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REPORTE DE CASO

Endogenous endophthalmitis and liver abscess due to presumed-Hypervirulent *Klebsiella pneumoniae*: a case report.

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Abstract

Pyogenic liver abscess is a high-incidence disease, in which hypervirulent (hypermucoviscous) *Klebsiella pneumoniae* (KP) has become more relevant due to its ability to spread and infect other tissues, among which endogenous endophthalmitis (EE) is the most common complication.

A patient with right-sided abdominal pain, vomiting, anorexia, fever, and jaundice was diagnosed with a KP liver abscess that was drained and treated with ampicillin/sulbactam plus metronidazole. Subsequently, he had a recurrence of the liver abscess plus rapidly progressive ocular symptoms that raised suspicion of EE. Due to the severity of the infection, eye enucleation was required and despite the natural resistance pattern, the patient only improved after meropenem was prescribed.

Any ocular symptoms in patients with KP liver abscess should raise suspicion of EE, contributing to an early diagnosis and treatment. It is possible that despite the antibiogram results, only broad-spectrum antibiotics may avoid vision loss and improve clinical outcomes.

Keywords (MeSH): Liver abscess, Endophthalmitis, Klebsiella pneumoniae, Eye enucleation.

Endoftalmitis endógena y absceso hepático con sospecha de *Klebsiella pneumoniae* hipervirulenta: reporte de caso.

Resumen

El absceso hepático piógeno es una patología frecuente, en la que *Klebsiella pneumoniae* (KP) hipervirulenta (hipermucoviscosa) ha cobrado relevancia por su capacidad de diseminarse e infectar otros tejidos, siendo la endoftalmitis endógena (EE) la complicación más común.

Se presenta un paciente con dolor en hemiabdomen derecho, vómito, anorexia, fiebre e ictericia quien fue diagnosticado con un absceso hepático por KP que fue drenado y tratado con ampicilina/sulbactam más metronidazol. Posteriormente, el absceso recurrió y presentó síntomas oculares rápidamente progresivos que hicieron sospechar EE. Debido a la severidad, requirió enucleación ocular y, a pesar del patrón de resistencia natural, solo mejoró al iniciar meropenem.

Cualquier síntoma ocular en pacientes con absceso hepático por KP debe hacer sospechar EE, contribuyendo a un diagnóstico y tratamiento oportuno. Es posible que, a pesar del antibiograma, solo los antibióticos de amplio espectro puedan eventualmente evitar la pérdida ocular y mejorar los desenlaces clínicos.

Palabras clave (DeCS): Absceso hepático, Endoftalmitis, Klebsiella pneumoniae, Enucleación del ojo.

Introduction

Pyogenic liver abscess is a high-incidence disease worldwide, most commonly caused by *Escherichia coli*, followed by *Klebsiella pneumoniae* (KP). In recent decades, cases related to KP, which has traditionally been described in East Asian countries, are becoming more frequent elsewhere[1].

KP is a gram-negative bacillus that has multiple virulence factors (such as the K1 capsular subtype and lipooligosaccharide) that allow it to spread to distant tissues. In fact, there are certain high-viscosity KP strains associated with a greater capacity to infect distant tissues (such as the eyes, meninges, or others)[2]. This subtype is called Hypervirulent (hypermucoviscous) KP and has been associated with invasive liver abscess syndrome, of which endogenous endophthalmitis (EE) is the most frequent complication[1,2].

Endophthalmitis is a rare, potentially sight-threatening inflammation of the vitreous humor (vitritis), caused by coagulase-negative *Staphylococcus, S. aureus,* or *Candida,* among others. EE is caused by hematogenous bacterial dissemina-

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tion, usually from endocarditis, liver abscesses, or indwelling catheters. As bacteria translocate through the blood-ocular barrier, they elicit an inflammatory response that rapidly can cause vision loss and the need for enucleation[3].

Although the incidence of this disease is low, the rapid progression of the ocular compromise requires early diagnosis and prompt treatment to avoid further damage[3]. Moreover, due to the lack of clinical practice guidelines and inadequate response to usual treatments, the visual prognosis of patients is poor[2,4]. Consequently, the recognition of early signs of ocular infection and proper treatment in patients with KP liver abscess are important elements to prevent adverse outcomes.

