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► **To cite this version:**

Marguerite Monié, Laurence Drieux, Bernadette Nzili, Michèle Dicko, Catherine Goursot, et al.. *Klebsiella pneumoniae necrotizing fasciitis of the leg in an elderly French woman*. *Clinical Interventions in Aging*, 2014, 9, pp.1171-1174. 10.2147/CIA.S60812 . hal-01313003

HAL Id: hal-01313003

<https://hal.sorbonne-universite.fr/hal-01313003>

Submitted on 9 May 2016

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Klebsiella pneumoniae necrotizing fasciitis of the leg in an elderly French woman

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Abstract: *Klebsiella pneumoniae* necrotizing fasciitis is a rare infection in regions outside of Asia. Here, we present a case of necrotizing fasciitis of the leg caused by *K. pneumoniae* in a 92-year-old French woman hospitalized in a geriatric rehabilitation unit. The patient initially presented with dermohypodermatitis of the leg that developed from a dirty wound following a fall. A few hours later, this painful injury extended to the entire lower limb, with purplish discoloration of the skin, bullae, and necrosis. Septic shock rapidly appeared and the patient died 9 hours after the onset of symptoms. The patient was Caucasian, with no history of travel to Asia or any underlying disease. Computed tomography revealed no infectious metastatic loci. Blood cultures showed growth of capsular serotype K2 *K. pneumoniae* strains with virulence factors RmpA, yersiniabactin and aerobactin. This rare and fatal case of necrotizing fasciitis caused by a virulent strain of *K. pneumoniae* occurred in a hospitalized elderly woman without risk factors. Clinicians and geriatricians in particular should be aware of this important albeit unusual differential diagnosis.

Keywords: necrotizing fasciitis, *Klebsiella pneumoniae*, elderly

Introduction

First described by Hippocrates in the fifth century BC, the term “necrotizing fasciitis” was coined by Wilson in 1952.^{1,2} Necrotizing fasciitis is an acute, progressive, invasive, and severe infection that spreads along fascial planes, producing inflammation and necrosis of the adjacent muscle, subcutaneous fat, and skin. The incidence of necrotizing fasciitis is about 4 per million world population, and mortality rates as high as 73% are noted.³ Necrotizing fasciitis is classified into two types: type 1 polymicrobial necrotizing fasciitis (a mix of aerobic and anaerobic bacteria) and type 2 monomicrobial necrotizing fasciitis, caused mainly by *Streptococcus pyogenes* but also by *Klebsiella pneumoniae*.⁴ Initial empiric broad-spectrum antibiotic coverage is needed in cases of necrotizing fasciitis, directed against aerobic Gram-positive cocci, Gram-negative rods, and a variety of anaerobes as recommended by the Infectious Diseases Society of America.⁵ *K. pneumoniae* is an enteric Gram-negative rod mostly implicated in hospital-acquired urinary tract infections, pneumonia, septicemia, and intra-abdominal infections. In Asia, *K. pneumoniae* necrotizing fasciitis was reported for the first time in 1996 in patients with comorbidities including diabetes mellitus, hepatobiliary disease, malignancy, and acquired immunodeficiency syndrome.⁶⁻¹¹

Case report

A 92-year-old French woman with a history of hypertension, atrial fibrillation, and dementia with Lewy bodies (Mini-Mental State Examination score 23/30) was initially admitted to an acute geriatric unit at La Pitié Salpêtrière University Hospital,

Paris, France, following regular falls at home. Her falls were due to sick sinus syndrome (bradycardia of 30 beats per minute, necessitating implantation of a pacemaker), and orthostatic hypotension. The patient was then transferred to a geriatric rehabilitation care unit at Charles Foix Hospital in the Paris area. She was clinically stable during her stay in the rehabilitation unit, and her medication was rabeprazole and mianserin. An initially clean 2 cm wound was noticed on the right leg upon her arrival at the rehabilitation care unit. Initially no fever or inflammation was reported, and the wound was managed with local antiseptic dressings and daily monitoring.

