



Invasive *Klebsiella Pneumoniae* Liver Abscess Syndrome. Analysis of Three Cases in Angola



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Abstract

Liver abscess is a disease that is defined as collection bordered by a fibrotic capsule in the hepatic parenchyma and its frequency and etiology varies according to its geographic latitude. *Klebsiella pneumoniae* (Kp) was described for the first time in Taiwan in 1980 and it rapidly spread through the east Asia. Due to migration of people from those countries to all the continents today there are cases in Europe, North America, South America and Australia. There is an especially virulent Kp serotype that causes a syndrome with high mortality rate due to its extrahepatic complications known as Hypervirulent Invasive *Klebsiella pneumoniae* Syndrome (HIKPS). We describe three patients with HIKPS, there are no similar cases known in Angola but in the African continent cases were reported in South Africa, Nigeria and Morocco. The Hypervirulent Invasive Kp Syndrome is a reality in Angola, generally associated to cryptogenic origin and diabetic patients, and is characterized by bacteremia with metastatic infection and even with an adequate treatment, it has a high morbidity and mortality rate. Initially its diagnosis can go unnoticed so a high index of clinical suspicion for an early diagnosis and management is important.

Keywords: Liver abscess; Hypervirulent *Klebsiella pneumoniae*

Abbreviations: Ksp: *Klebsiella* Specie; CT: Computed Tomography; Kp: *Klebsiella pneumoniae*; ERCP: Endoscopic Retrograde Cholangiopancreatography; HIKPS: Hypervirulent Invasive *Klebsiella pneumoniae* Syndrome

Introduction

Liver abscess is a disease that is defined as collection bordered by a fibrotic capsule in the hepatic parenchyma and its frequency and etiology varies according to its geographic latitude [1-3]. Generally, they are classified into two groups, pyogenic and amebic, but there are other etiologies such as *Mycobacterium tuberculosis* [4,5], fungal and parasites [2]. The etiology of pyogenic liver abscess has changed in the last few years due to scientific and technical advancements and strong antibiotics; Intraabdominal infection (appendicitis, diverticulitis) via portal vein used to be the most common cause in the last century but nowadays it was replaced by biliary tract infection in the last decades of the twentieth century [1-5].

First world countries report as a primary cause the biliary tract instrumentation (ERCP), reconstructive biliary surgery, hepatic transplant, treatment of liver tumor, interventional

radiology (chemoembolization) and radio ablation [1,5-8]. In Asia, the cryptogenic cause (apparently without etiological cause) is predominant, and in countries of Eastern Asia especially in Taiwan, the *Klebsiella pneumoniae* (Kp) substitutes the *Escherichia Coli* as the agent responsible of the formation of the pyogenic liver abscess in the last three decades [1-8]. Kp was described in Taiwan for the first time in 1980 and it rapidly spread through all east Asia reporting 23% in China, 52% in Hong Kong, 72% in South Korea [1]. As a result of the vast migration of people from those countries to all the continents, in nowadays series and isolated cases are reported in Europe, North America, South America and Australia [1-9].

There is a specific Kp virulent serotype that causes a syndrome with high mortality rate due to its extra-hepatic septic complications known as Hypervirulent Invasive liver Abscess

Syndrome with bacteremia, metastatic infection, peculiar ultrasound and Computed Tomography (CT) findings that are associated to its cryptogenic cause and diabetic patients [1-10]. Three cases with the invasive liver abscess syndrome associated to Kp were reported in our institution, we don't have knowledge of other similar cases reported in Angola but there were cases reported in other African countries such as South Africa [11], Nigeria [12] and Morocco [13].

The aim of the authors is to alert the medical community in the country and the rest of Africa about this dangerous syndrome responsible of high mortality rate.

Case Presentation

On table 1, described three patients with HIKPS, all Angolans, without travel background to Asian countries, all male between the ages of 39 and 65. Two of them were diabetic, the microbiological agent found was *Klebsiella specie* (Ksp), one of them was positive to Kp in the blood culture and pus culture collected from the liver

abscess.

The three patients had clinically and radiologically the HIKPS, characterized by bacteremia, metastatic infection, peculiar ultrasound and tomography characteristics which are going to be explained next. From the imaging point of view (ultrasound and abdominal tomography with contrast): the wall or capsule were poorly demarcated, were single, multilocular and with presence of gas in all patients. We could also prove distant metastasis (tomography diagnosis) in the three patients, been the most frequents in the lung, mediastinum, muscle groups, bone and brain as well as the hepatic and portal vein thrombophlebitis. One patient presented septic pulmonary thromboembolism, there was not rupture of the abscess into the abdominal cavity. The therapeutic used was the ultrasound guided percutaneous drainage and there was the necessity to evolve to a laparotomy in two of them. All patients evolved to multiple organ failure that led to their death.