This article aims to describe the case of a patient treated at the Hospital Universitario Nacional (HUN) in Bogotá, Colombia, with a typical clinical presentation of a KP pyogenic liver abscess that spread and caused endogenous endophthalmitis, configuring the previously described invasive liver abscess syndrome. Then a discussion of the case and conclusions are presented to raise awareness of early recognition and therefore improve outcomes of patients with similar characteristics. This case report was approved by the ethics committee of the Hospital Universitario Nacional. The clinical information and images included in this article were approved by the patient through written informed consent.

Case presentation

A 77-year-old male patient with a past medical history of type 2 diabetes mellitus and systemic arterial hypertension, comes to the physician after 4 days of fever and right-sided abdominal stabbing pain, associated with jaundice, vomiting, and anorexia. Current medications included losartan, metformin, and sitagliptin. He was admitted to the hospital, and an abdominal ultrasound showed a liver abscess, then an empiric treatment with Ampicillin/sulbactam and metronidazole was started. Percutaneous drainage was performed and cultures of it grew KP with a natural antimicrobial susceptibility pattern. The patient's condition improved and was discharged with oral antibiotic treatment (sultamicillin and metronidazole) for 20 days.

Five months after discharge, the patient was readmitted with the same clinical presentation, but additionally, he presented with right conjunctival hyperemia (Figure 1A). Within the requested laboratory tests, a complete blood count reported leukocytosis (17.130 cells/mL) with neutrophilia (15.708 cells/mL), thrombocytopenia (117.000 cells/mL), hyperbilirubinemia (total bilirubin 1,81, direct bilirubin 0,07 mg/dL, indirect bilirubin 1,74 mg/dL) and impaired renal function (Creatinine 1,72 mg/dL, Blood Urea Nitrogen 25,6 mg/dL), then treatment with ampicillin/sulbactam and metronidazole was restarted. In addition, a contrast-enhanced computed tomography (CT) of the abdomen and pelvis showed a focal lesion of 200 cc in the left liver lobe consistent with the diagnosis of recurrent liver abscess, in consequence, laparoscopic drainage was performed. A culture of the sample was taken in which the same bacteria yielded again.

On the third day at the hospital, the patient had an episode of impaired level of consciousness, (drowsiness), dyspnea, and oxygen desaturation, therefore was transferred to the intensive care unit and a Venturi mask oxygen therapy was started. Consequently, sepsis of abdominal origin was considered, whereby a broad-spectrum antibiotic coverage was achieved with Piperacillin/Tazobactam for 4 days plus metronidazole, with the following clinical improvement.

During the hospitalization, on the fourth day, the patient developed headache and right retroocular pain. The Ophthalmology group performed a clinical evaluation where they found chemosis, proptosis, palpebral edema, corneal edema, and partial ophthalmoplegia. A contrast-enhanced CT of the orbits was carried out and pre- and post-septal inflammatory changes with ocular proptosis were found and a diagnosis of EE was ruled-in secondary to the hematogenous spread from the liver abscess, for which urgent ophthalmological management was initiated with topical moxifloxacin.

On the seventh day, the patient presented lethargy and worsening ocular symptoms, which raised the suspicion of neuroinfection. As a consequence, piperacillin/tazobactam was changed to ceftriaxone in order to allow adequate blood-brain barrier penetration. Additionally, due to persistent headache and limitation in ocular movements, thrombosis of venous sinuses was ruled out by a contrast-enhanced CT with angiography of the head.

Although the antibiotic therapy was guided by the natural antimicrobial susceptibility pattern of KP, the clinical status did not improve, raising the suspicion of hypervirulent (hypermucoviscous) KP (Figure 1B). Consequently, the antibiotic therapy was switched to meropenem for 42 days, an ocular enucleation was performed, and the patient's condition improved slowly. The primary cause of the abscess was never identified, and no follow-up imaging was performed. However, the infection was adequately controlled, and the patient was discharged to continue the antibiotic therapy in the outpatient setting for 4 weeks. Once the treatment ended, he was scheduled for an ocular prosthesis procedure. Observe the clinical case timeline during the hospitalization in Figure 2.

