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Case Report

Bilateral Endogenous Bacterial Endophthalmitis with Asynchrony for 14 Months due to *Klebsiella pneumoniae*: A Case Report

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Keywords
Endogenous endophthalmitis · Bilateral asynchrony · *Klebsiella* · Liver abscess · Case report

Abstract
Introduction: The aim of this study was to describe a very rare case of endogenous bacterial endophthalmitis caused by *Klebsiella pneumoniae* in both eyes with a difference in the onset of symptoms of 14 months in an immunocompetent patient. ***Case Presentation:*** A 66-year-old immunocompetent man presented with asynchronous bilateral endogenous endophthalmitis produced by the *K. pneumoniae* bacterium at the starting point of a liver abscess after cholecystectomy surgery, causing endophthalmitis 1 year and 2 months apart between an eye and another. The first was diffuse anteroposterior endophthalmitis in the left eye that ended in visual loss and phthisis bulbi due to delayed initial diagnosis and established treatment, and the second was focal endophthalmitis in the right eye that preserved the organ and resulted in a vision of 20/20 due to early suspected diagnosis and rapid instituted treatment. ***Conclusion:*** To our knowledge, this is the first published case of a long asynchronous bilateral endogenous bacterial endophthalmitis caused by *K. pneumoniae* with a prolonged difference of 14 months in the onset of symptoms between one eye and another. This case is a vision-threatening ophthalmologic emergency that can be associated with life-threatening systemic morbidities. The early diagnosis of infection represents a challenge for clinicians, ophthalmologists, and microbiologists.

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Introduction

Endogenous endophthalmitis (EE) is a potential cause of blindness caused by the hematogenous spread of germs from primary extraocular focus. It is classified as focal or diffuse according to the degree of involvement, anterior or posterior depending on the location, and panophthalmia if sclera and orbit are also affected. Its incidence is low, 2–8% of all cases of endophthalmitis [1], but it can increase in people with chronic pathologies, immunocompromised patients, and those undergoing invasive procedures. Fungi are the most frequently implicated germs, mainly *Candida albicans*. In endogenous bacterial endophthalmitis (EBE), there is greater proportion of Gram (−) and more aggressive Gram (+) bacteria. Gram (−) germs like *Klebsiella*, *Escherichia*, *Pseudomonas*, and *Neisseria* are more common in Asian populations, whereas Gram (+) germs like *Staphylococcus*, *Streptococcus*, and *Listeria* are more common in Western populations. *Klebsiella pneumoniae* is the most commonly reported EBE pathogen worldwide. It is more common in Asia, but its incidence in the rest of the world is increasing. Diabetes and hepatobiliary disease are important predisposing factors, and liver abscesses are the main source of infection because of their entry through portal circulation. Patients with liver abscesses caused by *Klebsiella* have a 3% risk of developing EBE [2]; although in countries where this specific pathology is common (Taiwan), the association with endophthalmitis exceeds by 10% [3]. Most cases of EBE are unilateral. There are few reported cases of bilateral EBE in the literature, and asynchronous bilateral cases are even rarer. Most cases are simultaneous or occur with a very short time difference between eyes (about a week). The aim of this paper was to describe a very rare case of EBE produced by *K. pneumoniae* from a liver abscess in both eyes with a difference in the onset of symptoms over a period of 14 months in an immunocompetent patient.

Case Presentation

A 66-year-old male, rural worker, presented for consultation due to left eye pain and acute vision loss for 1 month. An ophthalmologist in his town prescribed commercial antibiotic eye drops for 30 days without a precise diagnosis and without reporting improvement. Regarding his personal history, he only underwent cholecystectomy 2 months before the onset of ocular symptoms. He did not report a history of diabetes, endocarditis, malignant neoplasia, or any disease that could have reduced his immunity.

