Caruntu and Radu, J Clin Case Rep 2018, 8:5
DOI: 10.4172/2165-7920.10001121

Journal of Clinical Case Reports

Case Report Open Access

Sepsis with *Klebsiella pneumoniae* Complicated with Renal Abscess in Immunocompetent Host: A Case Report

Caruntu FA and Radu MN*

Department of Medicine, National Institute for Infectious Diseases, Adulti Grozovici Street, Romania

Abstract

Introduction: The inflammatory response to an infectious trigger may evolve to sepsis and septic shock most frequently at the extremes of age and in immunosuppressed patients. *Klebsiella pneumoniae* is a gram-negative bacillus that is part of the saprophytic flora of the digestive tract. Bacteremia with commensal germs may be secondary to a localized infectious event from where bacteria crosses vascular endothelium.

Case presentation: We are presenting the case of a 17-years-old patient, admitted to the National Institute of Infectious Diseases "Prof. Dr. Matei Bals" in June 2017, on the 4th day of illness. Symptoms started 8 hours after meal with nausea, vomiting, fever, and temporo-spatial disorientation. Clinical manifestations and paraclinical investigations have established the diagnosis of sepsis with *Klebsiella pneumoniae*.

Results: Although antibiotic treatment was promptly initiated according to the antibiogram, complications of bacteremia still occurred, and patient developed renal abscess. Evolution was favorable under antibiotic treatment and correction of modified biological parameters, the patient being discharged cured after 21 days.

Discussion: The particularity of the case is given by the immunocompetent profile of the patient who developed sepsis with commensal germ. Intestinal inflammation secondary to a food poisoning has facilitated bacterial translocation. Bacterial lipopolysaccharide (LPS) is transported by binding proteins to CD14 receptor from the effector cells (neutrophils, monocytes, macrophages). This receptor facilitates the interaction between LPS and TLR 4. As a result, synthesis of proinflammatory factors: cytokines, chemokines, prostaglandins are stimulated.

Conclusion: *Klebsiella pneumoniae* causes an increased level of endotoxemia. Consequently, the risk of sepsis is higher even in immunocompetent patients.

Keywords: Diagnosis; Gram negative bacillus

Introduction

Klebsiella pneumoniae, part of Enterobacteriaceae family, is a Gram negative commensal bacillus of the intestinal tract that represents the second cause of bacteremia after *E. coli*. The bacteria cell wall contains the lipopolysaccharide endotoxin as a virulence factor responsible for the systemic inflammatory reaction. Bacteremia with commensal germs occurs after the intestinal epithelium is affected, the acute phase reaction being already started. Bacterial translocation is facilitated by the initial local inflammation which results in bacteremia [1].

Case Presentation

A 17-years-old female patient without a past medical history is transferred in National Institute of Infectious Diseases "Prof. Dr. Matei Bals" during June 2017 on the 4th day of the disease from a Malta's hospital where she was admitted for a digestive symptomatology occurred 8 hours after meal. The onset was with epigastralgia, afterwards, nausea and vomiting (about 11/24 hours) accompanied by chills and fever (39°C) and intolerance to oral nutrition and hydration.

After about 24 hours, she was admitted to the hospital with altered general state, fever (39.4°C), abdominal discomfort more accentuated in the epigastrium, signs of dehydration present: dehydrated skin and mucous membranes, hypotension corrected by intravenous rehydration and temporo-spatial disorientation.

Laboratory samples revealed significant neutrophilia (29,000 cells/mm^3), inflammatory syndrome (C-reactive protein - 142 mg/dl), normal liver tests and renal function, pulmonary radiography with no pathological changes and normal abdominal ultrasound.

Results

Antibiotic and hydration treatments have been initiated. 24 hours after admission, the patient maintained febrile with altered general state, high inflammatory syndrome (prot C reactive-348 mg/dl) and neutrophilia. The patient developed minimal anemia (Hb-11.2 g/dl) and thrombocytopenia (PLT -110 000/mm^3). Hemocultures came out positive with *Klebsiella pneumoniae* susceptible to the administered antibiotic.

