

Case report

***Citrobacter freundii* pyothorax complicating tuberculous pleurisy in an immunocompetent patient**

Abstract

Purulent tuberculous pleurisy is a severe form of tuberculosis. Co-infection tuberculosis and *Citrobacter freundii* in purulent pleurisy is rarely described in the literature. Early recognition of this pleural co- infection is necessary for a better prognosis of the patient. We report the first case of pyothorax secondary to *Citrobacter freundii* and Mycobacterium tuberculosis in an immunocompetent patient in the Pneumology Department of the Yalgado Ouédraogo University Hospital (Burkina Faso). The present case highlights the challenges and lessons learned in the management of a pyothorax of tuberculosis and *Citrobacter freundii* origin. Good clinician-biologist collaboration is necessary for the proper therapeutic management of patients to improve their prognosis.

Key words: *Citrobacter freundii*, Mycobacterium tuberculosis, pyothorax, tuberculosis, Burkina Faso.

Introduction

Tuberculous pyothorax is a severe form of tuberculosis [1]. Although this form of purulent pleurisy is common in immunocompromised patients, it can also occur in immunocompetent individuals. Bacterial superinfections can complicate the picture, making diagnosis and management complex. *Citrobacter freundii* is a Gram-negative bacterium, a member of the group three enterobacteria. It is a facultative anaerobic, motile, oxidase-negative bacillus, which generally uses citrate as its sole carbon source [2]. It accounts for around 0.8% of Gram-negative infections [3]. Tuberculous pyothorax associated with *Citrobacter freundii* infection is rarely described in the literature. Early recognition of this pleural co-infection is necessary for a better prognosis of the patient. We report here the case of an immunocompetent patient hospitalized for pyothorax secondary to *Citrobacter freundii* and Mycobacterium tuberculosis in the Pneumology Department of the Yalgado Ouédraogo University Hospital (Ouagadougou-Burkina Faso).

Case presentation

The patient was a 55-year-old farmer with known hypertension and no other pathological antecedents. He was admitted for a hacking cough with mucopurulent sputum associated with MRCm stage III dyspnea, all evolving in a chronic, febrile context.

On admission, the patient's conscious state was good, with a Glasgow score of 15, a general condition of stage 3 according to the WHO status performance index, and moderate dehydration. His peripheral oxygen saturation was 91% on room air, and he had a systemic inflammatory response syndrome with hyperthermia at 38°C, a heart rate of 98 beats per minute and a respiratory rate of 26 cycles per minute. He had a right-sided liquid pleural effusion syndrome, which was clarified on a frontal chest X-ray, which revealed a homogeneous opacity with a watery tone and no air bronchogram, occupying the entire right hemi-thorax (figure 1). This was confirmed by an exploratory pleural puncture, which brought back a purulent fluid.

The Xpert MTB Rif® test on pleural fluid isolated mycobacterium tuberculosis sensitive to Rifampicin; the test on sputum was negative. Pleural fluid culture isolated *Citrobacter freundii* sensitive to amikacin, fosfomicin and piperacilin-tazobactam. The blood count came back with thrombocytosis at 586,000 ul, mild hypochromic microcytic anemia with hemoglobin at 11.4 g/dl and normal white blood cells at 5880 ul. Abdominal ultrasound, retroviral serology, liver function (transaminases, HBS antigen) and renal function were unremarkable.

The diagnosis of polymicrobial tuberculous pyothorax and *Citrobacter freundii* was made. The patient underwent antituberculosis treatment according to the protocol in force in Burkina Faso, consisting of a combination of Rifampicin/Isoniazide/Pyrazinamide/Ethambutol combined with non-specific antibiotic therapy consisting of piperaciline-tazobactam 4.5mg every eight (8) hours and injectable amikacin 1g every 24 hours, rehydration and thoracic drainage on the right.

The evolution was favorable, marked by an improvement in clinical signs and re-expansion of the lung parenchyma on the follow-up chest X-ray (figure 2). He was discharged 20 days after admission with outpatient appointments.

