

# A case of invasive infection caused by a highly virulent strain of *Klebsiella pneumoniae* displaying hypermucoviscosity in a patient with hepatic involvement without liver abscess

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## SUMMARY

*Klebsiella pneumoniae* is an opportunistic nosocomial pathogen belonging to the *Enterobacteriaceae* family that is associated with a wide range of infections. In the 1980s a new hypervirulent (hypermucoviscous) variant of *Klebsiella pneumoniae* (hvKP) emerged in southeast Asia and is now increasingly spreading to Western countries due to an invasive syndrome. hvKP isolates can cause serious, life-threatening community-acquired infections in younger healthy hosts, including liver abscess, pneumonia, meningitis and endophthalmitis. We present a case of an 83-year-old man who was examined in the Medicine Department of San Camillo Hospital in Treviso for dehydration in gastroenteritis. Since he presented fever on admission, microbiological investigations were performed and

empiric antibiotic therapy with cefotaxime was started. Blood analysis showed a high level of cholestasis indexes and transaminases. Blood cultures were found positive for *K. pneumoniae* that showed hypermucoviscosity. The hypermucoviscous phenotype of this *K. pneumoniae* isolate was easily identified by the "string test". Abdominal computed tomography and ultrasonography did not show presence of liver abscesses. After a few days of antibiotic therapy the patient's clinical condition improved. Correct microbiology identification of this kind of strain was essential for appropriate clinical management.

**Keywords:** *Klebsiella pneumoniae*, hypervirulent, hypermucoviscous, string test, clinical management.

## INTRODUCTION

*Klebsiella pneumoniae* is an opportunistic nosocomial pathogen with a worldwide distribution belonging to the *Enterobacteriaceae* family that is associated with a variety of infections [1, 2]. Although the most common clinical syndromes

associated to this kind of microorganism infections involve the urinary tract, lungs, abdominal cavity, intra-vascular devices, surgical sites and soft tissues, in the past two decades a new type of invasive syndrome has been associated to characteristic strains of *K. pneumoniae* exhibiting a particular hypermucoviscous phenotype. These strains emerged primarily in Southeast Asia and the syndrome they cause shows a hepatic involvement and usually is characterized by bacteremia, liver abscesses and metastatic infection [3-5]. The characteristic liver abscesses are called primary or

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cryptogenic because they occur in the absence of biliary tract disease or another focus of infection within the abdomen, so the source of the infection is unknown [6]. Extrahepatic complications due to bacteremic dissemination, such as endophthalmitis, meningitis and abscess formation, have also been reported [4].

Even if the first cases were reported in 1980s from Taiwan, subsequently there were reports of this disease from other East Asian countries and now they are emerging also in western countries [7-13]. The hypermucoviscous phenotype of this *K. pneumoniae*, also called hypervirulent *K. pneumoniae* (hvKP), is thought to contribute to invasive virulence by impairing phagocytosis [7,9,11,14]. The molecular mechanism that causes this kind of infections involves multiple factors, furthermore, several studies have indicated that hypermucoviscosity is associated with the mucoviscosity-associated gene A (*magA*) and the regulator of mucoid phenotype A (*rmpA*) genes [4-6, 15-17].

All the isolates grow in sticky colonies on agar plates and they can be easily identified using a "string tests". This test is positive when an inoculation loop or needle is able to generate a viscous string >5 mm in length by stretching bacterial colonies on an agar plate [11].

We herein report a case of an Italian patient with monomicrobial bacteremia caused by an infection with hvKP, admitted in our hospital for dehydration in gastroenteritis associated with fever and alteration of liver function tests.

## ■ CASE REPORT

An 83-year-old man was examined in the Emergency Department of Treviso Hospital for dysphagia, nausea, vomiting, aphasia and mental confusion. Physical examination did not show any abnormalities and chest X-ray was negative. So, he was transferred to the Medicine Department of San Camillo Hospital in Treviso with a diagnosis of dehydration due to gastroenteritis of unknown etiology. At the admission, the blood tests revealed a white blood cell count of 10,500/mm<sup>3</sup>, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values of 187 and 314 U/L respectively, gamma-glutamyl transpeptidase (GGT) of 527 U/L, alkaline phosphatase (ALP) level of 139 U/L and total bilirubin of 4.5

mg/dL, moreover he presented a concentration of ultrasensitive C-reactive protein of 20.45 mg/dL, while the serologic viral markers (anti-HCV and HBsAg) were negative. We also extended our investigation to other "minor" viral etiology such as EBV and CMV that demonstrated the presence of IgG antibodies for CMV, VCA and EBNA, while Anti-CMV IgM, Anti-VCA IgM and Anti-EA IgG resulted negative, showing a previous infection for both of them.

