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Scientific letters

Multiple organ failure by serotype K1 *Klebsiella pneumoniae*☆

Afectación multiorgánica por Klebsiella pneumoniae *serotipo K1*

Liver abscess syndrome caused by *Klebsiella pneumoniae* (*K. pneumoniae*) is a community-acquired infection characterised by primary liver abscess, bacteraemia and metastatic complications (lung, brain and psoas abscesses; osteomyelitis; meningitis; and endophthalmitis) with high mortality (10–40%). It occurs in immunocompetent patients, and the main risk factor is diabetes.[1]

Case report

A 67-year-old diabetic patient had a history of ischaemic cardiomyopathy and hypertension. In 2006, he had bilateral pneumonia, calculous cholecystitis and septic shock caused by *K. pneumoniae*. In 2007, he contracted community-acquired pneumonia (*K. pneumoniae* in sputum), and in 2008, he underwent laparoscopic cholecystectomy.

He attended the emergency department due to signs and symptoms for 48 h of a sudden decrease in visual acuity, fever (39 °C) and headache. He was diagnosed with posterior uveitis of the right eye, and treatment with corticosteroids was started. One day later, he was in very poor general condition, with severe holocranial headache, phonophobia, photophobia, fever (38 °C) and abdominal pain on palpation.

Complementary studies revealed significant hyperglycaemia, mild hypertransaminaemia, mild impairment of renal function, clear lumbar puncture fluid, pleocytosis and abnormal cerebrospinal fluid protein level. An electrocardiogram, chest X-ray, head CT scan and echocardiogram were normal. An abdominal ultrasound showed a 12-mm abscess on the left lobe of the liver.

Empirical therapy with intravenous ceftriaxone and vancomycin, as well as intravitreal ceftazidime and vancomycin was started. *K. pneumoniae* susceptible to all antibiotics except ampicillin was isolated in CSF, urine and blood cultures. The isolate was sent to a reference laboratory to confirm the suspected K1 serotype.

Six days after admission, due to the patient's poor clinical course, it was decided to enucleate the right eye. *K. pneumoniae* was again isolated in the vitreous humour.

The patient had a lower level of consciousness and left-sided hemiparesis. A whole-body CT scan was performed which showed multiple cerebral haemorrhages, pulmonary nodules, 2 abscessified collections in liver segment IV and left-sided perirenal free fluid. Treatment was changed to meropenem, amikacin and linezolid. A planned colonoscopy was performed which showed no abnormalities.

In subsequent ultrasound scans, hepatic fluid collection had reached 40 mm. Radiologically guided percutaneous drainage was unsuccessfully attempted. Treatment with meropenem, ceftriaxone and azithromycin was continued up to 8 weeks. Neurological recovery and resolution of brain, lung and liver lesions were achieved.

Discussion

K. pneumoniae is a Gram-negative enterobacterium that colonises the nasopharynx and gastrointestinal tract. Hypermucoviscosity is a characteristic possessed by only some *K. pneumoniae* strains that is associated with greater pathogenic power. Serotype K1 strains are positive for the magA gene, associated with hypermucoviscosity, which is part of the capsular operon of serotype K1 and essential for synthesising exopolysaccharides. The mucoid phenotype A (rpmA) regulator plasmid is the transcriptional activator which forms part of the molecular mechanism which in turn amplifies polysaccharide synthesis. Its virulence has also been associated with the aerobactin gene, a siderophore which maintains a constant flow of iron to the bacterium, thereby increasing its lethality.[2–4]

These strains cause liver abscesses with metastatic impairment (endogenous endophthalmitis and CNS infections).[5] This syndrome is an emerging infectious disease, initially reported in Asia but also documented in non-Asian patients and patients whose only risk factor is diabetes (which alters phagocytosis in Kupffer cells). Other authors think that the serotype K1 is the only risk factor for developing septic complications, including in immunocompetent patients.[6,7]

Few cases have been reported in Spain.[8,9] This is the first with multi-organ impairment documented at our hospital. The patient was a representative of an airline with journeys to eastern countries and had lived in the United Arab Emirates for 4 years. Therefore, we thought that he may have acquired *K. pneumoniae* outside of Spain and that it may have found its way into his biliary tract despite the correct antibiotic treatment.

