EUROPEAN JOURNAL OF EMERGING MICROBIOLOGY AND INFECTIOUS DISEASES

A FATAL CASE OF PNEUMOCEPHALUS LINKED TO HYPERMUCOVISCOUS, HYDROGEN-PRODUCING KLEBSIELLA PNEUMONIAE (K63) IN DIABETIC KETOACIDOSIS

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V0LUME01 ISSUE01 (2024)
Published Date: 02 December 2024 // Page no.: - 1-12

ABSTRACT

Imagine air trapped inside the skull – that's pneumocephalus, a rare but incredibly dangerous condition, especially when it's caused by gas-producing infections. This report shares the tragic story of a patient who developed extensive pneumocephalus and ultimately passed away. The culprit was a particularly aggressive strain of Klebsiella pneumoniae, a bacterium that not only produced a lot of sticky mucus but also generated hydrogen gas, all while the patient was battling severe diabetic ketoacidosis (DKA). When the patient arrived, his health was rapidly declining, and scans showed widespread air and multiple pockets of infection (abscesses) in his brain. Lab tests confirmed the highly virulent nature of the K. pneumoniae strain. Despite our best efforts with intensive medical care, the patient unfortunately succumbed within 48 hours. This case serves as a stark reminder of how incredibly dangerous certain K. pneumoniae strains can be, especially for people whose immune systems are weakened, like those with DKA, leading to incredibly fast and severe brain infections. Getting a quick diagnosis through scans and starting strong, targeted antibiotics are vital, but even then, the outlook for such widespread infections remains grim.

Keywords: Pneumocephalus, Klebsiella pneumoniae, Hypermucoviscous, Hydrogen-producing, Diabetic Ketoacidosis, Brain Abscess, Central Nervous System Infection, K63.

INTRODUCTION

Imagine the brain, a delicate organ, suddenly having pockets of air or gas trapped inside its protective casing – that's pneumocephalus. It's a condition that can be a minor finding, or, as in our case, a terrifying and life-threatening emergency. The reasons it happens are varied: sometimes it's from an injury, sometimes after surgery, or sometimes it just appears spontaneously, perhaps from a sinus infection that finds its way into the skull [4]. When air builds up, especially under pressure (what we call tension pneumocephalus), it can literally squeeze the brain, affecting blood flow and causing severe damage. This is why a quick and accurate diagnosis, often through advanced brain scans, is so crucial – it helps us figure out how to best help the patient.

Understanding Pneumocephalus: A Silent Intruder

Pneumocephalus, derived from the Greek words "pneuma" (air) and "kephale" (head), refers to the abnormal presence of air or gas within the intracranial cavity. While seemingly benign in small quantities, its presence signals a breach in the normally sealed cranial vault, creating a potential pathway for pathogens and exerting mechanical pressure on delicate brain structures. Clinically, pneumocephalus can manifest along a broad spectrum, from asymptomatic cases discovered incidentally on imaging to severe neurological emergencies. The symptoms often depend on the volume, location, and rate of air accumulation. Small, stable collections of air might cause only mild headaches or no symptoms at all. However, as the volume of intracranial air increases, it can lead to more pronounced symptoms such as severe, throbbing headaches (often described as "sloshing" or "gurgling" sounds by the patient, known as the "bruit de moulin" or "mill wheel murmur"), nausea, vomiting, dizziness, altered mental status, seizures, and focal neurological deficits like weakness or sensory changes.

The underlying causes of pneumocephalus are broadly classified into three main categories:

1. Traumatic Pneumocephalus: This is the most common etiology, accounting for approximately 70% of all cases. It typically results from head injuries that cause fractures of the skull, particularly those involving the skull base. Fractures in areas like the frontal bone, ethmoid bone, sphenoid bone, or temporal bone can create a direct communication between the intracranial space and adjacent air-filled cavities, such as the paranasal sinuses (frontal, ethmoid, sphenoid) or mastoid air cells. The air

can then enter the cranial cavity through this defect, often exacerbated by a "ball-valve" mechanism where coughing, sneezing, or Valsalva maneuvers force air in but prevent its escape.

2. Iatrogenic Pneumocephalus: This category arises as a complication of medical or surgical procedures. Neurosurgical interventions, especially those involving craniotomy, skull base surgery, or procedures near the paranasal sinuses, are frequent culprits. Other iatrogenic causes include lumbar punctures, spinal anesthesia, placement of intracranial monitoring devices, and even dental procedures or endoscopic sinus surgery. In these scenarios, the dura mater, the tough outer membrane protecting the brain, is inadvertently breached, allowing atmospheric air to enter.

3. Spontaneous Pneumocephalus: This is the rarest category, occurring without a clear history of trauma or recent surgical intervention. It can be associated with a variety of underlying conditions:

- Infections: This is the category most relevant to our case. Gas-forming bacterial infections within the brain (e.g., brain abscesses, empyema) or adjacent structures (e.g., osteomyelitis, sinusitis, mastoiditis) can produce gas as a metabolic byproduct, which then accumulates intracranially.
- Tumors: Intracranial tumors, particularly those that are necrotic or involve air-filled spaces, can erode into the cranial cavity.
- Vascular Lesions: Rarely, conditions like cerebral aneurysms or arteriovenous malformations can lead to pneumocephalus.
- Congenital Defects: Pre-existing defects in the skull or dura can predispose individuals to spontaneous air entry.

