Hospital-Acquired *Citrobacter* Meningitis Complicated by Pneumocephalus in a Neonate

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Citrobacter koseri, a facultative gram-negative bacillus, colonizes the intestine and environmental reservoirs. In neonates, especially preterm infants, it can cause severe central nervous system infections (eg, meningitis, encephalitis, abscesses), often with fatal outcomes. Pneumocephalus, an accumulation of intracranial gas, is a rare but deadly complication. We report a preterm female infant admitted to the neonatal intensive care unit (NICU) for respiratory distress who developed high fever and sepsis; blood culture results were positive for *C. koseri*. Rapid neurological deterioration with seizures occurred, and a cranial computed tomography scan showed extensive pneumocephalus. Despite intensive care, the infant died at 17 days. Autopsy and histology revealed widespread purulent meningitis and meningoencephalitis, pneumocephalus, cerebral hemorrhages, acute edema, and ventricular dilation. An environmental investigation traced the origin of the infection to the bathroom sinks, confirming the nosocomial nature of the pathogen. This case highlights the high virulence of *C. koseri* in neonates, the catastrophic potential of pneumocephalus, and the crucial importance of strict infection control in NICUs.

INTRODUCTION

Neonatal infections caused by *Citrobacter koseri* pose a significant clinical challenge because of their potential severe complications. We present the case of a preterm female infant who developed sepsis secondary to *C. koseri*, which was ultimately determined to be of nosocomial origin. The clinical course was further complicated by the development of pneumocephalus, an uncommon and serious complication associated with this gas-producing pathogen.

Case Report

This report details the case of a female infant born at 30 weeks and 3 days' gestation via cesarean section, with a birthweight of 1050 g (making her very low birth weight [VLBW]). The pregnancy was complicated by premature rupture of membranes (PROM) 1 month prior to delivery, for which the mother had been hospitalized.

Immediately after birth, the infant was admitted to the neonatal intensive care unit (NICU) for respiratory distress syndrome. Her overall clinical condition gradually improved until the eighth day, when she began to exhibit regurgitation and vomiting. The underlying cause became evident on the 16th day, when she developed hyperpyrexia, elevated inflammatory markers, and clinical signs of sepsis. Her condition rapidly worsened over the next 2 days, with the onset of seizures and an electroencephalogram showing markedly and diffusely depressed activity.

abstract

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Dr Di Maria drafted and wrote the original manuscript, including the literature review. Prof D'Errico and Dr Bolcato brought the present case to attention, conceptualized and designed the case report, and coordinated and supervised the process. Dr Radaelli and Dr Concato critically reviewed and revised the manuscript. Dr Buffon performed the histological analyses and provided interpretation and evaluation of the histological slides. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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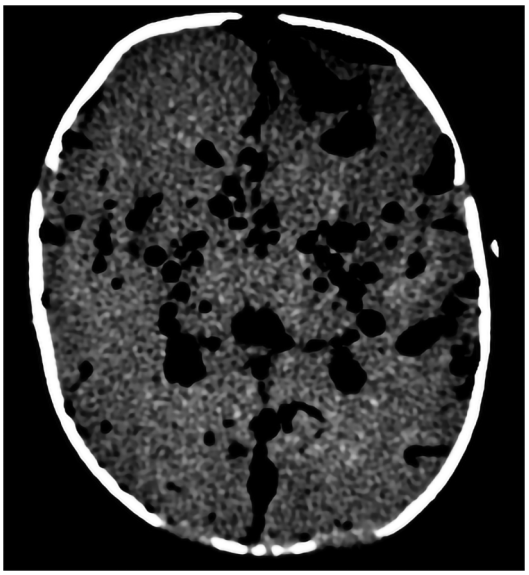

FIGURE 1.
Axial view of the CT scan.
Abbreviation: CT, computed tomography.

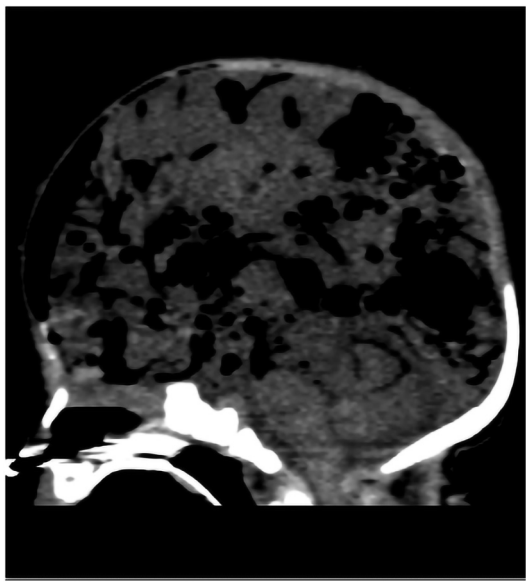

FIGURE 2.
Sagittal view of the CT scan.
Abbreviation: CT, computed tomography.

