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CASE REPORT

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Community-acquired *Klebsiella pneumoniae* systemic infection complicated with rhombencephalitis

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Abstract

Rhombencephalitis is a rapidly progressing disease that should be taken into consideration in a patient with abrupt onset of cerebellar ataxia with rapid neurologic deterioration (tetraparesis, coma) after vascular etiology has been ruled out.

KEYWORDS

coma, *Klebsiella pneumoniae*, rhombencephalitis, systemic infection

1 | INTRODUCTION

Rhombencephalitis (RE) refers to inflammatory diseases of the rhombencephalon. The most common cause of RE is the infection with Listeria monocytogenes followed by enterovirus. We report a case of community-acquired *Klebsiella Pneumoniae* systemic infection with CNS involvement in an adult patient without significant comorbidities.

The term rhombencephalitis refers to inflammatory diseases involving the hindbrain (brainstem and cerebellum).

It was described for the first time by two scientists, Edwin Bickerstaff and Philip Cloake in 1951[1,2] to designate inflammatory affections of the rhombencephalon.

Rhombencephalitis has a wide range of etiologies, which can be divided into infectious, autoimmune, and paraneoplastic causes.

The most common infectious agent is Listeria monocytogenes, followed by enterovirus 71 and herpesviruses. The most common autoimmune cause is Behcet's disease, and the most frequent paraneoplastic syndrome is caused by small-cell lung cancer.[3]

In Gram-negative CNS infections, a primary focus may be found in neonates, traumatic, or neurosurgical patients, but in adults without a history of surgical operations, the primary focus of the infection could not be detected in up to 60% of cases.[4]

The most common presentations of *Klebsiella pneumoniae* (*K. pneumoniae*) CNS infection in adult are meningitis and brain abscess, but cerebritis and cerebral hemorrhage were also reported.[5]

Here, we report a case of *K. pneumoniae* septicemia associated with CNS involvement in an immunocompetent patient, without neurosurgical or trauma history.

2 | CASE PRESENTATION

We present a case of an immunocompetent 60-year-old male patient admitted to the Neurology Department with sudden onset of difficulty in walking, poor balance, slurred speech, and complaints of mild headache.

His past medical history included hypertension and a chronic right sciatica, for which he received symptomatic treatment with NSAIDs and paravertebral infiltration with steroids.

At the time of admission, he was afebrile, alert, and without signs of meningism. No facial asymmetry or

palpebral ptosis was noted. He had bilateral gaze-evoked nystagmus, gait ataxia, bilateral cerebellar dysmetria, and dysarthria. Laboratory findings are as follows: minimal hepatic cytolysis, inflammatory syndrome with leukocytosis (WBC = 22×10^9 cells/L, 90% neutrophils, erythrocyte sedimentation rate = 40 mm/h, and C-reactive protein = 18 mg/L).

An emergency brain CT angiography was performed, and no acute lesions were observed.

Given the sudden onset of symptoms, a cerebrovascular accident (CVA) in the vertebrobasilar region was suspected and treatment with antiplatelet and statins was initiated.

Within a few hours of hospitalization, his condition worsened, and he presented several episodes of projectile vomiting and became less responsive (somnolence alternating with agitation). Further on, his neurological status deteriorated rapidly and he developed tetraplegia with bilateral Babinski sign. He became comatose (GCS = 3 points), with nonreactive mydriatic pupils and was immediately transferred to the intensive care unit (ICU).

At this point, the authors considered the following differential diagnoses: an encephalitic process involving the brainstem, brainstem compression, cerebral edema with brain herniation, and venous thrombosis, and therefore, additional investigations were performed.

The patient was referred for an emergent brain MRI which showed bilateral cerebellar lesions, hyperintense in T2/FLAIR, diffuse edema involving bilateral cerebellum, medulla, and pons (Figure 1). Neither contrast-enhanced lesion nor leptomeningeal enhancement was shown.

The initial diagnosis of CVA in the vertebrobasilar region was rejected, because both CT angiography and MRI showed fully intact vasculature (arteries and veins), and so was the suspicion of venous thrombosis. The aspect of the lesions on MRI was suggestive for encephalitis.

A lumbar puncture was performed, and cerebrospinal fluid examination revealed a leukocyte count of 75/mm^3 , a protein concentration of 1230 mg/dL, and a glucose concentration of 87 mg/dL (blood glucose: 156 mg/dL).

In the ICU department, the patient became febrile, with marked inflammatory syndrome. Empiric antibiotic therapy was initiated with intravenous vancomycin 1.5 g every 12 hours, ampicillin 2 g every 6 hours, and meropenem 2 g every 8 hours, associated with acyclovir 500 mg every 8 hours, to cover for bacterial and viral infections.