At 9 am on day 28, the patient developed fever with erythema and edema of the right leg, and lymphangitis ascending from the wound. Dermohypodermatitis was diagnosed and antimicrobial treatment was started with intravenous amoxicillin 3,000 mg/day. A venous Doppler was performed and did not show thrombosis. At 3 pm, the injury extended to the entire lower limb, with purplish discoloration of the skin, bullae, and necrosis. The patient complained of severe pain at this time, requiring administration of morphine. Leg movements were limited. This was suggestive of necrotizing fasciitis of the right leg.

Blood cultures were performed and empiric broad-spectrum antibiotic therapy was commenced. Amoxicillin was switched for an intravenous combination of piperacillin 8 g/day and tazobactam 1 g/day and intravenous gentamicin 150 mg/day. The patient's condition rapidly deteriorated. Vitals included a blood pressure of 93/50 mmHg, a heart rate of 91 beats per minute, a body temperature of 34.3°C, a respiratory rate of 32 breaths per minute, and an oxygen saturation of 84% in ambient air. Reduced consciousness was noted. In the context of a distended abdomen and dyspnea, a computed tomography scan was performed, but revealed neither pneumoniae nor abdominal or pelvic infection.

Laboratory findings were as follows: white cell count, 4.6 cells/mm³; hemoglobin, 13.0 g/dL; platelet count, 15.1×10⁴ cells/mm³; C-reactive protein, 70 mg/dL; blood glucose, 1.4 mmol/L; procalcitonin, 43 ng/mL; troponin, 3.73 µg/L; pH 7.19; HCO₃⁻, 14.4 mmol/L; and blood lactate, 9.0 mmol/L. Urine analysis showed no infection.

The patient developed septic shock requiring fluid challenge. Extension of the necrotic disease process to the entire lower limb and her precarious medical condition prompted transfer to La Pitié Salpêtrière Hospital for urgent aggressive surgical debridement of her necrotic tissues and appropriate multimodal therapy, including mechanical ventilation, inotropic support, and antibiotic administration in an

intensive care unit. Unfortunately, the patient died of septic shock at 6 pm upon arrival at La Pitié Salpêtrière Hospital.

Bacterial investigation

Blood cultures were incubated in an automated BacT/ALERT system (Organon Teknika, bioMérieux, Inc, Durham, NC, USA) and grew *K. pneumoniae*. On blood agar, the isolate grew as hypermucoviscous colonies and showed a positive string test (Figure 1). This isolate harbored the wild-type resistant phenotype of *K. pneumoniae*, ie, resistance to amoxicillin, piperacillin, and ticarcillin. A multiplex polymerase chain reaction was performed to determine the capsular serotype of the strain.^{12,13} The presence of known virulence factors was determined by polymerase chain reaction using primers described elsewhere.¹⁴ Two reference strains of capsular serotypes K1 (NTUH K2044) and K2 (CG43) were used as controls.¹⁵ The isolate was the capsular K2 serotype and carried the regulator of the mucoid phenotype RmpA, and two siderophores, ie, aerobactin and yersiniabactin. Multilocus sequence typing was performed using the international multilocus sequence typing scheme from the Institut Pasteur, Paris, France (<http://www.pasteur.fr/mlst>) and revealed that the isolate belonged to sequence type ST86.

Discussion

We report here a rare French case of necrotizing fasciitis caused by *K. pneumoniae*, which is a common causative pathogen in monomicrobial necrotizing fasciitis in Asia, especially in Taiwan, in patients with risk factors.^{16,17} Some cases have been documented in Europe and the USA, mainly in patients who had travelled to Asia or were of Asian descent.^{7,8,18–20} The majority of cases described to date have been in Asians, raising the question of a genetic predisposition versus geographic strain acquisition.²¹ Our patient was