Concurrently, a cranial computed tomography (CT) scan revealed the presence of intracranial gas localized within the cerebral tissue, ventricular system, and subdural space (Figures 1–3).

From birth, the infant received prophylactic antibiotic therapy with ampicillin, gentamicin, and fluconazole, administered for 9, 6, and 7 days, respectively, owing to the placement of a central vascular catheter. On the day that sepsis became clinically apparent, a blood sample was obtained, and empirical antibiotic therapy with vancomycin and amikacin was started following the onset of gastrointestinal symptoms and the identification of gram-negative bacilli in the preliminary blood culture. Two days after the infant's death, a multidrug-sensitive *Citrobacter koseri* strain was definitively identified as the causative agent.

She died 17 days after birth, and an autopsy was conducted to determine the precise cause of death and assess any potential liability on the part of the health care providers or the hospital responsible for her care. External examination revealed cyanosis of the extremities. Macroscopic findings included the release of abundant gas on opening the cranium, inflammatory changes in the meninges, a vacuolated appearance of the brain on section, parenchymal hemorrhages, and ventricular dilation. Tissue samples were collected, and histological examination conducted using hematoxylin and eosin staining demonstrated severe purulent meningitis, encephalitis with acute inflammatory foci, intraparenchymal cerebral hemorrhage, and acute cerebral edema (Figures 4 and 5). The cause of death was determined to be sepsis secondary to *C. koseri*, culminating in meningoencephalitis with diffuse pneumocephalus and cerebral

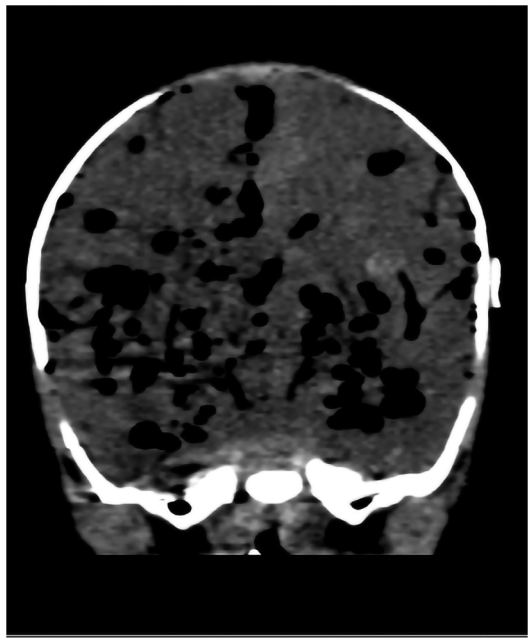

FIGURE 3.
Coronal view of the CT scan.
Abbreviation: CT, computed tomography.

hemorrhage. Using CT scan data, a three-dimensional reconstruction was performed via the Anatomage Table, a virtual dissection platform at the University of Trieste, which clearly delineated the spatial distribution of gas vacuoles within the cerebral parenchyma (Figure 6).

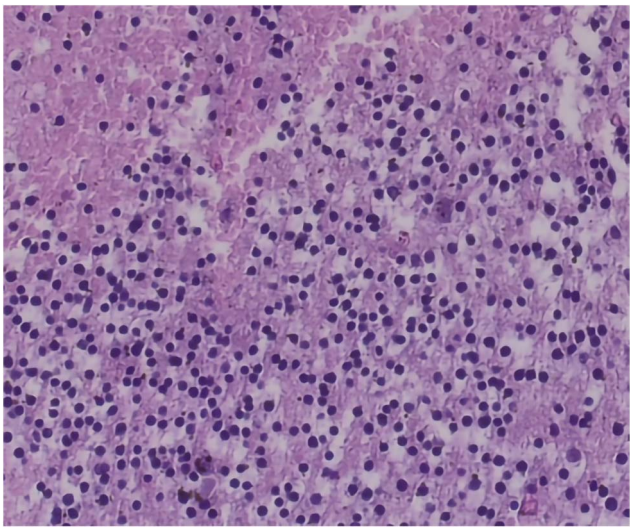

FIGURE 4.
Sample taken from the parietal lobe. The presence of abundant inflammatory infiltrate is evidence of the cerebral infectious process.