A particularly dangerous form is tension pneumocephalus, where a large volume of air accumulates under pressure, acting as a mass lesion. This can lead to rapid neurological deterioration, brain compression, and potentially fatal cerebral herniation. Radiologically, tension pneumocephalus is often characterized by the "Mount Fuji sign" on CT scans, where the frontal lobes are separated by a large collection of air, resembling the iconic Japanese mountain. The rapid accumulation of intracranial gas, regardless of its origin, can exert direct pressure on brain tissue, compromise cerebral blood flow, and precipitate a cascade of detrimental physiological responses. These include elevated intracranial pressure (ICP), reduced cerebral perfusion pressure (CPP), and ultimately, irreversible brain injury if not promptly addressed. Therefore, timely and accurate diagnosis, primarily through advanced imaging techniques, is paramount for guiding effective management strategies and improving patient outcomes.

Klebsiella pneumoniae: A Versatile and Evolving Pathogen

Klebsiella pneumoniae is a Gram-negative, non-motile, encapsulated, facultative anaerobic bacillus belonging to the family Enterobacteriaceae. It is a ubiquitous bacterium found in various environments, including soil, water, and the human gastrointestinal tract, where it can be a commensal organism. However, K. pneumoniae is also a formidable opportunistic pathogen, responsible for a wide spectrum of infections in humans. Historically, it has been a common cause of hospital-acquired (nosocomial) infections, particularly pneumonia (often necrotizing), urinary tract infections, bloodstream infections (bacteremia), and surgical site infections. Its ability to form biofilms and its intrinsic resistance to certain antibiotics contribute to its persistence in healthcare settings.

In recent decades, a significant shift in the epidemiology and clinical presentation of K. pneumoniae infections has occurred with the emergence and global spread of hypermucoviscous Klebsiella pneumoniae (hvKp) strains [6]. Unlike classical K. pneumoniae (cKp) strains, which primarily affect immunocompromised or critically ill patients, hvKp strains possess enhanced virulence factors that enable them to cause severe, life-threatening infections in otherwise healthy individuals. These infections are often characterized by their invasive and metastatic nature, meaning they can spread from a primary site of infection to distant organs. Common metastatic complications include endophthalmitis (a severe eye infection), meningitis, brain abscesses, and necrotizing fasciitis. The global rise of hvKp, particularly in Asian countries, represents a significant public health concern, posing new challenges for diagnosis and treatment.

The heightened virulence of hvKp strains is attributed to a constellation of specific virulence factors:

1. Hypermucoviscous Phenotype: This is the most striking and defining characteristic of hvKp. It refers to the excessive production of an extracellular polysaccharide capsule, which gives colonies a highly viscous, stringy appearance (a positive "string test"). This thick capsule acts as a formidable shield, protecting the bacterium from host immune defenses. It effectively evades phagocytosis by macrophages and neutrophils, resists complement-mediated killing, and reduces the efficacy of antimicrobial agents. This protective barrier allows hvKp to survive and disseminate within the host more effectively than cKp strains.

2. Capsular Serotypes: Specific capsular serotypes are strongly associated with hvKp strains and their enhanced pathogenicity. The most prevalent hypervirulent capsular types are K1 and K2, but other serotypes such as K5, K20, K54, K57, and, importantly for our case, K63, have also been identified as hypervirulent [6]. These specific capsule structures are often linked to particular sequence types (STs) identified through multilocus sequence typing

(MLST), such as ST23 (commonly associated with K1) or ST11 (often associated with K2). The K63 capsular serotype, though less frequently reported than K1 or K2, is recognized for its significant virulence potential.

3. Siderophores: HvKp strains often produce an abundance of siderophores, small, high-affinity iron-chelating compounds that are crucial for bacterial growth in iron-limited environments like the human body. Key siderophores associated with hvKp include aerobactin (encoded by the iucABCD-iutA operon), enterobactin, and yersiniabactin. Efficient iron acquisition is a critical determinant of bacterial survival and proliferation within the host, contributing significantly to the invasive potential of hvKp.

4. Other Virulence Genes: A range of other genes contribute to hvKp virulence, including magA (mucoviscosity-associated gene A) and rmpA (regulator of mucoid phenotype A), both of which are involved in regulating capsule synthesis and contributing to the hypermucoviscous phenotype. Other genes related to adherence, serum resistance, and toxin production may also play roles.