Given that at the admission to San Camillo Hospital the patient presented fever (38°C), blood (two sets) and urine cultures were carried out and empiric antibiotic therapy with cefotaxime (2g bid IV) was started. Blood samples were incubated into BD BACTEC™ 9050 Blood Culture System. Urine culture was negative. After 48 hours, the BACTEC™ System gave alarm for bacteria growth in all the blood samples and then Gram staining was performed showing presence of Gram-negative rods. All the positive samples were cultured on BD Chocolate Agar (GC II Agar with IsoVitaleX), BD Columbia Agar with 5% Sheep Blood and BD MacConkey II Agar at 37°C for 24 h.

Colonies grown on plates were identified as *Klebsiella pneumoniae* after biochemical identification with Sensititre™ GNID plates using Sensititre™ ARIS® System (ThermoScientific, TREK Diagnostic Systems). Given that the colonies showed a mucoid morphology, the "string test" was performed with a sterile loop: stretching of bacterial colonies on agar plate showed the formation of a viscous string with a length exceeding 5 mm (string test positive), confirming the hypermucoviscous phenotype.

Antimicrobial susceptibility testing was carried out with broth microdilution method using Sensititre™ ITGNEGF panel (ThermoScientific, TREK Diagnostic Systems), that provide results related to the minimum inhibitory concentration (MIC). All MIC values were evaluated with EUCAST Clinical Breakpoint for bacteria (v 7.1) [18]. The strain was susceptible to all tested antimicrobials (amoxicillin/clavulanic acid, cephalosporins, carbapenems, aminoglycosides, fluoroquinolones and trimethoprim/sulfamethoxazole) including cefotaxime, so the therapy remained unchanged. Chest X-ray and head computed tomographies (CTs) did not indicate any foci of infection. Even if abdominal CT and ultrasonography did not show liver abscesses, hepatic involvement was

demonstrated by the gradual improvement of clinical symptoms and the progressive reduction of liver enzymes levels after the antibiotic therapy was started. No abnormal changes in the bile ducts were observed in the abdominal CT and ultrasonography showed marked signs of cholecystectomy. Indeed, at discharge, after a two-week course of treatment fever disappeared and blood test analysis showed a decrease of the inflammation markers, specifically we found a white blood cell count of 4,860/mm<sup>3</sup>, AST and ALT values of 47 and 96 U/L respectively, GGT of 279 U/L, ALP level of 117 U/L and a concentration of ultrasensitive C-reactive protein of 0.77 mg/dL. Total bilirubin was within the normal range after 5 days of treatment (0.9 mg/dL).

## ■ CONCLUSIONS

Even if the first case of hypervirulent (hypermucoviscous) variant of *K. pneumoniae* infection was identified in southeast Asia in 1980s, recently also in Western countries, including Italy, it is possible to see an increase of cases of severe infections (mainly liver abscess with bacteremia) caused by this kind of strains. For this reason, an immediate and specific phenotypical characterization is important because these strains are capable of causing severe infections of community origin, even in previously healthy young patients.

Although epidemiologic features are still being defined, colonization, particularly intestinal colonization, appears to be a critical step leading to infection. However, the route of entry remains unclear. In case of discovery of strains with this phenotype in blood culture, it could be helpful to immediately communicate with the clinician who is in charge of the patient and to suggest the execution of a liver ultrasonography for the detection of abscess lesions or further diagnostic investigations. The "string test," which reflects the hypermucoviscous phenotype, is the best laboratory-based surrogate method presently available because an unequivocal genotypic and/or phenotypic markers for hvKP is lacking. However, this test is not routinely performed in clinical laboratories so the incidence of hvKP infection and the clinical spectrum of disease could be underestimated. In fact, in a number of reports describing *Klebsiella* infection, information on the character-

istics needed to assist in differentiating between classic *K. pneumoniae* and hvKP are lacking [11]. In literature, most of hvKP infections present mainly liver abscess with bacteremia and some cases without liver abscess syndrome, but with involvement of other body districts, are described [19-20]. The distinctive trait of our case report is that even if abdominal CT and ultrasound examination did not show liver abscess, the gradual improvement of clinical symptoms and the progressive reduction of liver enzymes levels after antibiotic therapy let to think that there was a relevant hepatic involvement caused by the hvKP strain. With this report, we want to emphasize the importance of a timely communication and the interaction between microbiologist and clinicians in order to have a better patient management, especially when infection is due to strains with particular features.

## Conflict of interest and funding source

None declared

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