The patient is transferred to INBI on the 4th day of disease with improved general condition, with low grade fever, pale teguments and mucous membranes, peripheral and upper limbs edema, soft embossed subcutaneous epigastrium tissue, meteorized abdomen sensitive during deep palpation, liver palpable 3 cm below costal margin, palpable spleen lower pole, free, painless percussion of kidney loins, no neck stiffines, slightly disorientated, focus difficulty, retrograde amnesia (she does not remember important events from the previous day) and somnolence. The urine output was normal and intestinal transit is slowed down.

The laboratory tests on the day of admission up revealed: improved neutrophilia (7020 cell/mm^3), anemia (Hb-11g/dl) and

***Corresponding author:** Radu MN, Department of Medicine, National Institute for Infectious Diseases, Adulti Grozovici Street, Bucharest, 021105 Romania, Tel: 0040722597702; E-mail: drmnradu@gmail.com

Received May 16, 2018; **Accepted** May 24, 2018; **Published** May 29, 2018

Citation: Caruntu FA, Radu MN (2018) Sepsis with *Klebsiella pneumoniae* Complicated with Renal Abscess in Immunocompetent Host: A Case Report. J Clin Case Rep 8: 1121. doi: 10.4172/2165-7920.10001121

thrombocytopenia (98000/mm^3) with D-dimers (4 × N), persisting inflammatory syndrome (C reactive protein - 201mg/dl), Fibrinogen - 670 mg/dl) with positive procalcitonin (10 ng/ml). Symptoms of cholestasis with GGT-6 × N and normal transaminases, pancreatic enzymes 2 × N, increased triglycerides-2.5 × N, severe hypoproteinemia (4.9 g/dl) with hypoalbuminemia, normal blood sugar, urine protein traces, but with 24 h urinary protein normal, negative uroculture.

There were performed:

• Abdominal ultrasound - mild hepatomegaly with left hepatic lobe -7.3 cm and right hepatic lobe -16 cm.

• Upper endoscopy - normal.

• Abdominal radiography – abnormal intestinal gas.

• Pulmonary radiography – normal

Antibiotic treatment, hydro-electrolytic rebalancing and hypoproteinemia correction are continued. The patient still had food intolerance but improves fluid intolerance.

On the 5th day of disease, physical asthenia, somnolence and abdominal meteorism are maintained with intestinal transit occurring after micro-enema. The patient accused discomfort in the right upper quadrant of the abdomen.

It was decided to perform abdominal CT that shown increased liver size (22.5 cm cranio-caudal diameter) with slightly non-homogeneous structure in the native and post administration of iodine-based contrast material by the presence of periportal hypodensities that surround vascular axis suggestive for edema; no intrahepatic and extrahepatic bile ducts dilatation; pericholecystic low volume fluid; splenomegaly 14cm; the left kidneys presents in the renal cortical area para-fluid densities in the middle third of the posterior valve (9/5 mm and 8/4 mm) and in the lower third of the posterior valve (20/12 mm); lombo-aortic and interaortico-cave lymph nodes.

Considering the complication of bacteremia with renal abscess development, heart ultrasound was performed, and endocarditis has been excluded. Anemia and thrombocytopenia, inflammatory syndrome (C reactive prot-197 mg/dl), altered values for pancreatic and triglyceride enzymes, hyporeninemia, presence of D-dimers, cholestasis accentuation (GGT-8 × N, BT-1.5 × N), hepatic cytolysis (ALT-2.5 × N and AST-3 × N) were maintained.

During the hospitalization, the patient's progression was slowly favorable. Because of the left kidney abscess development, antibiotic treatment was continued for 21 days. Repeated urocultures during hospitalization were negative. Hemocultures after antibiotic initiation were negative. The inflammatory syndrome normalized in the 16th day. The patient is discharged cured after 21 days of admission.

Discussion

Although antibiotic treatment was early initiated and blood cultures became rapidly negative, the systemic inflammatory response was secondary to endotoxemia. Like *Neisseria meningitidis*, *E. coli* and Klebsiella pn produce high levels of endotoxins. It seems that the risk of developing sepsis is not directly correlated with the density of bacteria in the blood (exception being sepsis with S. aureus), so positive hemocultures do not necessarily have a poorer prognostic compared to negative hemocultures. Following the clinical, biological and imagistic evolution of the patient, we were able to identify both the endotoxin trigger response and also the consequences of inflammatory and hypoxic injury at different levels.