Discussion

Purulent pleurisy or pyothorax or empyema is the presence in the pleural space of a thick, sometimes fetid purulent fluid containing a majority of neutrophils altered with germs on direct examination [4]. Tuberculous pyothorax is a rare complication of pulmonary tuberculosis, which can occur even in immunocompetent patients. In our case, this infection was complicated by co-infection with *Citrobacterfreundii*, a bacterium rarely encountered in pleural infections. Only 2 cases of *C. freundii* pyothorax isolated from young subjects have previously been reported [5, 6].

Citrobacter species are commonly found in water, soil, food and the intestinal tract of animals and humans. They can cause a variety of infections affecting the urinary tract, hepatobiliary tract, respiratory tract, wounds, bone and central nervous system [7]. Mortality has been reported to range from 16.6% to 48.3% [8-10]. Polymicrobial infection is known to increase mortality and length of hospital stay in adults [8-10]. The association of *C. freundii* and *M. tuberculosis* has rarely been described in the literature, particularly in a country endemic for tuberculosis. This underlines the singularity of our observation and the importance of multidisciplinary management of patients with infectious pleural complications.

Diagnosis is based on pleural fluid analysis (Xpert, culture and antibiogram). In our case, this analysis identified both *M. tuberculosis* and *C. freundii*. Clinical manifestations of tuberculosis can mask the symptoms of bacterial superinfection, thus delaying diagnosis.

From a therapeutic point of view, treatment must be initiated as early as possible, as delaying treatment can lead to complications and even be life-threatening. Several studies have noted that the use of a cephalosporin within 14 days favours the emergence of multi-resistant strains [11]. A study carried out in India revealed a high degree of resistance to third- and fourth-generation cephalosporins, as well as to piperacillin, gentamicin and ciprofloxacin [12].

Prognosis depends on rapid diagnosis and appropriate treatment. In our case, pleural drainage and adjustment of anti-tuberculosis and antibiotic treatment based on susceptibility testing resulted in a favorable outcome. However, this unusual association of these germs in an immunocompetent patient underlines the need for increased vigilance in the management of pleural infections.

Conclusion

The present case highlights the challenges and lessons learned in the management of a pyothorax of tuberculous origin associated with *C. freundii* infection. Clinical symptomatology is nonspecific, and analysis of the effusion fluid is necessary for accurate and early diagnosis. Good collaboration between clinician and biologist is essential to ensure proper therapeutic management of patients and to improve their prognosis.

Consent

Written informed consent has been obtained from the patient for publication of this case report and accompanying images.

Ethical approval

It does not apply to

Reference

1. Souhi Hicham et al. Tuberculous pyo-pneumothorax: about 18 cases. Pan African Medical Journal. 2016; 24:26.
2. Janda JM, Abbott SL, Cheung WKW and Hanson DF. Biochemical identification of citrobacteria in the clinical laboratory, *Journal of Clinical Microbiology*, 1994; 32(8):1850-54.
3. Lavigne JP, Defez C, Bouziges N, Mahamat A, Sotto A. Clinical and molecular epidemiology of multidrug-resistant bacteria *Citrobacter* Infections with *P. spp.* in a French university hospital. *Eur J Clin Microbiol Infect Dis* 2007; 26(6):439-41.
4. Fantin B., Touaty E.: Purulent pleurisy. *Encycl Med Chir, Poumon* 1988; 60(41):1-15.
5. Warnow IE, Ayoola YA, Daniel A, Raymond MP, Abubakar ML, Adeniji RY. *Citrobacter freundii*: A Cause of Cardiac Tamponade and Empyema Thoracis in a Nigerian Child. *J Cardiovasc Echogr*. 2020; 30(2):121-123.

