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First Case of Liver Abscess in Scandinavia Due to the International Hypervirulent *Klebsiella Pneumoniae* Clone ST23

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Abstract: This is the first case report from Scandinavia of a pyogenic liver abscess caused by a *Klebsiella pneumoniae* isolate belonging to the international hyper virulent clone ST23. The patient, an 85-year old Caucasian, had no history of foreign travel or any classical predisposing factors for infection. The isolate was hypermucoviscous of capsular serotype K1 and carried the virulence factors aerobactin, allS, kfu and rmpA.

Keywords: *Klebsiella pneumoniae*, liver abscess, ST23.

INTRODUCTION

Klebsiella pneumoniae is a well known opportunistic nosocomial gram-negative pathogen often associated with a history of alcohol abuse or diabetes mellitus [1]. However, recently a new pattern of community acquired infections has evolved in patients from Taiwan and other Asian countries. These infections are characterised by being invasive and often metastatic with a particularly high frequency of pyogenic liver abscesses [2-7].

Traditionally the somatic antigen (O-antigen, O1) and the capsular antigen (K-antigen, K1 and K2) have been regarded as the most important *K. pneumoniae* virulence factors [1]. Hypervirulent liver abscess isolates have also been shown to be associated with the specific virulence factors aerobactin, allS, kfu and rmpA [5, 8]. RmpA (regulator of the mucoid phenotype) is associated with hypermucoviscosity thereby making the organism resistant to phagocytosis. Aerobactin and kfu are involved in iron acquisition whereas allS is associated with aerobic and anaerobic allantoin metabolism and only found in K1 isolates [8-10]. The *magA* gene was originally proposed as a virulence factor but has been shown to be a constitutive part of the K1 capsule polysaccharide gene cluster [11].

Investigation of the population structure of *K. pneumoniae* by multilocus sequence typing (MLST) has revealed a clonal structure with the hypervirulent capsular serotype K1 isolates associated with pyogenic liver abscesses belonging to sequence type (ST) 23 [9, 12, 13]. In addition to Taiwan and Southeast Asia, sporadic cases of *K. pneumoniae* liver abscess, often connected with travel or migration, have been reported from USA, Canada, Spain, France, Belgium, and Sweden [14-24]. Only the cases from France and Poland have been investigated by MLST and the isolates shown belong to ST23 [23, 25]. This is the first case report of a pyogenic liver abscess caused by the hyper-virulent ST23 *K. pneumoniae* clone found in Scandinavia.

CASE REPORT

An 85-year old Caucasian man was admitted to the hospital with a history of 2-3 weeks of anorexia, fatigue, headache and dyspnoea. The patient had prior to hospitalization taken penicillin per os (p.o.) for seven days for pneumonia without effect. His only medical history was a pacemaker implementation one year previously, due to III degree AV-block. After admission the patient was treated with intravenous (i.v.) G-penicillin and gentamicin on suspicion of pneumonia and endocarditis. Chest X-ray and echocardiography were normal. Unfortunately, blood and urine cultures were taken after institution of antibiotics and showed no growth. Due to poor clinical response antibiotics were changed first to i.v. mecillinam on day 7, and later to i.v. cefuroxime on day 9.

Due to elevated alkaline phosphatase an abdominal ultrasound and CT were performed on day 14 showing an abscess measuring 10.5 x 7.2 x 8.7cm in the right liver lobe. By ultrasonic guided abscess drainage, 20 cubic cm of pus giving growth to *K. pneumoniae* was removed. Antibiotics were stopped after two days and the patient was discharged without any further treatment or follow up.

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The patient was re-admitted to the hospital 109 days later due to collapse at home. On suspicion of urosepsis he was treated with i.v. cefuroxime and later supplemented with gentamicin. Liver ultrasound showed no abscess, but as blood culture showed growth of *K. pneumoniae* a new CT scanning was performed. The CT scan showed a new liver abscess about 2 cm in diameter, in close relation to the original liver abscess. The original liver abscess area was reduced to about 3 cm in diameter, and was hypodense with possible signs of infections/edema. Ten days after admission antibiotics was changed to ciprofloxacin p.o. for 41 days. After discontinuation of antibiotics, the patient was followed weekly with blood samples, and was after one month declared free from infection, as both CRP and leukocytes had remained normal.

The patient had no history of foreign travel and also no contact with people from Southeast Asia. Eighteen months after the last follow up the patient was doing well and had no sign of relapse.

The *K. pneumoniae* blood isolate was hypermucoviscous as shown by the formation of a mucoviscous strings when a loop was passed through a colony. Capsular serotype was K1 and it belonged to ST23 as determined by the *K. pneumoniae* MLST scheme described by Diancourt *et al*. [26]. The isolate was positive for the following virulence factors: aerobactin, allS, kfu and rmpA as revealed by polymerase chain reaction using specific primers [27].

DISCUSSION

Historically, *K. pneumoniae* was seen as a primary pulmonary pathogen, clinically associated with community acquired pneumonia, characterized by sudden onset of high fever and hemoptysis ("currant jelly sputum") and often had a fatal outcome [2]. Studies from USA and elsewhere from the 1920s and onwards have shown that the incidence of community-acquired *K. pneumoniae* pneumonia has declined, although it can still be found, in *e.g*. South Africa [2, 15-17]. However, a new disease entity, with primary liver abscesses with metastatic spread in otherwise healthy patients caused by highly virulent strains of ST23, is seen with increasing frequencies in Southeast Asia [3, 6-8].

The finding of one of these virulent strains in a Danish patient, with none of the normal predisposing factors (DM or alcoholism) and without a travel history or known connection to persons of Southeastern Asia origin, can have at least two possible explanations: i) these strains are endemic, circulating at all times in low numbers in the community, or ii) our patient was part of an infectious chain with the ST23 clone, which we were unable to elucidate at the time. This clone has been found in faecal samples from healthy subjects in Hong Kong, Singapore, Taiwan and South Korea, which may at least partially explain the high incidence of *K. pneumoniae* liver abscesses in these regions [28, 29]. The clear association of most cases from USA and Europe with Asian origin or travel history speaks most strongly for possibility ii. The implication is that hypervirulent *K. pneumoniae* clones could develop into an important worldwide health problem. This should encourage clinical microbiology laboratories to be more vigilant and rapidly refer isolates suspected of belonging to these virulent clones to reference laboratories for further characterization. This case report also emphasizes on the importance of follow-up to ensure a proper treatment and response to antibiotics in liver abscess patients to avoid relapse.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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