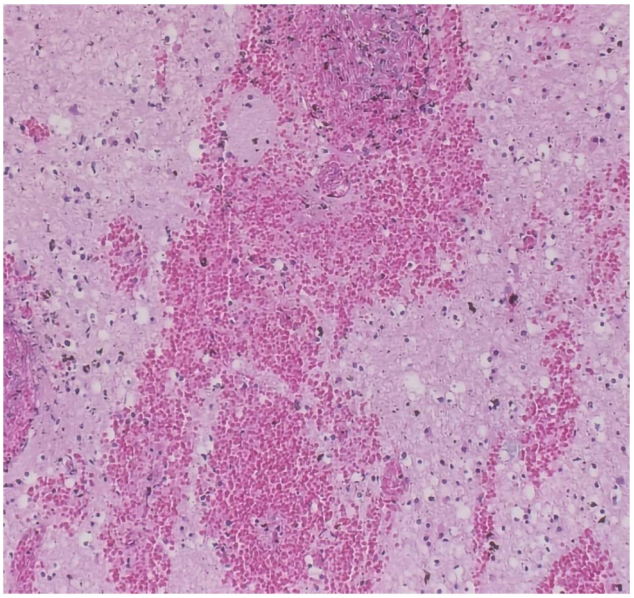

FIGURE 5.
Sample taken from the left parietal lobe. Cerebral hemorrhage is clearly visible.

DISCUSSION

Citrobacter spp are gram-negative bacilli with facultative anaerobic metabolism capable of breaking down glucose, leading to the formation of gas byproducts. These organisms are commonly found in the intestinal tracts of humans and animals and are also widespread in various environmental sources, including water, soil, and food.[1] *C. koseri* and *C. freundii* are the primary species responsible for the majority of *Citrobacter* infections.[2]

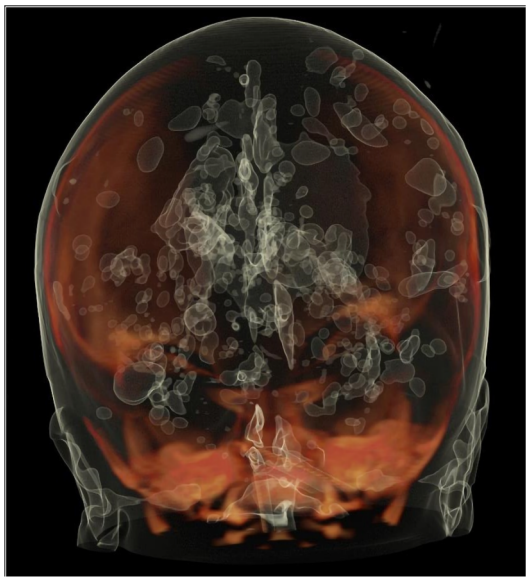

FIGURE 6.
Three-dimensional images reconstructed using the coronal view of the CT scan.
Abbreviation: CT, computed tomography.

A distinctive characteristic of this group of bacteria is their ability to cause significant nosocomial outbreaks that can persist for prolonged periods, ranging from several months to even years.[1,3] In most cases, health care personnel's hands have been identified as a primary source of transmission, reflecting horizontal transmission originating in the clinical environment.[1] The *Citrobacter* spp can thereby be classified within the broader category of health care-associated infections (HAIs), which are defined as infections acquired during medical treatment in hospitals that were not evident or incubating at the time of admission.[4] This species is accounted for causing approximately 3% to 6% of all *Enterobacteriaceae* infections isolated in hospital settings.[3]

Vertical transmission represents an additional pathway through which *Citrobacter* infections can occur, with neonates potentially acquiring the organism during delivery if the maternal birth canal is colonized.[5] When symptoms manifest within hours of birth, vertical transmission should be considered the likely route of infection. However, confirmatory diagnostic methods are often lacking, and identification of the pathogen in the mother frequently remains undetermined.[1,6]

Citrobacter species are capable of causing a broad spectrum of infections, despite being considered a low-virulence organism, including those affecting urinary and respiratory tracts, the abdominal cavity, skin and soft tissues, eyes, bones, the bloodstream, and the central nervous system (CNS).[3]

Two populations are at highest risk for *Citrobacter*-related clinical disease: immunocompromised individuals

of any age, and newborns, especially preterm infants (gestation age of younger than 37 weeks), who are also particularly in danger of vertical germ transmission.[1,5,6]

Of all the *Citrobacter* CNS infections in the neonatal population, *C. koseri* has been identified as the most-frequently implicated species.[1] This is attributed to the presence of a specific outer membrane protein that confers a marked tropism for meningeal tissue.[1,5] Meningitis, encephalitis, and brain abscesses represent the most-frequent clinical manifestations in neonates, constituting the majority of reported cases in literature.[7,8] Notably, *C. koseri* is responsible for up to 80% of all neonatal brain abscesses, a significantly higher proportion compared with other causative agents,[6] and is associated with high mortality and a high rate of long-term neurological complications among survivors.[9]