Examination of the right eye was normal with 20/20 visual acuity (VA). The left eye could only see light. External examination revealed inflammation of the left upper and lower eyelids without restriction of ocular motility. The findings also revealed purulent conjunctival discharge, conjunctival hyperemia and edema, iris rubeosis, posterior synechiae, cataract, very low ocular pressure (2 mm Hg), and severe vitritis, which did not allow observation of the retina (shown in Fig. 1). Left ocular ultrasound showed multiple hyperechogenic punctate images and low-reflectivity mobile membranes filling vitreous cavity consistent with severe vitritis and retina impressed applied. Endophthalmitis was diagnosed, and emergency pars plana vitrectomy was performed. A small ocular perforation was found at 6 h, through which purulent material was draining. We performed lensectomy, vitreous sample extraction for direct examination and culture, and intravitreal injection of broad-spectrum antibiotics: vancomycin (1 mg in 0.1 mL) and ceftazidime (2.25 mg in 0.1 mL). Penetrating ocular trauma through the inferior orifice was suspected despite being repeatedly denied by the patient. Oral antibiotics were prescribed (ciprofloxacin 500 mg every 12 h), along with fortified vancomycin and ceftazidime eye drops

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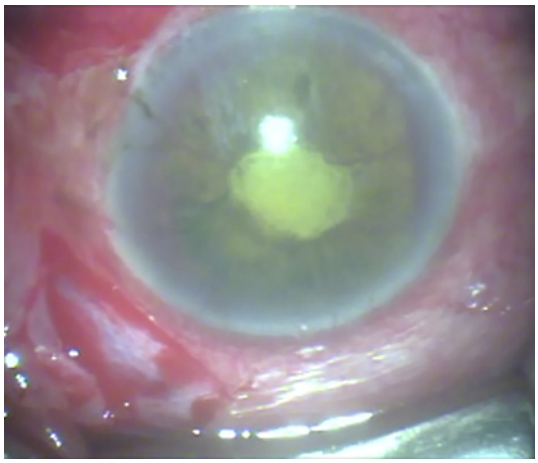

Fig. 1. Left eye biomicroscopy: diffuse anteroposterior endophthalmitis.

alternated every 30 min and atropine 1% eye drops every 12 h. Direct examination reported the presence of Gram (−) bacteria, and vitreous culture reported *K. pneumoniae* sensitive to ciprofloxacin, ceftazidime, and imipenem, so the previously indicated protocol was continued. Due to the nature of germs, diagnostic suspicion was changed from ocular trauma to endogenous origin, and ocular perforation was interpreted as the site of spontaneous drainage of 1-month-old vitreous abscesses. The patient was referred to the infectious diseases department, but because he no longer felt pain, he decided to conduct consultations in his town.

He returned to our service 14 months after the first consultation due to sudden and painful vision loss in other eye – right – of 1 day. As a new history, he reported being admitted to a local hospital for abdominal pains and having received intravenous antibiotics without specifying their names. Examination revealed a severe decrease to 20/800 VA in his right eye that did not improve with pinhole; biomicroscopy revealed conjunctival edema and hyperemia, fibrinoid reaction in the anterior chamber, and a 1.5-mm hypopyon (shown in Fig. 2); ocular pressure was 10 mm Hg; and fundus examination revealed moderate vitritis with the applied retina (shown in Fig. 3). Left eye had phthisis bulbi. Emergency vitreous puncture was performed in the right eye with sample collection and injection of vancomycin and ceftazidime at usual doses. Fortified vancomycin and ceftazidime and atropine 1% eye drops and oral ciprofloxacin were administered at usual doses. Urgent consultation with the infectious diseases department was indicated, which decided to hospitalize the patient for further studies. A sample was taken for blood culture, and antibiotic treatment was started with intravenous imipenem at usual doses (500 mg every 6 h). Ocular evolution was slowly favorable, with VA improving to 20/80 in the first days, disappearance of hypopyon, ocular pressure of 4 mm Hg, and vitritis improvement.