Table 1: Clinical manifestation, epidemiology and imaging study of the patients.

Characteristics	Patient 1	Patient 2	Patient 3
Nationality	Angolan	Angolan	Angolan
Travel background to Ásia	No	No	No
Age	56	65	39
Gender	M	M	M
Diabetes Mellitus	No	Yes	Yes
Previous diseases (30 days)	Malária	Malária	Malária
Etiology	Cryptogenic	Cryptogenic	Cryptogenic
Microbiology abscess	<i>K Specie</i>	<i>K Specie</i>	<i>K Pneumoniae</i>
Microbiology hemoculture	Negative	<i>K Specie</i>	<i>K Pneumoniae</i>
Abscess capsule ultrasound or CT	Poorly demarcated	Poorly demarcated	Poorly demarcated
Number of abscesses	single	single	single
Uni ou multilocular	Multilocular	Multilocular	Multilocular
Abdominal cavity perforation	No	No	No
Presence of gas	Yes	Yes	Yes
Thrombophlebitis of portal and/or hepatic vein	No	Portal and hepatic	Portal
Septic pulmonary thromboembolism	No	No	Yes
Metastatic infection	Yes	Yes	Yes
Pleural effusion	Yes	Yes	Yes
Ultrasound guided percutaneous drainage	Yes	Yes	Yes
Exploratory laparotomy	No	Yes	Yes
Multiorgan failure	Yes	Yes	Yes
Death	Yes	Yes	Yes

Source: Patients clinical history. Multiperfil Clinic. Luanda. Angola.

Discussion

Klebsiella pneumoniae is a bacillar, Gram-negative bacteria, facultative anaerobic, non-motile and encapsulated, widely spread

through the environment and it grows in mammals' mucous surfaces; in human beings it colonizes the nasopharynx and the gastrointestinal tract [9]. *Klebsiella pneumoniae* is responsible for the infections of a variety of systems such as respiratory, urinary

and digestive, surgical site infections, cholangitis and peritonitis [14], generally associated to patients with medical history of alcohol abuse and diabetes [15].

In the majority of cases, pyogenic abscesses are polymicrobial and the *Escherichia coli* is the most frequent agent [16,17] and they respond well to a combined treatment of drainage with antibiotics. In the last century, mid '80s, pyogenic liver abscesses caused by specific hypervirulent *Klebsiella pneumoniae* strains appeared as an important epidemiologic problem in East Asia and nowadays they constitute the cause of more than 80% of the pyogenic liver abscesses in Asia [17,18]. In the last decade, cases of hypervirulent *Klebsiella pneumoniae* pyogenic liver abscesses were notified in the whole world [1-18] regardless of its Asian origin like in the three patients described in our study in which all of them were Angolans without travel background to those endemic countries.

Typically, *Kp pneumoniae* is responsible for the severe cryptogenic liver abscesses frequently associated to uncommon distant septic metastatic locations: endophthalmitis, meningitis, myositis, osteomyelitis among others in immunocompetent hosts [16,19]. Several studies have been demonstrating that the invasive *Kp* strains infect the liver through the portal circulation starting from the bacterial translocation of the intestinal epithelium [14,18-20]. It is interesting to comment that the studied patients has as a past medical history malaria by falciparum 30 days before the liver abscess diagnosis and according to studies made in rats by Denny and cols [2], infection by plasmodium have different effects on the homeostasis of the intestinal microbiota that could contribute to a enteric bacteremia associated to malaria.

Diabetes mellitus is considered as a risk factor for *Kp* liver abscess and its complications, it is proposed that hyperglycemia interferes in the polymorphs leukocytes chemotaxis and therefore compromises the phagocytosis of the K1 and K2 encapsulated

serotypes that are considered as hypervirulent strains [19] and it is related to a bad control of these patients glycemia as a possible cause of the metastatic septic complications [14,21].

In relation to the etiology, *Kp* liver abscesses rarely have a biliary, portal, pos surgical, traumatic, or tumoral cause, generally they have a cryptogenic cause. Studies in animals suggests that *Kp* crosses the intestinal barrier and produces the liver abscess [18,22]. Although a pathognomonic image hasn't been defined for the hypervirulent *Kp* liver abscess, they tend to present imaging characteristics of immaturity [6,23]. The Ultrasound shows solid masses with irregular or ill-defined margins with internal debris images and incomplete liquefaction [6,23].