A rare but devastating complication of *C. koseri* CNS infections is pneumocephalus, a condition characterized by the presence of air within the epidural, subdural, or subarachnoid spaces; the brain parenchyma; or the ventricular system.[10] The primary causes of pneumocephalus are traumatic, typically involving air entry through skull fractures. However, spontaneous cases can also occur, particularly in the context of infections caused by gas-producing bacteria.[11,12]

To our knowledge, this represents one of the few reported cases of neonatal pneumocephalus secondary to *C. koseri* infection.[5,13–17] The patient, a preterm infant born at 30 weeks and 3 days' gestation, presented with early signs of sepsis, including lethargy and poor oral intake, which are clinical features that have been commonly observed in previously documented cases.[5,13,14,17]

The neonate exhibited significant risk factors for infection, including VLBW and prematurity. This case was classified as an HAI, as evidenced by the absence of infection signs during the immediate postnatal period, delayed sepsis onset, and placental histopathology revealing no infection strongly supported the exclusion of vertical transmission.

The empirical antibiotic regimen, consisting of vancomycin and amikacin, was likely inadequate for treating *C. koseri*, which is less susceptible to amikacin alone but is susceptible to third-generation cephalosporins, carbapenems, piperacillin–tazobactam, and trimethoprim.[9]

Following the reported case, a thorough investigation identified bathroom sinks used for rinsing infant bottles as the source of infection. The cultures and subsequent analyses, performed using pulsed-field gel electrophoresis, confirmed that it was the same strain of *C. koseri*, thereby confirming the nosocomial origin of the infection. A second case was documented 11 months later, prompting the implementation of enhanced procedures to prevent bacterial dissemination. These included isolation of colonized neonates; reinforced hygiene protocols for parental contact; assessment of health care staff adherence to hand hygiene and device disinfection; and universal screening of neonates using nasopharyngeal, conjunctival, and biweekly urine cultures for at least 4 weeks. Environmental contamination was monitored via surface- and object-sampling, and decontamination was conducted using chlorine solutions. Despite these measures, 4 additional clustered cases occurred 16 to 18 months after the initial case, leading to further strengthened surveillance protocols. Neonates were separated into 3 dedicated rooms with color-coded zones (ie, red for positive results, yellow for pending culture results, and green for negative results). Screening was intensified, with rectal and nasopharyngeal swabs at birth and every 48 hours. Random screening of healthy neonates was conducted at birth and discharge. Sampling of formula milk, air, and water was performed, alongside screening of all health care personnel via oropharyngeal, inguinal, and hand swabs. Detailed epidemiological investigations were carried out on all infants with *C. koseri* positivity to identify potential sources of infection. Adherence with infection prevention practices was evaluated, and dedicated pathways for parental access were established. Since implementing these comprehensive procedures, no further cases of *C. koseri* infection have been detected.

Although cases of vertically transmitted *C. koseri* infections (eg, those linked to chorioamnionitis) have been documented in scientific literature, this is a documented case of *C. koseri* meningoencephalitis resulting from horizontal transmission and classified as an HAI.[18]

In a comparable case of hospital-acquired CNS infection, the health care-associated classification was dismissed despite the absence of environmental screening to substantiate this conclusion.[8]

Although *C. koseri* is not traditionally classified as a prototypical nosocomial pathogen, mounting evidence has highlighted its emerging role in HAIs. A 2024 systematic review identified 13 *Citrobacter* spp outbreaks between 1991 and 2020, with 85% of infections occurring in hospitalized patients and 54% of outbreaks proving difficult to control. These events were frequently linked to hospital environmental reservoirs such as sinks, toilets, contaminated food supplies, and injection materials.[19] Among the studies examined, 4 specifically reported nosocomial outbreaks involving *C. koseri* and *C. freundii* in pediatric departments and/or in the NICU.[19]

CONCLUSIONS

This report describes a severe case of meningoencephalitis complicated by pneumocephalus in a preterm infant caused by *C. koseri*. The case underscores the critical importance of stringent infection control measures in NICUs to prevent severe outcomes associated with this rare but highly pathogenic nosocomial organism. It further highlights the necessity for enhanced clinical recognition, preventive strategies, and rigorous hygiene protocols to

mitigate the risk of hospital-acquired infections in vulnerable neonatal populations.

CONSENT

Written permission was obtained from the patient's guardian(s) to publish this case and the corresponding photos or imaging studies.

ABBREVIATIONS

CNS: central nervous system
CT: computed tomography
HAI: health care-associated infection
NICU: neonatal intensive care unit
PROM: premature rupture of membranes
VLBW: very low birth weight

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