Laboratory tests were normal, except for an elevated erythrocyte sedimentation rate (30 mm/h), elevated C-reactive protein (48 mg/L), and liver tests showing elevated alkaline-phosphatase (141 U/L) and gamma-glutamyl-transpeptidase (84 U/L) levels. The ELISA test for human immunodeficiency virus was negative. Vitreous culture was negative, but blood culture revealed *K. pneumoniae* (same germs responsible for endophthalmitis in other eye previous year). Abdominal ultrasound revealed an irregular hypoechogenic image of 37 × 37 mm in the right hepatic lobe and absent gallbladder (shown in Fig. 4). To confirm these findings, computed tomography of the abdomen was performed, which revealed an enlarged liver due to a hypodense lesion in the right lobe with peripheral enhancement after intravenous administration of a contrast substance (shown in Fig. 5). Based on these findings, a diagnosis of chronic liver abscess was made, and image-guided percutaneous surgical

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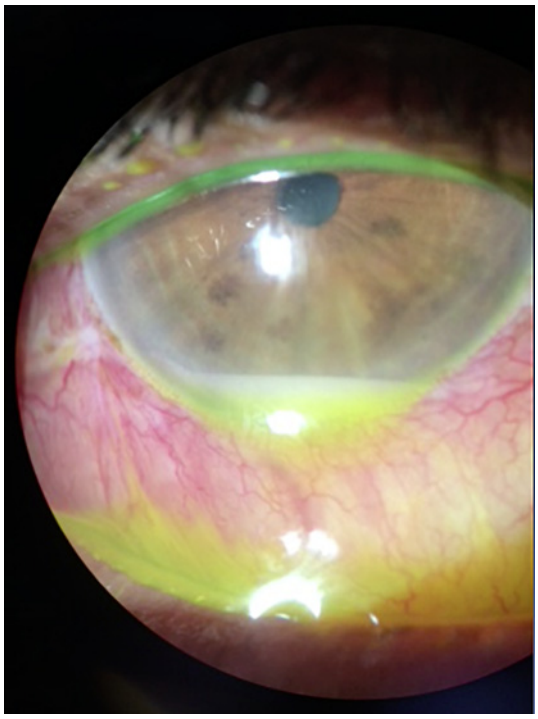

Fig. 2. Right eye biomicroscopy: focal endophthalmitis.

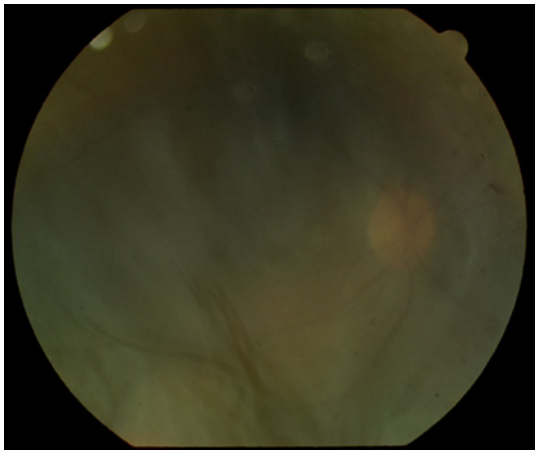

Fig. 3. Right eye retinography: moderate vitritis and applied retina.

drainage was performed. General and ocular evolution was good without complications, and antibiotics were progressively reduced. At 6 months, the best-corrected VA had improved to 20/25, ocular pressure was 17 mm Hg, and the retina and vitreous were normal (shown in Fig. 6). The ocular infectious episodes and hospitalizations for previous abdominal causes were not repeated.

After 5 years, the patient presented progressive and painless visual decrease in his right eye (to 20/200) due to nuclear cataract. Uncomplicated phacoemulsification was performed, obtaining 20/20 VA. Now, 7 years after the onset of symptoms, the patient still has 20/20 best-corrected VA in the right eye, transparent intraocular lens and eye fundus with applied retina, clean vitreous, and chorioretinal atrophy in lower nasal periphery with pigment dispersion around (shown in Fig. 7).