Thus, the stages of systemic inflammatory response secondary to bacteremia with gram negative commensal germs in the previously healthy patient, following the local intestinal inflammation episode of a food poisoning, by crossing the vascular endothelium and the occurrence of endotoxemia are highlighted. The lipopolysaccharide (LPS) is transported by the binding proteins to the CD14 receptor immune cells (Ne, Mo/Ma). This receptor facilitates the interaction between LPS and TLR4. It transmits signals inside cells that stimulate the synthesis of proinflammatory factors: cytokines, chemokines, prostaglandins resulting in systemic inflammatory response. The systemic response is mediated by the brain, liver and spleen1.

The CNS response is achieved in two ways:

- The first path through the vagus nerve is the afferent, after detection of local inflammation by the axonal receptors of the cytokines, the hypothalamo-pituitary-adrenal axis, the autonomous system and the center of thermoregulation in the hypothalamus and efferent are activated, with cholinergic anti-inflammatory response.
- The second path is through circumventricular organs located near neuroendocrine and neurovegetative nuclei. This area is deprived of the blood-brain barrier and expresses components of the native and adaptive immune system.

Sepsis is associated with early acute clinical encephalopathy by changes in mental status, attention defficite, incoherent thinking, behavioral changes, to delirium. The explanation is given by the presence of CD14 receptors in microglial cells. Microglial cells are small cells that are part of the neural support group (neuroglial cells). Unlike the neuroglial cells of neuroectoderm from which nervous tissue originates, the microglial cells originate from the embryonic mesoderm from which the blood cells and the immune system derive. They act as macroface and are activated by inflammation in the central nervous system. Thus, the LPS-LBP-CD14 complex stimulates through TLR4 receptors central production of proinflammatory cytokines-IL-1ß, IL-6, TNF-α. The result is a local progressive inflammatory reaction, production of nitric oxide, oxygen free radicals etc. Nerve transmission abnormalities occur in the CNS, for example: the concentration of dopamine, norepinephrine, serotonin is increased while maintaining the unchanged level of GABA, which induce behavioral changes from the onset of sepsis. Somnolence, concentration difficulty, retrograde amnesia was maintained in the 4th and 5th day even in the absence of fever and after hydration correction [2,3].

The liver is the largest gland of our body and has a central role in metabolic and immunologic homeostasis. Like the spleen that opsonizes the bacteria, the liver contributes to bacterial clearance. Both the circulation and the hepatic structure are involved in keeping this homeostasis in sepsis [4,5].

The liver has a double irrigation:

- 1/3 is provided by the hepatic artery.
- 2/3 is provided by the venous portal system by combining in sepsis the effect of splanchnic vasoconstriction, bacterial translocation in the intestine and the contribution of mesenteric arteries.

The greatest adaptation to sepsis is achieved in the liver artery when the phenomenon of "hepatic artery buffer response" appear. This is actually a reversal of the sense of blood flow in the artery in

response to the decrease in blood flow in the portal vein in order to maintain the normal hepatic blood intake. The effect is achieved by vasodilatation in the liver artery providing blood perfusion even at low systemic blood pressure. Thus TAs induce decreased flux in the mesenteric arteries with decreased portal blood flow whereas flow in the hepatic artery increases but with reversal of the direction resulting in the compensation of the portal circulation with superior oxygen from the arterial blood. During endotoxemia, due to the decrease in blood flow intestinal, this compensation mechanism is very important.

Although it is possible to compensate the oxygen deficiency secondary to hypotension, the needs of oxygen in the liver are increased in sepsis and hypoxic imbalance is frequent.

Hepatic cells are represented as 60% hepatocytes, 10% to 20% Kupffer, the rest of them being endothelial cells from hepatic sinusoids, mononuclear, neutrophils. Their role is to mediate the inflammatory response. LPS-TLR4 interaction is favored by the LPS-LBP-CD14 complex, thus, stimulating Kupffer cells proinflammatory cytokines production: TNF-alpha, IL-1, IL-6 [4,5].

Besides the role of mediating the inflammatory response, the liver also has a metabolic role in sepsis by producing acute phase proteins with plasmatic increase of: C reactive proteine, alpha1-antitrypsin, fibrinogen, prothrombin and haptoglobin. Glycogenolysis and gluconeogenesis increase and the production of antithrombin and albumin decreases, albumin being negative acute phase protein [4,5].