6. Diego Andrés R.L.: Empyema necessitatis due to *Citrobacter freundii*: Case report. *Rev. Fac. Med.* 2018; 66 (4): 639-42
7. Mohanty S, Singhal R, Sood S, Dhawan B, Kapil A, Das BK. *Citrobacter* infections in a tertiary care hospital in northern India. *J Infecter.* 2007; 54:58-64.
8. Kim BN, Woo JH, Ryu J, Kim YS. Extended-spectrum cephalosporin resistance and mortality in patients with *Citrobacter freundii* bacteremia. *Infection* 2003; 31:202-7.
9. Drelichman V, Band JD. Bacteremia due to *Citrobacter diversus* and *Citrobacter freundii*. Incidence, risk factors and clinical outcome. *Arch Intern Med* 1985; 145:1808-10.
10. Liu LH, Wang NY, Wu AY, Lin CC, Lee CM, Liu CP. *Citrobacter freundii* Bacteremia: mortality risk factors and prevalence of resistance genes. *J Microbiol Immunol Infect* 2018; 51:565-72.
11. Shih C.-C. Shih, Chen Y.-C. Chang S.-C. , Luh K.-T., Hsieh W.-C. Bacteremia due to *Citrobacter* species: importance of primary intra-abdominal infection. *Clinical Infectious Diseases*, 1996; 23 (3): 543-549.
12. Shahid M. *Citrobacteriapp.* Simultaneously harboring bla-CTX-M, blaTEM, blaSHV, blaampC and the insertion sequences IS26 and orf513: an evolutionary phenomenon of recent concern for antibiotic resistance, *Journal of Clinical Microbiology*, 2010; 48 (5): 1833-1838.

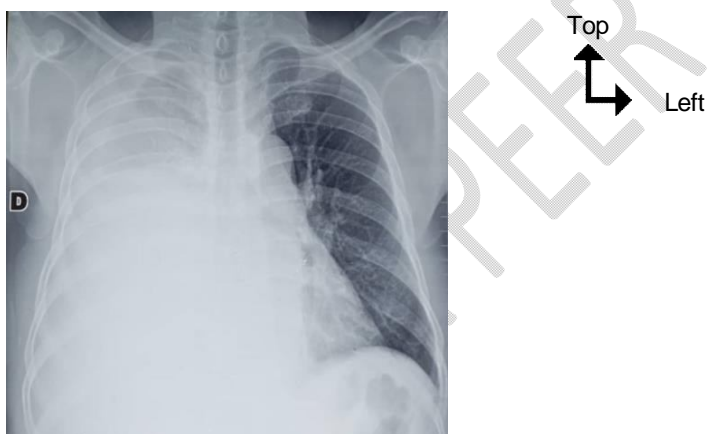


Figure1: Frontal upright chest X-ray showing homogeneous opacity without air bronchogram occupying almost the entire right hemithorax, suggesting pleurisy of great abundance.

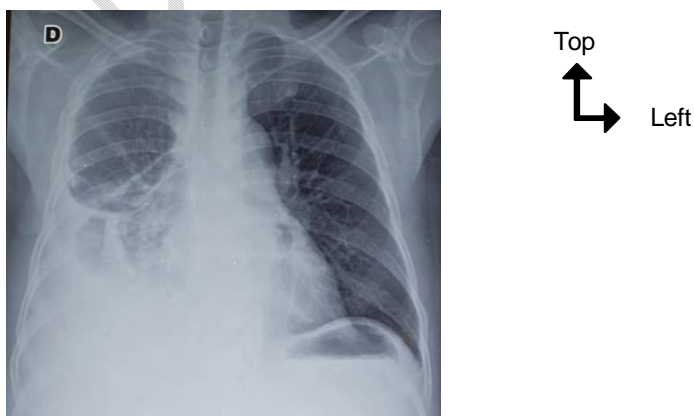


Figure 2: Front and upright chest X-ray showing favourable evolution of pleurisy on the right after placement of a chest drain (right basal homogeneous opacity filling the right cardiothoracic and cardiophrenic cul de sacs).

UNDER PEER REVIEW