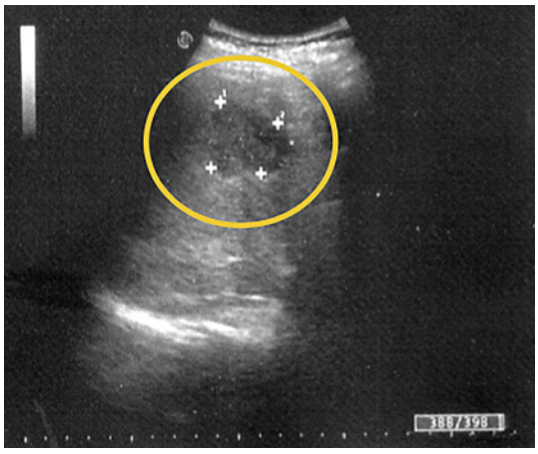

Fig. 4. Liver ultrasound: hypoechogenic image of the right hepatic lobe (abscess).

Discussion

In summary, this is a case of a 66-year-old immunocompetent man who presented with asynchronous bilateral EBE caused by *K. pneumoniae* from a liver abscess after cholecystectomy, causing endophthalmitis 14 months apart between eyes, with different visual results due to different times in diagnosis and start of treatment. This prolonged difference of 14 months was much longer than the published bilateral EBE cases (simultaneous or 1 week between eyes).

In 2013, Kashani and Eliott published that EBE is rare (2–8%), but with very poor visual prognosis (90% achieve light vision or worse); bilateral in 14–25%; diabetes mellitus is the most common risk factor (68%); pyogenic liver abscesses are caused by Gram (−) organisms and produce transient bacteremia and intermittent symptoms; and mortality has declined from 90% to less than 10% with early diagnosis and timely treatment [1]. Liver abscesses have been implicated as the primary focus of EBE mainly on the Asian continent [4], although our patient did not have Asian ancestors nor did he live on that continent. According to Chen's 20-year review, most liver abscesses were single (74%), located in the right lobe (60.6%), and had a maximum diameter of 5.6 cm, which is consistent with ultrasound findings of our patient [3].

Binder did not find extraocular focus in up to 44% of cases, so they argued that transient bacteremia could be the cause of endophthalmitis [5]. In a study by Park, ocular symptoms developed before the diagnosis of liver abscesses in 66.7% of cases, as in our patient [6].

The right eye would be affected twice as often as the left, probably because of closer and more direct blood flow to the right carotid artery [7]. However, in our case, the first eye affected was the left one and coincides with reviews by Chen and Chung (54.2 and 60.5% in the left eye) [2, 4].

Jackson found only 12% bilaterality in EBE [8], while in Chen's review, bilaterality was 15.4% [3]. In other reviews from Hong Kong, it was even higher (26.3 and 28.6%) [4, 9]. Therefore, bilaterality, as observed in our patient, occurs in a minority of cases.

In particular cases of EBE caused by liver abscesses, germs are multiresistant and antibiograms showed that carbapenems had the greatest antibiotic effects. Considering the antibiogram results in our patient, we decided to start systemic treatment with intravenous imipenem. Gram (+) bacteria are susceptible to vancomycin, and Gram (−) microbes are sensitive to ceftazidime. These are currently recommended as initial empirical therapy and were the ones used in our patient. In severe cases, vitrectomy can be beneficial because it eliminates microorganisms, inflammatory environment, and toxic

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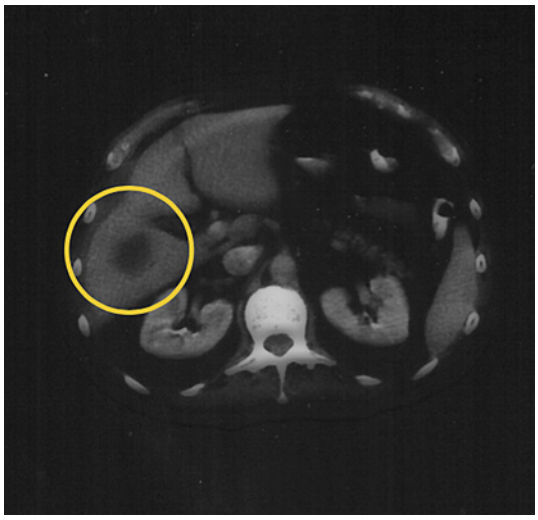

Fig. 5. Abdominal computed tomography: enlarged liver due to a hypodense lesion in the right lobe (abscess).