The CT findings include thin walls or badly demarcated, septum ruptures, necrosed debris, presence of air that translates into a delay in the abscess maturity [6,23]. There is also described: single abscess, more solid than liquid, multilocular, with a high percentage of association to portal and hepatic vein thrombophlebitis [18,24,25]. Lee & cols [23] propose as a criteria to imaging diagnosis of *Kp* liver abscess, the presence of (1) thin walls, (2) necrosed debris, (3) metastatic infection and (4) absence of biliary pathology.

According to their study in the Asian population, the presence of three criteria has 98% of specificity. All studied patients in this article had the Lee and cols criteria (Figure 1-3). Generally, it is suggested ultrasound guided percutaneous drainage as the gold standard treatment although this procedure might be jeopardized by a predominance of solid areas, abscess immaturity that could lead to its failure and complement it with surgery (laparotomy or laparoscopy) as it happened with two of the patients in this study. Hsieh & cols [26] suggest that an aggressive hepatic resection could have a better prognosis than a percutaneous drainage in those patients that are severely ill.



Figure 1: Liver abscess in the left lobe, poorly defined walls, presence of cellular debris and gas inside.



Figure 2: Liver abscess in the right lobe, poorly defined walls, presence of cellular debris and gas inside.

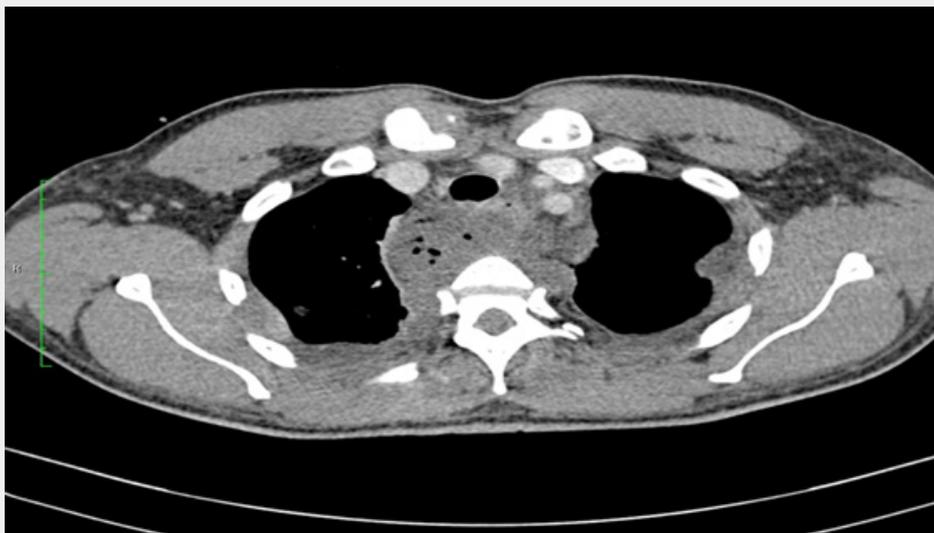


Figure 3: Mediastinal collection with gas inside (metastatic septic complication).

There is preference to third-generation cephalosporin, there can be also used ampicillin-sulbactam, aztreonam, and a quinolone [19]; though beta lactamase producer strains are not usual, in these cases the drug of election are the carbapenems.

The morbidity and mortality of the invasive Kp liver abscess syndrome is substantial, with a mortality between 35 and 42% [14-25]. Our study has several limitations as the sample is scarce, with limitations in isolating the Hypervirulent Kp (serotypes K1 and K2). Nevertheless, the hypervirulent invasive Kp liver abscess syndrome has a cryptogenic etiology, associated to diabetic patients, with characteristic imaging criteria (Lee criteria) with metastatic infections that were present in all three of the reported patients. Despite the appropriate treatment, including the

abscess drainage percutaneous or surgical in combination with aggressive antibiotics, the result was not good. The metastatic septic complication that led to the septic shock and multiple organ failure contributed to its fatal outcome.

Conclusions

The invasive liver abscess syndrome secondary to *Klebsiella pneumoniae* is a reality in Angola usually associated to cryptogenic cause and diabetic patients. It is characterized by bacteremia with metastatic septic complications that even with an adequate treatment has a high morbimortality. Its diagnosis could initially go unnoticed so a high index of clinical suspicion for an early diagnosis and management is important.

Recommendations

a) It is important for the medical community not only in Angola but also in the rest of the African continent and the world to take into consideration this unusual and dangerous diagnosis in our daily practice due to the extra-hepatic complications that are generally fatal.

Microbiologists must be alert and know that a positive culture for Kp with hyper viscosity is highly suggestive of invasive Kp, same with radiologists when they write the medical reports of peculiar ultrasonography and tomography images (Lee criteria) they should immediately notify the medical doctors to consider the possibility of this syndrome.

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