**: Skin abscess of right index finger with pus discharge and surrounding cellulitis in the right hand. **C**: Wound healing in progress at 4 days after surgical drainage of the abscess due to *Chromobacterium violaceum*.



observed, and presence of violet pigments was also noted when grown on Mueller Hinton agar (Figure 2) for antibiotic susceptibility test. Gram staining showed gram-negative bacilli and the isolates were subsequently identified by the automated microbial identification platform VITEK2 System with biochemical reaction results compatible to *Chromobacterium violaceum*. The isolate was sensitive to aminoglycosides, nitrofurantoin, trimethoprim/sulfonamides, quinolones and meropenem, and resistant to ampicillin, beta-lactam/beta-lactamase inhibitors, first-, second-, third- and fourth-generation cephalosporin. The antibiotic treatment was changed to intravenous meropenem and subsequently gradual resolution of the fever and the signs of inflammation of the skin lesion were observed. Over the next 4 days post-surgical drainage, she remained afebrile, the right middle finger wound was in healing without discharge or gapping (Figure 1c), the white blood cell count was normalized and was subsequently discharged home. Furthermore, subsequent investigations for HIV antibodies and neutrophil dysfunction yielded negative results.

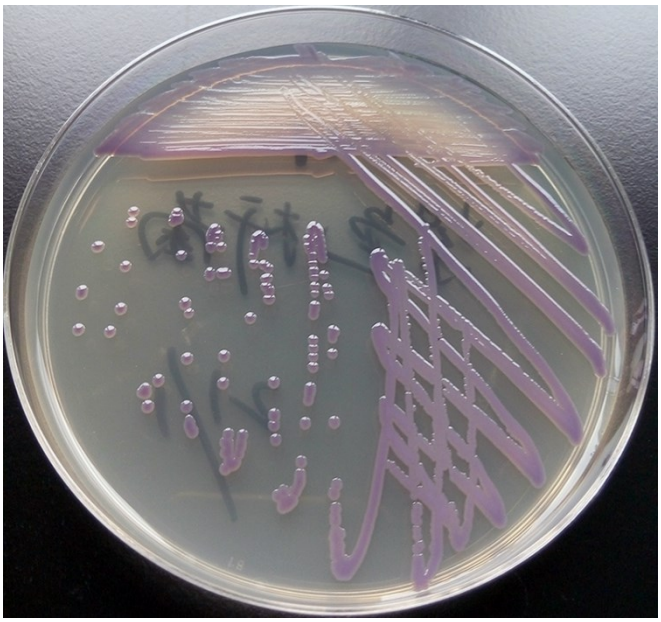
Discussion

This is the first case report of *Chromobacterium violaceum* skin abscess incubated during and manifested after *Mycoplasma pneumoniae* pneumonia in a pediatric patient without any known history of immunodeficiency, and patient survival after successful treatment with meropenem.

Chromobacterium violaceum is usually considered as an opportunistic pathogen in humans. Nevertheless, an increasing number of *Chromobacterium violaceum* infection cases have been reported in recent decades worldwide [14]. The clinical course is characterized by acute febrile illness, rapidly progressing to life-threatening fulminant sepsis and multi-organ failure requiring critical care, and characterized by a high mortality rate (50% to 80% in days to weeks after the infection) if left untreated. The significant risk factors for mortality in patients with *Chromobacterium violaceum* infection include the presence of localized abscess and the use of short clinical courses of inappropriate antibiotic treatments. Other risk factors include patient's young age and immunodeficiency status [10,13]. Relapse or recurrent infection have been reported at 6.6% [14,15].

The most common presenting symptoms of human *Chromobacterium violaceum* infection are fever, sepsis, skin lesions, abdominal pain, and clinical syndrome of localized skin and soft tissue infection, lymphadenitis and gastroenteritis [8,10,16]. During the infection progression bacteremia and disseminated infection involving various organ systems can result in urinary tract infection, arthritis, osteomyelitis, abscesses in lung, brain and other viscera, meningitis, endocarditis, endophthalmitis, otitis media, vaginitis, haemophagocytic syndrome and multi-organ failure [8,10,16].

Figure 2. Violet pigments of *Chromobacterium violaceum* on Mueller Hinton agar, after incubation at 37°C with 5% CO2 for 24 hours.



The routes of infection due to *Chromobacterium violaceum* are usually through direct inoculation into mucocutaneous break or ingestion of contaminated water. Most infected individuals usually report a preceding history of trauma or wound, and exposure to recreational or stagnant muddy water, or breast surgery or appendicectomy. Isolates of *Chromobacterium violaceum* have been detected in drinking water springs, pasteurized milk samples from a dairy plant, and in samples of tap water from operation theatres. In the latter case, water has been implicated in the nosocomial transmission of *Chromobacterium violaceum* with outbreak potential and public health issues [10,17-19].

The clinical presentation of fever and skin abscess in our patient was concordant with the most commonly reported manifestation of *Chromobacterium violaceum* infection. Fifty percent of the infected patients have localized abscess [14]. Due to the prompt diagnosis of the infection, the adequate surgical drainage and the use of the appropriate antibiotics, our patient survived to the infection, and progression to bacteremia and

disseminated infection was haulted despite our patient's young age.

The identification of *Chromobacterium violaceum* as the co-existing pathogen in our patient was prompted by the presence of non-diffusible violet pigmented colonies on blood agar, which facilitated diagnosis and treatment. About 91% of *Chromobacterium violaceum* strains give rise to pigmented colonies. However, there are infectious nonpigmented strains and there are also reports of co-infection with pigmented and nonpigmented strains making diagnosis even more difficult [20,21]. The organism produces a natural antibiotic called violacein encoded by a cluster of 4 genes, vioABCD, within a single operon. Its anti-cancerous and anti-bacterial activities would have potential implications in future clinical therapeutic or biotechnological applications with industrial benefits [13,22,23].