Screening for MRSA, ESBL, VRE, and CRE was performed upon ICU admission, and blood cultures were also taken within the first 24 hours of admission.

Chest radiograph was normal.

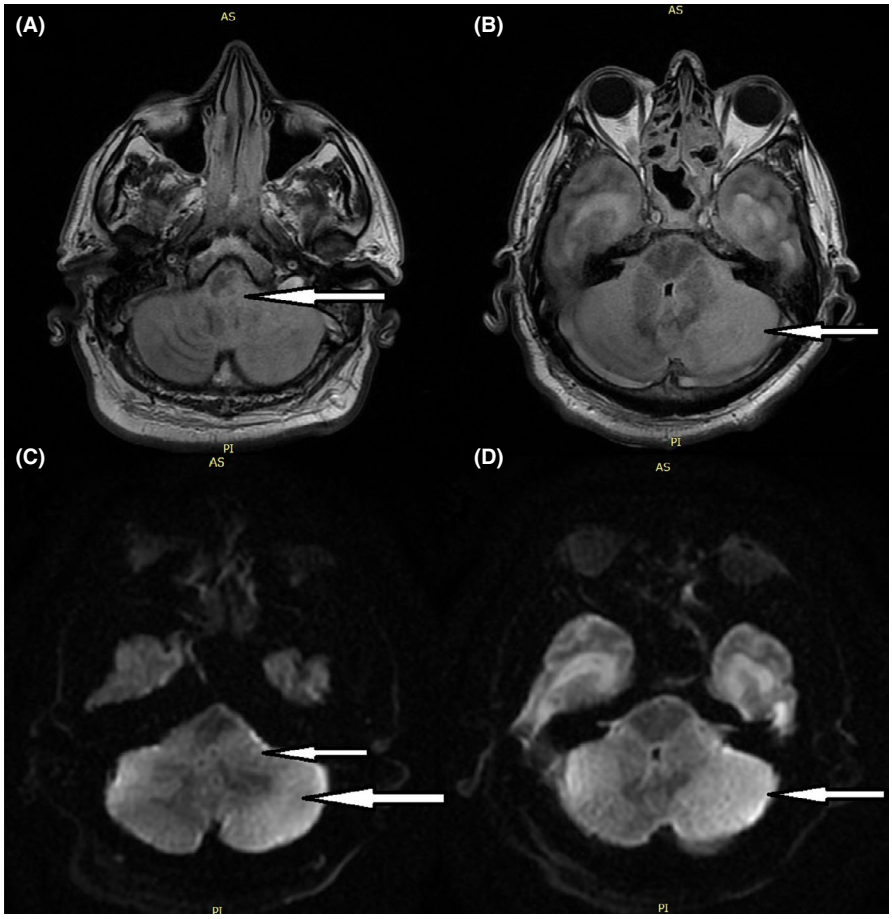

FIGURE 1 (1.5 Tesla): MRI axial fluid-attenuated inversion recovery (FLAIR) sequence (A, B) and diffusion-weighted image (DWI) sequence (C, D) showing bilateral, asymmetric, hyperintensity in the cerebellum with extension into the brainstem (A, C)

Cultures of CSF were positive for *K. pneumoniae* spp, and it was detected in blood and urine cultures as well, on the 5th day of admission. The isolated strain was susceptible to the majority of antibiotics.

Therefore, a diagnosis of systemic infection with *K. pneumoniae* complicated with rhombencephalitis was made and antibiotic treatment was adjusted according to the results of blood, urine, and CSF cultures.

Because Klebsiella spp. primarily attack immunocompromised individuals, the patient was tested for HIV and syphilis, with a negative result.

A abdomino-pelvic CT scan was performed, to rule out neoplastic disease, which could cause immune suppression. The examination revealed right iliopsoas muscle abscess (Figure 2). An ultrasound-guided drainage was performed, and the pus culture was also positive for K. pneumonia.

The initial screening for MRSA, ESBL, VRE, and CRE was negative, but a second screening was performed 9 days after ICU admission and Klebsiella CRE and ESBL was detected on perianal and rectal swabs.

2.1 | Outcome and follow-up

Despite intensive treatment, the patient's condition further deteriorated and he developed several complications such as pulmonary embolism, septic shock, for which he received appropriate treatment.