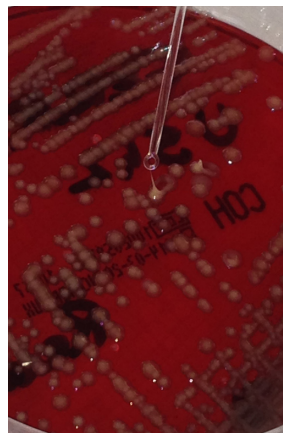


Figure 1 Hypermucoviscous *Klebsiella pneumoniae* colonies with positive string test.

a Caucasian woman who had not visited an endemic Asian area before the onset of infection. However, on review of her social history, she had lived in Paris' Chinatown and used to go to Asian restaurants in her neighborhood one year prior to her presentation. Her grandson, whom she met with frequently, used to travel to China for work. Is it possible that her acquisition of this *K. pneumoniae* was via food transmission or cross transmission? Epidemiologic factors are still being defined. Colonization, particularly intestinal colonization, appears to be a critical step leading to infection, although the route of entry remains unclear. Unfortunately, the patient was not screened for gut colonization with *K. pneumoniae*.

Moreover, this patient had *K. pneumoniae* necrotizing fasciitis without predisposing medical factors identified by her history, biology, or imaging (computed tomography).⁷⁻¹¹ No apparent underlying disease was identified, except for her very advanced age. Reasons for an increased susceptibility to *K. pneumoniae* necrotizing fasciitis in the elderly could include immunosenescence and malnutrition, as well as a large number of age-associated physiological changes.^{22,23} To the best of our knowledge, *K. pneumoniae* necrotizing fasciitis has not been reported previously in such an elderly patient.^{6,9,16,18,20}

In our patient, the necrotizing fasciitis occurred during hospitalization in a geriatric rehabilitation care unit and was considered health care-associated. Less than 12 hours elapsed between the onset of symptoms and the fatal outcome. This fulminant case is consistent with previous reports of monomicrobial *K. pneumoniae* necrotizing fasciitis rapidly leading to septic shock (within 72 hours).²⁴ As in other patients, systemic complications resulted in a fatal outcome, with no benefit from prompt and appropriate treatment with antibiotics and surgical debridement.²⁵ Advanced age, anemia, and thrombocytopenia are considered to be risk factors for mortality,²⁶ and *K. pneumoniae* necrotizing fasciitis has a poor prognosis in the elderly, as highlighted in this report. Important pharmacokinetic and pharmacodynamic changes also occur with advancing age.²⁷

Although no skin biopsy was performed, the leg wound was suspected to be the primary site of infection. The preceding local injury was probably the result of minor trauma in this patient, who was known to have falls. A systematic study of monomicrobial *K. pneumoniae* necrotizing fasciitis showed that the initial infectious site was often on the lower extremities;¹⁶ however, no preceding local factor was identified in half of the cases, and the infection showed a hematogenous spread, unlike the present case.^{16,18}

The bacteriological findings of a K2 serotype and virulence factors RmpA, yersiniabactin and aerobactin are consistent

with the epidemiological data. The K2 serotype reported in this case seems to be observed more often outside of Asia than the K1 serotype.²⁸ The K2 serotype also seems less likely to be responsible for distant abscesses than K1.²⁹ Our case can be added to the previous ones, and underscores the invasive and severe infectious nature of K2 *K. pneumoniae*.^{18,30,31}

Conclusion

Here we report a rare case of fatal necrotizing fasciitis from a leg wound caused by virulent *K. pneumoniae* in a 92-year-old French woman. No risk factors were identified. Advanced age, already considered to indicate a poor prognosis, could be a risk factor for developing *K. pneumoniae* necrotizing fasciitis. A combination of our aging population and increased travel may explain the spread of this emerging worldwide infectious disease.^{32,33} Clinicians and geriatricians in particular should be aware that this unusual emerging pathogen may be involved in the pathogenesis of necrotizing fasciitis and requires prompt and appropriate therapy.^{32,34}

Acknowledgments

Reference strains were kindly provided by S Brisse, Institut Pasteur, Paris, France. The authors thank S Wilks and S Curtis for English editing and language revision.

Disclosure

The authors report no conflicts of interest in this work.

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