Although *K. pneumoniae* liver abscess syndrome in our area may be very uncommon, we believe that it should be taken into account, especially in diabetic patients. Diabetes is a risk factor and is associated with a worse visual prognosis in patients with endophthalmitis.[2] Strict glycaemic control may prevent metastatic complications in patients infected with serotype K1 *K. pneumoniae*. Even with suitable treatment (third-generation cephalosporins which penetrate the vitreous and CNS well), an early diagnosis would allow prompt percutaneous drainage, which could prevent the development of metastatic foci.[10]

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Gema Barbeito-Castiñeiras[a,*], María Jesús Ladra González[b], María Jesús Domínguez Santalla[c], Carmen Rivero Velasco[d]

[a] *Servicio de Microbiología y Parasitología, Complexo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, A Coruña, Spain*
[b] *Servicio de Cirugía General y Digestiva, Complexo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, A Coruña, Spain*
[c] *Servicio de Medicina Interna, Complexo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, A Coruña, Spain*
[d] *Servicio de Medicina Intensiva, Complexo Hospitalario Universitario de Santiago de Compostela, A Coruña, Spain*

* Corresponding author.
E-mail address: Gema.Barbeito.Castineiras@sergas.es
(G. Barbeito-Castiñeiras).

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First case of ceftazidime/avibactam administration in home care. ESBL producing *Klebsiella pneumoniae* bacteremia☆

Primer caso de administración de ceftazidima/avibactam en hospitalización a domicilio. Bacteriemia por Klebsiella pneumoniae *BLEE multirresistente*

Dear Editor,

The increase in nosocomial infections caused by multi-drug resistant Gram-negative bacilli has necessitated the development of new antibiotics. In recent months, the FDA approved 2 new antibiotics, ceftolozane/tazobactam and ceftazidime/avibactam, for the treatment of intra-abdominal infections (together with metronidazole) and urinary tract infections.[1] Since June 2016, ceftazidime/avibactam has been approved in Europe for the treatment of nosocomial pneumonia, including those cases associated with mechanical ventilation and infections caused by Gram-negative aerobic microorganisms, with limited treatment options.[2] There is no documented evidence on the use of these drugs in the hospital at home (HAH) setting, a treatment modality that is not only less expensive, but also drastically reduces the possibility of intrahospital transmission of the bacteria.

We report the first case of ceftazidime/avibactam administration in a hospital at home programme. It discusses a 62-year-old patient with hypertension who had recently been diagnosed (February 2016) with acute myeloblastic leukaemia and was undergoing treatment with chemotherapy. He was admitted to haematology for a consolidation cycle, and had as a complication persistent bacteraemia caused by multidrug resistant extended-spectrum beta-lactamase (ESBL) *Klebsiella pneumoniae* secondary to sacral ulcer. Initially he received empirical treatment with imipenem/cilastatin and colistin. Given that his fever persisted and his blood cultures were positive again, the antibiogram was extended and showed sensitivity only to ceftazidime/avibactam and resistance even to ceftolozane/tazobactam (minimum inhibitory concentration of 8). Therefore, in view of the results, despite the fact that it was not among the approved indications at that time (it is now), it was decided to start treatment with ceftazidime/avibactam. Given his clinical stability, HAH services were contacted to complete treatment. They continued administering 2/0.5 g/8 h of ceftazidime/avibactam, which required pump infusion and 2 home visits (the drug is stable diluted and unrefrigerated for 12 h[1]). No outstanding incidents or related side effects occurred, and his monitoring rectal swab and blood cultures became negative.

Hospital-acquired infections are the sixth leading cause of death both in the United States and in Europe.[3] Those caused by Gram-negative bacteria have a special capacity for acquiring new mechanisms of resistance to antibiotics, especially if they are under antibiotic pressure. Since few new antibiotics have been developed in recent years, few treatment options are available to fight these infections. Cases of nosocomial bacteraemia caused by Gram-negative bacteria account for 30% of these infections. The most common microorganisms include species of *Klebsiella*, as in our case. The increase in resistance to broad-spectrum cephalosporins and carbapenems is also a particularly significant problem.[3] Among cases of nosocomial bacteraemia caused by *K. pneumoniae*, in the United States, 27.1% were resistant to third-generation cephalosporins, and 10.8% were resistant to carbapenems, with even higher rates of resistance in Europe.[3] Therefore, in this regard it is essential to have new therapeutic weapons such as ceftazidime/avibactam, an antibiotic approved on 25 February 2015. This antibiotic is active against a broad group of Gram-negative bacteria, *Enterobacteriaceae* and even *Pseudomonas aeruginosa*. However, it is minimally active against *Acinectobacter*, anaerobes and Gram-positive bacteria.[4] It is well tolerated (the most common side effects reported in the REPRISE study were gastrointestinal, in the same proportion in the 2 branches of the study–with and without ceftazidime/avibactam–with no other significant side effects).[5] In addition, it has demonstrated activity against *K. pneumoniae* carbapenemase, or KPC,[6] class A carbapenemases, encoded by plasmid genes, which would explain its greater capacity for spreading. Moreover, it should be noted that the antibiotic treatment directly observed in HAH units in Spain has proven to

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