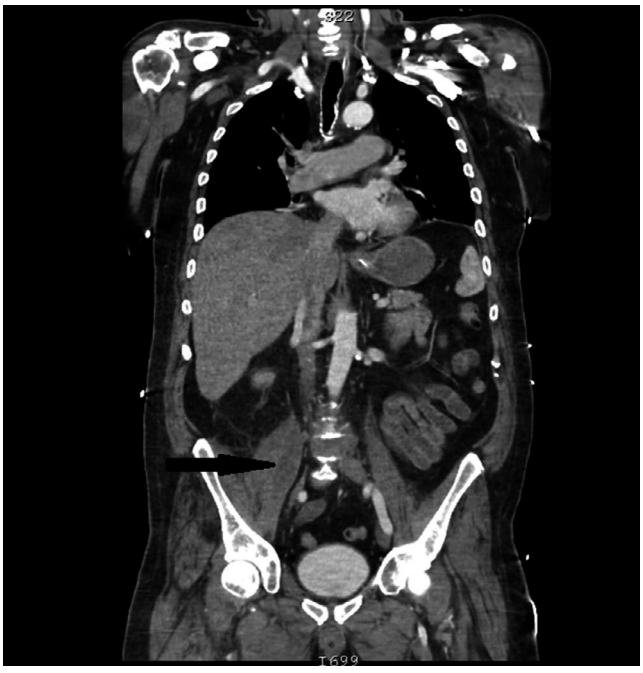

FIGURE 2 Contrast-computed tomography of the abdomen, pelvis, and thorax, with arrows pointing to right psoas muscles. Note the different sizes between right and left psoas muscle. The affected portion of the right psoas muscle is expand

However, he remained comatose, intubated, and ventilated without autonomous respiration, with a persisting GCS 3, absence of brainstem reflexes, and he died on the 14th day of hospitalization.

3 | DISCUSSION

Our patient was a 60-year-old male with no previous hospital admissions and no obvious risk factors for suppressed immune status, who developed a systemic infection with CNS involvement, with an unusual pathogen.

Rhombencephalitis is usually caused by Listeria monocytogenes, followed by herpes simplex virus (HSV) and enterovirus-71, while to our knowledge, no cases of *K. Pneumoniae* infection with CNS involvement presenting as rhombencephalitis have been previously reported.

Listerial rhombencephalitis has a characteristic biphasic course: For the first 2-4 days, there are nonspecific symptoms, such as fever, headache, nausea, and vomiting, followed by progressive asymmetrical cranial nerve palsies, cerebellar signs, hemiparesis, and impairment of consciousness. The onset of neurological deterioration is usually abrupt. The syndrome progresses rapidly and sometimes has a fatal outcome.[6]

In our case, the course of the syndrome was different, with mild headache presenting as the first symptom, followed by cerebellar signs, impairment of consciousness, quadriplegia, and ultimately fever, with rapid progression.

The cerebellar signs were consistent with bilateral cerebellar lesions, and the patient's weakness presumably resulted from the extensive brainstem lesion involving the corticospinal tracts. The coma was likely caused by the involvement of the reticular activating system.

The diagnosis is usually achieved by MRI findings and confirmed by CSF analysis in correlation with clinical manifestations.

Radiological findings reveal high signal intensities on T2-weighted, FLAIR, and DWI (hypointense on ADC map) images in the brainstem and cerebellum, with hypo- or isointense signal in T1. On Postgadolinium T1-weighted series, there is variable enhancement, depending on the etiology. MRI findings are not exclusive of any particular entity.[7]

CSF examination usually reveals moderate pleocytosis, normal/reduced glucose concentration, and elevated proteins. Positive CSF and blood cultures are the most specific findings for diagnosis.

In this case, CT scan upon admission was unremarkable, which is possible in the early course of the disease. When the clinical status of the patient deteriorated, an MRI was performed, which evidenced lesion characteristic for rhombencephalitis.

Combining CSF, blood, and urine cultures (blood cultures were taken within 24 hours of admission) with radiological

and clinical findings, we established the diagnosis of community-acquired *K. pneumoniae* septicemia complicated with rhombencephalitis.

Klebsiella species are Gram-negative bacteria, found ubiquitously in nature, including in plants, animals, and humans. It is the causative agent of several types of infections in humans, including respiratory tract infections, urinary tract infections (UTIs), and bloodstream infections (BSI).[8]

Klebsiella Pneumoniae strains can be divided into opportunistic, hypervirulent (hv) and multidrug-resistant groups. Most frequently, opportunistic strains cause hospital-acquired infection in patients with impaired host defenses.[9] Hypervirulent strains of *K. Pneumoniae* affect healthy people in community settings and can cause severe infections, such as pyogenic liver abscess, endophthalmitis, and meningitis.[10]

In recent years, new hypervirulent Kp strains have been associated with life-threatening infections with distant metastasis and, despite the presence of comorbidities in most patients, it is seen in younger, healthy patients as well,[11,12] as also observed in our case.

Given the aggressive course of the disease and the lack of response to antibiotic treatment, we presume that a hypervirulent strain of *K. pneumoniae* was involved in this case.