Hepatic dysfunction in sepsis occurs early as a result of inflammation and hypoxia. It consists of the subtle alteration of hepatocellular synthesis and clearance function. It is initially materialized by cholestasis due to decreased hepatobiliary transport and bile flow, and, if liver hypoxia persists, there is also hepatic cytolysis (Figure 1).

During hospitalization, the cholestatic syndrome increased, reaching the maximum values on the 5th day of illness (GGT-10xN, FA-1.5xN) and their normalization on 23rd day. The CT aspect with hepatosplenomegaly accompanies the biological modifications. According to the imagistic re-evaluation, hepatosplenomegaly improvement was achieved on the 12th day.

Correction of severe hypoproteinemia from admission was achieved on the 15th day of illness. Human albumin was administered for a short period although the need for such administration is questionable. The mechanism by which hypoalbuminemia occurs in sepsis would be explained by:

- Decrease of secondary synthesis of hepatocellular damage.
- Albumins are negative acute phase proteins, so TNF and IL-1 inhibit the production of proteins that are not essential to the inflammatory process, namely albumin, and stimulate the production of the important acute-phase proteins: fibrinogen, globulin, haptoglobin.
- Increased losses - renal (the patient shows traces of protein in the urine test, but proteinuria / 24h was normal) and through inflammatory enteropathy.
- Redistribution by increasing the vascular permeability with translocation in the extravascular space, the patient presenting the swelled appearance of the tegument along with the soft peripheral edema.

Biological blood tests have found a decrease near the lower limit of cholesterol and significant increased triglycerides that became normal in the 20th day. An alteration of lipid metabolism and lipoprotein ratio during sepsis, was identified as follows [6].

- Triglycerides and VLDL increase due to decreased hydrolysis of triglycerides. LPS and inflammatory cells induce free fatty acid production, increase hepatic synthesis of triglycerides, and decrease lipoprotein lipase activity, thus decreasing VLDL

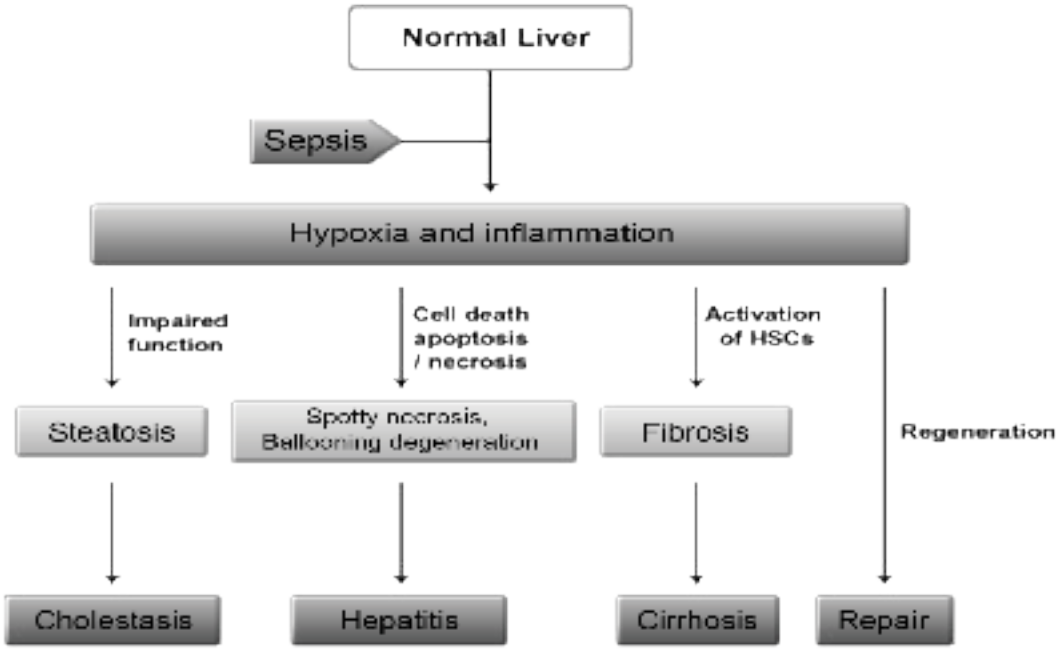

Figure 1: Hepatic dysfunction.

clearance and increasing plasma levels of triglycerides. The effect is increasing insulin resistance and possibly pancreatic reaction.