Discussion

In the present clinical case, a 77-year-old male patient with a medical history of type 2 diabetes mellitus and systemic arterial hypertension was diagnosed with a liver abscess caused by KP with a natural antibiotic susceptibility pattern. Despite the ty-

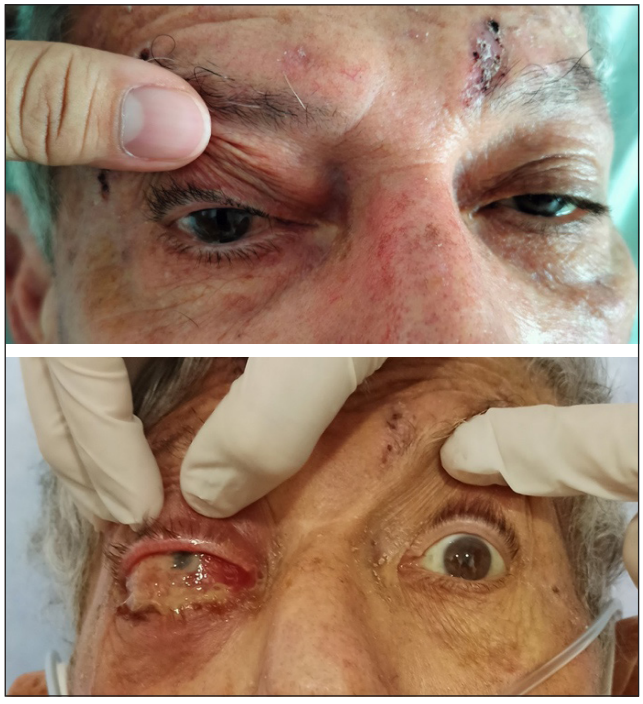

Figure 1. A. Upper picture. Conjunctival hyperemia during first day of readmisison. **B.** Lower picture: image taken after day 7 of readmision, showing worsening of the ocular inflammation and presence of hyperviscous secretions

pical clinical presentation and proper antibiogram-guided therapy and drainage, the patient developed EE, configuring the condition known as "invasive liver abscess syndrome".

In previous studies, diabetes mellitus has been identified as a risk factor for developing a KP liver abscess, but it has not been associated with etiologic agents other than KP[5]. The mechanism is not well understood; however, it has been found that poor glycemic control alters the phagocytic activity of neutrophils, especially KP serotypes K1/K2[6].

In all patients in whom liver abscess is confirmed by imaging, empiric antibiotic therapy should be initiated based on the suspected route of infection and local resistance patterns. The 2017 Surgical Infection Society guideline on intra-abdominal infection suggests starting with a single-agent regimen (e.g., piperacillin/tazobactam) or a combination therapy regimen (metronidazole plus a third-generation cephalosporin)[7]. Subsequently, antibiotic therapy should be switched to culture-specific antibiotics. In this case report, the initial management was metronidazole plus ampicillin/sulbactam.

Despite appropriate antibiotic management of the KP liver abscess, the patient developed the previously described ocular symptoms, hence, EE was suspected due to hematogenous dissemination. In Colombia, this clinical presentation has been described only 4 times, in which ocular pain, visual blurring, and eye redness were the most common symptoms and the outcome in all cases was ocular enucleation or total vision loss[8,9]. In a retrospective study, it was found that 87% of patients with KP endophthalmitis had poor visual acuity at the onset of the presentation[10]. For this reason, we suggest that any ocular symptom should be taken as an alarm sign in all patients diagnosed with KP liver abscess.

Currently, there is no recommendation with strong evidence for the treatment of EE due to invasive liver abscess syndrome, in consequence, there is a great variation in the described therapies. In the cases reported in Colombia, therapy consisted of anticholinergics, steroids, and systemic antibiotics such as metronidazole plus ceftriaxone or vancomycin. Intravitreal injections of amikacin, vancomycin, ceftazidime, topical ofloxacin, moxifloxacin, and oxytetracycline were also prescribed[8,9].