The frequency of Klebsiella as a CNS pathogen is increasing, with no improvement in prognosis over a 15-year period despite the availability of newer antibiotics. There is a higher mortality in BSI with Klebsiella and concomitant CNS spread.[13] BSI can be primary (no identifiable source) or, more often, secondary infection through dissemination from a known source. The most common sources of secondary BSI include the urinary tract, the gastrointestinal tract, intravenous or urinary catheters, and respiratory sites.[14]

The portal of entry of *K. pneumoniae* bacteremia is identified in only 32% of cases; it is usually urinary, digestive, and hepatobiliary. Other gateways—vascular, oral, or lung, were rarely found.[15]

In our case, it was difficult to establish the primary source of the systemic infection, given the multiple infected sites.

Klebsiella Pneumoniae psoas muscle abscess is a rare infection that has been described in case reports and small institutional series, mostly from Taiwan, where, since 1981, a distinctive syndrome of community-acquired *K. pneumoniae* septicemia with liver abscess has been reported.[16,17] Among those cases, 43 percent had concurrent urinary infection. This syndrome is notable for high mortality (10%-40%), and some cases have been complicated by meningitis or endophthalmitis.[18]

The psoas abscess is considered primary if the cause is hematogenous seeding from a distant site by bacteremia or sepsis, and secondary if there is a contiguous infectious source from vertebrae, pancreas, kidney, ureter, appendix, bowel, or hip joint.[19]

The psoas major originates along the outer surfaces of the vertebral bodies of T12 and L1-L3 and their associated intervertebral disks.

Taking into consideration the anatomy of the psoas muscle and the fact that the patient received paravertebral infiltration in the lumbar region for his sciatica, we cannot rule out the hypothesis that the psoas abscess was the primary source of infection.

Intramuscular injections can rarely result in serious infectious complications such as abscesses which may progress to bacteremia and generalized sepsis.

Due to the proximity of iliopsoas abscess to the vertebrae, it is possible that the adjacent structures could be infected via direct invasion, causing epidural abscess, osteomyelitis, or discitis. In this case, the abdomino-pelvic CT scan did not evidence any of this. We cannot exclude that the lumbar sciatic was caused in the first place by an infectious process in the lumbar region.

Another hypothesis is that the primary source of infection could be the urinary tract infection, which could lead to psoas abscess either by contiguity or hematogenous spreading, with CNS involvement.

Management of rhombencephalitis includes treating the underlying cause in addition to supportive management. Carbapenems are typically the drug of choice to treat severe infections caused by ESBL-producing bacteria.

Due to the selective pressure of treating ESBL infections with carbapenems, resistance has emerged and *K. pneumoniae* is the most common carbapenem-resistant Enterobacteriaceae (CRE), which can explain the inadequate response despite treatment with broad-spectrum antibiotics.

Another risk factor for poor outcome in this case was the association of community-acquired bacteremia with an ICU-acquired infection (*K. pneumoniae* CRE and ESBL).

Because Listeria and HSV are the most common treatable acute causes, it is recommended to start empiric therapy with ampicillin and acyclovir for all cases after CSF and blood samples have been obtained for cultures and the polymerase chain reaction (PCR). Antibiotics can be changed based upon MRI, culture results, and PCR results.

CNS infections represent a challenge for clinicians because of the poor concentration achieved by antibiotics in the CSF. In particular, if the isolated microorganism exhibits multiple resistances, the situation becomes critical because of the relative difficulty of reaching the high concentrations needed.

Despite advances in microbiology and imaging, rhombencephalitis can be a diagnostic challenge due to the multitude of possible differential diagnoses and the difficulty to determine etiology. In order to reduce mortality and morbidity, rapid diagnosis and adequate treatment are important. Overall mortality in rhombencephalitis is around 10%-15%.[20]

A particularity of this case was the systemic infection with *K. pneumoniae* and CNS involvement presenting as

rhombencephalitis in an immunocompetent patient, without known comorbidities or risk factors that could affect immunocompetence.

Another particularity of the case was the difficulty to establish the primary source of *K. pneumoniae* systemic infection, which remained unknown.

4 | CONCLUSIONS

This case shows an unusual and severe CNS complication of a systemic infection with *K. pneumoniae*-rhombencephalitis, which, to our knowledge, has not been reported before.

It illustrates the difficulty of identifying the original site of infection in the presence of several infected sites and bacteremia.

It also shows the devastating course that community-acquired *K. Pneumoniae* infection can have in an apparently immunocompetent patient, without significant comorbidities.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

AUTHOR CONTRIBUTIONS

DMS: is a consultant neurologist in charge of the patient and given approval of the final version of the paper. DLŞ: is a resident doctor, conception and design of the case report. MR: is a resident doctor, drafting the work and revising it for important intellectual content. AA: is a resident doctor, comparing the case report to the current literature. DFM: is a coordinator of the team.

ETHICAL APPROVAL

The ethical principles in this case were applied.

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