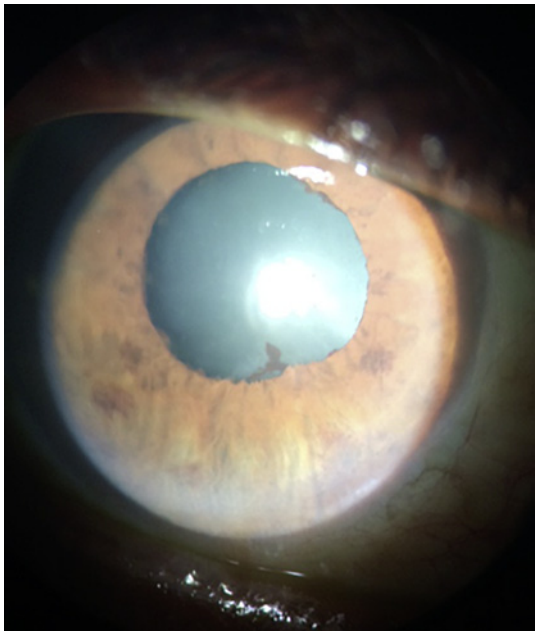

Fig. 6. Right eye biomicroscopy: normal anterior segment, only slight posterior synechiae.

substances present in the vitreous cavity and it can triple the chance of maintaining useful vision and reduce the probability of enucleation or evisceration by threefold. Currently, early vitrectomy is recommended. Then, given the suspicion of advanced endophthalmitis in the first eye (left), we performed vitrectomy, collected samples, injected vancomycin and ceftazidime as empirical antibiotics, and started oral ciprofloxacin. Given the subsequent appearance of similar but less advanced condition in the right eye, we performed vitreous puncture with sample collection and injection of same empiric antibiotics, and we again prescribed oral ciprofloxacin and urgently referred the patient to the infectious diseases department who began treatment with intravenous imipenem, taking into account results of vitreous culture of the left eye from the previous year until obtaining results of current blood culture that showed the same germs and same susceptibility. Wang concluded that in addition to vitrectomy, active treatment of primary lesions is essential; therefore, systemic antibiotics must be administered along with surgical

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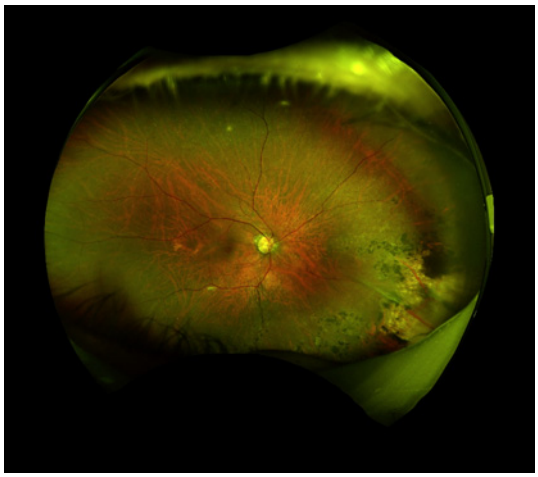

Fig. 7. Right eye wide-field retinography: Chorioretinal atrophy in the lower nasal periphery with pigment dispersion around.

drainage of liver abscesses [10]. This was unintentionally demonstrated in our case since the first eye was treated locally with vitrectomy and intravitreal antibiotics, but the patient did not receive adequate systemic treatment because he decided to return to his town; and EBE recurred in the other eye (right) 14 months later, again performing local therapy with intravitreal antibiotic injection and now systemic therapy with intravenous antibiotics and surgical drainage of the liver abscess. Only then was the disease cured without recurrence until today, after 7-year follow-up.

The visual prognosis is usually unfavorable, with 32% useful vision, 44% blindness, 25% enucleations or eviscerations, and an appreciable mortality rate of 5–14%. In a study by Ang, severe visual loss was found in 71 eyes of 61 patients with EBE due to *K. pneumoniae*, with a high probability of bilateral blindness [11]. Our patient presented an unfavorable result in his left eye with phthisis bulbi and an excellent result in his right eye with 20/20 VA, expressing his satisfaction with the treatments performed and the results obtained.