In our clinical case, as soon as EE was suspected, antibiotic management was changed to systemic ceftriaxone plus topical ocular moxifloxacin in accordance with the concept given by Ophthalmology. Despite an antimicrobial susceptibility profile indicating a natural KP pattern, the clinical response was unsatisfactory. For that reason, therapy was adjusted to meropenem, to cover a potentially multiresistant KP, and clinical improvement was achieved. Although the antibiogram does not indicate multi-resistance, it is possible that the use of broad-spectrum agents may improve the outcomes, as well as the multidisciplinary management, especially with the Ophthalmology group.

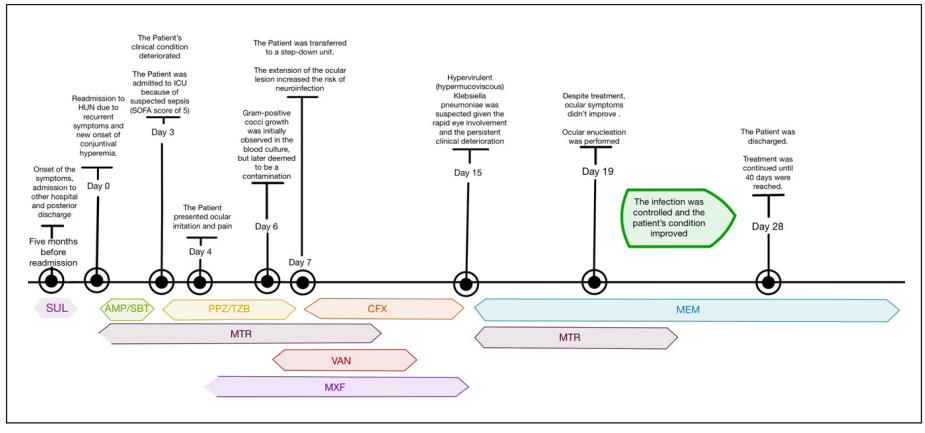

Figure 2. Timeline during the hospitalization

Genotyping would be useful to predict the small percentage of liver abscesses that will develop EE. A review of KP bacteremia found that some specific virulence factors were present in more than 86% of the cases of invasive liver abscess syndrome[11]. In this case report, as in most health centers in Colombia, it is not possible to access bacterial genotyping due to its high costs and unavailability, but according to the clinical course, hypervirulent (hypermucoviscous) KP was the most probable causative etiology.

Another way to promptly diagnose the hypervirulent (hypermucoviscous) KP phenotype is through the "string test". It is a simple and inexpensive test that consists of immersing an inoculation loop in the bacterial culture and slowly withdrawing it. If the colonies can be stretched 5 mm or more, they are considered to have this phenotype[12]. However, further research is required to evaluate its accuracy.

In conclusion, we strongly recommend suspecting EE in all patients with KP liver abscess who develop any ocular symptom, which must be diagnosed and treated as soon as possible. There is currently insufficient evidence to support specific antibiotic management for ocular infection and outcomes have been unfavorable in most cases, despite the culture-guided antibiotic therapy. It is possible that broad-spectrum therapy may improve the outcomes of these patients.

Ethical considerations

Protection of people and animals. No experiments were performed in animals nor humans for the elaboration of this project.

Confidentiality of the data. The authors declare that the text does not contain data that allows patient identification.

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Contribution of authors. Literature review: HI, NG, SD, NC. Case analysis: HI, NG, SD, NC. Production of the text: HI, NG, SD, NC. All authors contributed, read, and agreed with the version of the manuscript.