- Endotoxemia modulates the HDL composition and size: phospholipids are decreased as apolipoprotein A, serum amyloid A and phospholipase A2 secretion increase dramatically and the number of small and medium molecules decreases although the total HDL count remains constant. It is important given the role of these molecules in bacteria: HDL binds LPS by participating in bacterial clearance and induction and release of inflammatory cells with involvement in early inflammatory response.

The pancreatic reaction expressed by the increase in serum levels of pancreatic enzymes was observed on day 6, normalized on day 20 and is due to the following

- Changes in lipid metabolism with increased plasma triglycerides.
- Increase of endothelial lipase necessary for HDL remodeling which is followed by amyloid A dominance
- Secondary to the inflammatory response by IL-1b, IL-6, TNF-α that activates NF-KB involved in apoptosis.
- Hypoxia secondary to oxygen consumption in the intestines with Ph decreasing at this level. In sepsis, cardiac output is raised thus blood flow increases in the colon and gallbladder but decreases in the pancreas.
- Oxidative stress by the release of reactive oxygen species. Antioxidants and enzymes that neutralize these radicals (e.g. glutathione, thiamine) seem to decrease [7].

Case Particularity

It is due to the immunocompetent profile of the patient who develops systemic inflammatory response and sepsis with commensal bacteria complicated with renal abscess although antibiotic treatment was promptly initiated after admission to the first hospital and sensitivity was confirmed by the antibiogram.

There are 3 scenarios of systemic inflammatory response and sepsis, as follows:

1. The pathogenic bacteria can cause sepsis in the previously healthy individuals while the commensal bacteria, in order to invade, requires the epithelial barrier to be compromised in patients in which acute phase reaction is already initiated. A local inflammatory process is firstly activated by invasion of extravascular tissue. Bacteremia occurs when the local defense process cannot control the infection.
2. Bacteria can penetrate directly into the bloodstream without initial local extravascular inflammation. Bacteremia, if it is not controlled by circulating antibodies or complement, can cause invasion and infection of vascular endothelium cells or to various bloodstream cells by releasing endotoxins or other proinflammatory molecules. E.g., *Neisseria meningitidis*, viruses, rickettsia etc. The basis for the pathogenesis of this scenario is the absence of the host's rapid inflammatory response.
3. Others are e.g., Gram positive bacteria - superantigens activate lymphocytes T→ releasing cytokines which are responsible for the systemic inflammatory reaction → sepsis

The patient presented falls under Type 1 scenario.

Conclusion

Klebsiella pneumonia represents a frequent cause of bacteremia in immunodepressed and also in immunocompetent patients. Bacteremia with commensal germs occurs as a result of a localized infectious event from where the bacteria translocate the vascular endothelium. Based on this affected area, we can suspect the germs involved. *Klebsiella pneumoniae* causes an increased level of endotoxemia. Consequently, the risk of sepsis and complications of sepsis is higher even in immunocompetent patients. Understanding of the immunologic and metabolic response might contribute to the development of new therapies that could be used along with antibiotic treatment in sepsis.

References

1. Douglas M, Bennett's (2014) Principles and practice of infectious diseases. 2: 1.
2. Ziaja M (2013) Septic encephalopathy. Curr Neurol Neurosci Rep 13: 383.
3. Sonnevile R, Verdonk F, Rauturier C, Klein IF, Wolff M, et al. (2013) Understanding brain disfunction in sespsis. Ann Intensive Care 3: 15.
4. Yan J, Li S, Li S (2014) The role of the liver in sepsis. Int reviews of immunol. pp: 498-510.
5. Soultati A, Dourakis SP (2005) Liver dysfunction in the intensive care unit. Annals of gastroenterology 18: 35-345.
6. Eckardsteinv, Kardassis A(2015)High density lipoproteins. Handbook of Experimental Pharmacology book series 224: 483-508.
7. Chaari A, Hakim KA, Bousselmi K, Etman M, El Bahr M, et al. (2016) Pancreatic injury in patients with septic shock: A literature review. 8: 526–531.