In the published literature, we can highlight 4 cases of unilateral EBE due to *K. pneumoniae* in immunocompetent patients with liver abscesses who had poor visual outcome despite local and systemic antibiotic treatment [12–14]. A recent Malaysian study published 3 cases of unilateral EBE due to *K. pneumoniae* [15]: first due to pneumonia, second due to left renal and basal ganglia abscesses, and third due to pneumonia and a history of colon adenocarcinoma. Unfortunately, the 3 eyes went to phthisis.

Bilateral EE is usually more frequent in series with fungal etiological agents. Reported cases of bilateral EE due to bacteria (EBE) are extremely few in the literature, and asynchronous bilateral cases are even rarer. A similar case of bilateral EBE secondary to *K. pneumoniae* and liver abscess was found in a 57-year-old man with no significant history, but, unlike our case, endophthalmitis was simultaneous in both eyes and, at the time of diagnosis, the patient already had septicemia with hepatic, ocular, urinary, and pulmonary involvement [16]. Other cases of simultaneous bilateral EBE were published but caused by other bacteria: 1 case due to *Staphylococcus warneri* caused by a *Vespa crabro* hornet sting with poor visual result [17]; one case due to *Streptococcus pneumoniae* from endocarditis with no light perception in the right eye and 20/25 VA in the left eye [18]; another case due to methicillin-resistant *Staphylococcus aureus* from the suture and pelvic abscesses after removal of screws inserted at the time of surgical repair of a tibial fracture with 20/20 VA in both eyes [19]; another case due to *Escherichia coli* with bilateral EBE complicated by necrotizing scleritis, orbital cellulitis, and scleral perforation [20]; another case due to methicillin-resistant *Streptococcus aureus* from endocarditis, osteomyelitis, and septic

polyarthralgia with poor visual result [21]; and another case due to *Staphylococcus aureus* infection of a burn from an electronic cigarette device with complete recovery of both eyes [22]. In 2004, Christensen published 4 cases of bilateral EBE: a man with endocarditis and advanced simultaneous bilateral panophthalmia due to *Streptococcus pneumoniae* leaving 20/100 VA in both eyes, a man with subdural abscess at the lumbar level with bilateral EBE (5 days difference between eyes) due to *Streptococcus pneumoniae* leaving no light perception in both eyes, another man with type 2 diabetes and urinary tract infection with bilateral EBE (5 days difference between eyes) due to *Staphylococcus aureus* leaving 20/30 VA in the right eye and less than 20/400 in the left eye, and finally a woman with abscess in a left hip prosthesis and simultaneous bilateral EBE due to *Morganella morganii* leaving no light perception in both eyes [23].

Finally, to our knowledge and after exhaustive literature search, this is the first published case of asynchronous bilateral EBE caused by *K. pneumoniae* with a prolonged difference of 14 months in the onset of symptoms between eyes. The origin was a liver abscess that formed after cholecystectomy and persisted silent for 17 months without adequate treatment, which produced transient bacteremia and caused endophthalmitis 14 months apart between eyes. First, diffuse anteroposterior endophthalmitis occurred in the left eye that ended in phthisis bulbi due to delay in initial diagnosis and established treatment. Then, focal endophthalmitis occurred in the right eye, preserving the organ and 20/20 VA due to early diagnostic suspicion and rapid treatment. The most likely hypothesis is that this is a hypervirulent strain of *K. pneumoniae*.

This case illustrates that EBE is a vision-threatening ophthalmologic emergency that can be associated with life-threatening systemic morbidities. Given that prognosis is associated with early treatment, early diagnosis represents a challenge for clinicians, ophthalmologists, and microbiologists. The CARE Checklist was completed by the author for this case report and attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000540471).

Statement of Ethics

This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines. Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the participant for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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This study was not supported by any sponsor or funder.

Author Contributions

Pedro Javier Nuova is the sole author of this work.

Data Availability Statement

Data are present in clinical records from the Sanatorio Modelo of Tucumán, but the data are not publicly available due to privacy reasons. Nevertheless, they are available upon reasonable request to the corresponding author Pedro Javier Nuova.

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