References

1. Chen J, Zhang M, Chen J, Ning Y, Cai X, Zhang L, Xu H, et al. Cryptogenic and non-cryptogenic liver abscess: A retrospective analysis of 178 cases revealed distinct characteristics. J Int Med Res. 2018 Sep;46(9):3824-3836. doi: 10.1177/0300060518781256. Epub 2018 Aug 9. PMID: 30091401; PMCID: PMC6136014.
2. Lin ZW, Zheng JX, Bai B, Xu GJ, Lin FJ, Chen Z, et al. Characteristics of Hypervirulent Klebsiella pneumoniae: Does Low Expression of rmpA Contribute to the Absence of Hypervirulence? Front Microbiol. 2020 Mar 17;11:436. doi: 10.3389/fmicb.2020.00436. PMID: 32256482; PMCID: PMC7090111.
3. Gajdzis M, Figuła K, Kamińska J, Kaczmarek R. Endogenous Endophthalmitis-The Clinical Significance of the Primary Source of Infection. J Clin Med. 2022 Feb 23;11(5):1183. doi: 10.3390/jcm11051183. PMID: 35268274; PMCID: PMC8911070.
4. Hussain I, Ishrat S, Ho DCW, Khan SR, Veeraraghavan MA, Palraj BR, et al. Endogenous endophthalmitis in Klebsiella pneumoniae pyogenic liver abscess: Systematic review and meta-analysis. Int J Infect Dis. 2020 Dec;101:259-268. doi: 10.1016/j.ijid.2020.09.1485. Epub 2020 Oct 6. PMID: 33035676.
5. Yang CC, Yen CH, Ho MW, Wang JH. Comparison of pyogenic liver abscess caused by non-Klebsiella pneumoniae and Klebsiella pneumoniae. J Microbiol Immunol Infect. 2004 Jun;37(3):176-84. PMID: 15221038..
6. Jung-Chung Lin, L. K. Siu, Chang-Phone Fung, Hsiao-Hui Tsou, Jaang-Jiun Wang, Chiung-Tong Chen, Shu-Chuan Wang, Feng-Yee Chang, Impaired Phagocytosis of Capsular Serotypes K1 or K2 Klebsiella pneumoniae in Type 2 Diabetes Mellitus Patients with Poor Glycemic Control, The Journal of Clinical Endocrinology & Metabolism, Volume 91, Issue 8, 1 August 2006, Pages 3084–3087, https://doi.org/10.1210/jc.2005-2749
7. Mazuski JE, Tessier JM, May AK, Sawyer RG, Nadler EP, Rosengart MR, et al. The Surgical Infection Society Revised Guidelines on the Management of Intra-Abdominal Infection. Surg Infect (Larchmt). 2017 Jan;18(1):1-76. doi: 10.1089/sur.2016.261. PMID: 28085573.
8. Solarte Iván, Otto Sussmann, and Paola García. "Endoftalmitis y septicemia por Klebsiella pneumoniae." Acta Médica Colombiana 2001 Septiembre-Octubre; 26(5).
9. Jaramillo-Aristizábal María Clara, Jaramillo-Lozano James Eduardo, Cuevas-Peláez Miguel. Endoftalmitis endógena asociada a absceso hepático por Klebsiella pneumoniae. Descripción de tres casos y revisión de la literatura. Iatreia. 2016 June; 29(2): 228-236. https://doi.org/10.17533/udea.iatreia.v29n2a11.
10. Ang M, Jap A, Chee SP. Prognostic factors and outcomes in endogenous Klebsiella pneumoniae endophthalmitis. Am J Ophthalmol. 2011 Feb;151(2):338-44.e2. doi: 10.1016/j.ajo.2010.08.036. Epub 2010 Dec 18. PMID: 21168820.
11. Yu VL, Hansen DS, Ko WC, Sagnimeni A, Klugman KP, von Gottberg A, et al; International Klebsiella Study Group. Virulence characteristics of Klebsiella and clinical manifestations of K. pneumoniae bloodstream infections. Emerg Infect Dis. 2007 Jul;13(7):986-93. doi: 10.3201/eid1307.070187. PMID: 18214169; PMCID: PMC2878244.
12. Hagiya H, Watanabe N, Maki M, Murase T, Otsuka F. Clinical utility of string test as a screening method for hypermucoviscosity-phenotype Klebsiella pneumoniae. Acute Med Surg. 2014 May 19;1(4):245-246. doi: 10.1002/ams2.40. PMID: 29930857; PMCID: PMC5997228.