Our patient did not have any immunodeficiency state, such as chronic granulomatous disease (CGD), neutrophil dysfunction, HIV infection, or any other immunodeficiency, that would have predisposed her to the infection [7,10]. Moreover, she did not have any apparent history of trauma, injury, wound or exposure that would have allowed direct inoculation of organisms to the skin so as to establish the infection. Nevertheless, it is believed that *Chromobacterium violaceum* infection in our patient was incubated during *Mycoplasma pneumoniae* infection and manifested sequentially. *Mycoplasma pneumoniae* is well known as a great mimicker, therefore almost any organ system can be affected. The most common extra-pulmonary manifestation is exanthematous skin rash with or without mucosal lesions [4,24]. *Mycoplasma pneumoniae* infection in our patient was evidenced by the elevated *Mycoplasma pneumoniae*-specific IgM antibodies, which typically appear within 1 week after the infection, with a more prominent response in children than in adults, and around 2 weeks before detectable IgG antibodies [4]. This preceding episode of acute infection of *Mycoplasma pneumoniae* in our patient may have caused unnoticed cutaneous lesions as an extra-pulmonary manifestation of the *Mycoplasma pneumoniae* infection. Even a minute skin crack or break in our patient's skin may have resulted in reduced local immunity, which in turn may have facilitated the subsequent entrance of *Chromobacterium violaceum* pathogens leading to infection as well as skin abscess.

Moreover, *Mycoplasma pneumoniae* has been shown to induce transient depression of T-lymphocyte function and depletion of CD4 T-cells, and a transient anergy state during the acute phase of infection [25]. Temporary suppression of the immune system has also been shown in pediatric patients acutely infected by *Mycoplasma pneumoniae* [25]. In addition, blood lymphocytes from patients in acute phase of *Mycoplasma pneumoniae* infection have been shown to have a decreased response to purified protein derivatives *in vitro* [26]. Hence, it has been suggested that *Mycoplasma pneumoniae* infection causes transient depression of cell-mediated immunity [26]. It appears possible that the depressed cell-mediated immunity during the acute *Mycoplasma pneumoniae* infection predisposed our patient to the development of *Chrombobacterium violaceum* infection which manifested as skin abscess. The interval of 3 days between the resolution of the *Mycoplasma pneumoniae* infection symptoms and the onset of the *Chromobacterium violaceum* infection symptoms in our patient is compatible with the median incubation period reported for *Chromobacterium violaceum* (3 days median, range 1 to 90 days) [14]. It is also concordant with the sequential manifestation of *Mycoplasma pneumoniae* pneumonia and *Chromobacterium violaceum* skin abscess in our patient. Co-infection of *Mycoplasma pneumoniae* with respiratory viruses has been previously reported, but co-infection or superinfection with bacteria other than *Streptococcus pneumoniae* or *Haemophilus influenzae* have rarely been reported. There is no previous report of sequential *Mycoplasma pneumoniae* infection followed by *Chromobacterium violaceum* skin abscess in a pediatric patient without any known immunodeficiency or any other predisposing factor.

Mycoplasma pneumoniae is a well-recognized respiratory pathogen in children and adults, infecting the upper and lower respiratory tract leading to upper respiratory tract infection, bronchitis, bronchiolitis, tracheobronchitis, community-acquired pneumonia, and associated with asthmatic exacerbation. *Mycoplasma pneumoniae* are primarily mucosa-associated organisms capable of intracellular existence, and closely associated with epithelial cells extracellularly. Our patient did not have apparent extra-pulmonary manifestations of *Mycoplasma pneumoniae* infection which are mainly due to indirect effects rather than the presence of the organism in the target organs or systems. Commonly reported infections involve the central nervous system with aseptic meningitis, encephalitis, transverse myelitis, and the cardiovascular system with myocarditis, pericarditis or acute myocardial infarction. Less commonly reported manifestations involve the gastrointestinal tract with pancreatitis, cholestatic hepatitis; haematologically

resulting into hemolytic anaemia, coagulopathy, presence of cold agglutinins, vasculitis and immunologically involving kidney, musculoskeletal with arthritis, myalgia, and rhabdomyolysis [4,25].

Chromobacterium violaceum is characteristically resistant to penicillin, first- and second-generation cephalosporins, and has a variable susceptibility to third-generation cephalosporins, carbapenems and aminoglycosides, resulting from the presence of numerous ORFs associated with various drug resistance mechanisms in particular beta-lactam and multidrug resistance genes [25,26]. It is hypothesized that these genes are essential for *Chromobacterium violaceum* survival in competing with other bacteria in different ecosystems, because isolates from environment have demonstrated a higher level of antibiotic resistance than laboratory reference strains [27,28]. The persistent fever in our patient did not respond to cefoperazone-sulbactam but improved after adequate drainage of the abscess in combination with the administration of meropenem.

In conclusion, the first case of a pediatric patient without apparent significant exposure history or immunodeficiency who survived after *Chromobacterium violaceum* skin abscess incubated during and manifested after *Mycoplasma pneumoniae* pneumonia was reported. The management of *Chromobacterium violaceum* infection requires its prompt inclusion in the differential diagnosis, and the consideration of its characteristic multidrug resistance nature and high case-fatality rate by timely and appropriate use of antibiotics.

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