A particularly relevant aspect of K. pneumoniae pathogenesis, especially in the context of pneumocephalus, is its ability to produce gas. Certain strains of K. pneumoniae are potent gas producers, primarily through the fermentation of carbohydrates, especially glucose [8]. This metabolic process yields various gaseous byproducts, predominantly hydrogen (H2) and carbon dioxide (CO2). This characteristic is central to the development of emphysematous infections, such as emphysematous pyelonephritis (a severe kidney infection) and emphysematous liver abscesses. In confined anatomical spaces, the accumulation of these gases can lead to severe pressure effects and tissue destruction, exacerbating the clinical picture. The presence of gas within a brain abscess, as seen in our case, is a strong indicator of this metabolic capability and significantly complicates management by contributing to elevated intracranial pressure.

Diabetic Ketoacidosis (DKA) and Immunocompromise: A Recipe for Vulnerability

Diabetic ketoacidosis (DKA) is an acute, life-threatening complication of diabetes mellitus, primarily occurring in individuals with type 1 diabetes but increasingly seen in type 2 diabetes, especially during periods of severe stress or infection. It results from a profound deficiency of insulin, leading to uncontrolled hyperglycemia, increased lipolysis (breakdown of fats), and excessive production of ketone bodies (beta-hydroxybutyrate, acetoacetate, and acetone), which are acidic. The accumulation of these ketones leads to a severe metabolic acidosis, a hallmark of DKA. Clinically, DKA is characterized by hyperglycemia, ketonemia, and metabolic acidosis, often accompanied by dehydration, electrolyte imbalances, and altered mental status.

Patients experiencing DKA are profoundly immunocompromised, rendering them highly susceptible to severe and opportunistic infections [2]. This immune dysfunction is multifaceted and contributes significantly to the increased risk of severe infections:

1. Neutrophil Dysfunction: Neutrophils, critical components of the innate immune system, are severely impaired in uncontrolled diabetes and DKA. Their functions, including chemotaxis (movement towards infection sites), phagocytosis (engulfment of pathogens), and oxidative burst activity (production of reactive oxygen species to kill pathogens), are all compromised. This means that the body's first line of defense against bacterial invaders is significantly weakened.

2. Impaired Cellular Immunity: While less pronounced than neutrophil dysfunction, components of cellular immunity, such as T-cell function, can also be affected in diabetes. Chronic hyperglycemia can lead to glycation of proteins, including those involved in immune signaling, further impairing immune responses. The lymphopenia observed in our patient (low CD4+ and CD8+ counts) is a direct indicator of this compromised cellular immunity, making the patient more vulnerable to a wide range of pathogens.

3. Hyperglycemic Environment: High blood glucose levels themselves can create a favorable environment for bacterial growth. Many bacteria, including K. pneumoniae, thrive in glucose-rich environments. Furthermore, hyperglycemia can directly impair the function of immune cells and promote inflammation.

4. Acidosis: The metabolic acidosis characteristic of DKA can also negatively impact immune cell function and alter host physiology in ways that favor bacterial proliferation and virulence.

5. Compromised Blood-Brain Barrier (BBB): Crucially, chronic hyperglycemia and the metabolic disturbances associated with diabetes have been shown to compromise the integrity of the blood-brain barrier (BBB) [2]. The BBB is a highly selective semipermeable membrane that normally protects the central nervous system (CNS) from circulating pathogens, toxins, and inflammatory cells. In diabetes, chronic inflammation, oxidative stress, and structural changes in the endothelial cells and tight junctions of the BBB can increase its permeability. This breach allows bacteria from a distant primary infection site (e.g., the lungs, liver, or urinary tract) to bypass this critical defense mechanism and gain entry into the brain parenchyma and cerebrospinal fluid. Once inside the CNS, the bacteria can rapidly proliferate in the relatively immune-privileged environment, leading to severe infections like meningitis and brain abscesses.

The convergence of a highly virulent, gas-producing pathogen like hvKp and the profound immunocompromised state induced by DKA creates an exceptionally dangerous synergy. The patient's weakened immune system is unable to mount an effective defense,

while the compromised blood-brain barrier provides an easy entry point for the aggressive bacterium. This combination often leads to rapidly progressive, severe, and often fatal infections, particularly within the central nervous system.

The Rarity and Severity of K. pneumoniae-Associated Pneumocephalus

While K. pneumoniae is a well-recognized cause of brain abscesses, the specific complication of extensive pneumocephalus due to hydrogen-producing K. pneumoniae in the context of diabetic ketoacidosis remains exceedingly rare. Previous reports in medical literature are scarce, with only a limited number of cases documented over the past few decades [5, 10, 11]. These rare case reports consistently highlight the severity of such infections and their often-fatal outcomes, particularly when associated with underlying diabetes.

To provide context for the extreme rarity and severity of our patient's condition, we have compiled a summary of previously reported cases of K. pneumoniae-associated pneumocephalus in non-operative and non-traumatic patients. This table, drawing insights from the limited existing literature, emphasizes commonalities such as the frequent association with diabetes and the often-grim prognosis.

Table 1: Summary of Previously Reported Cases of K. pneumoniae-Associated Pneumocephalus (Non-operative, Non-traumatic)

Case No.	Year Reported	Gender	Age (Years)	Underlying Conditions	Primary Symptoms	Imaging Findings (Key)	Treatment (Key)	Outcome	Source of K. pneumoniae (if known)	Reference
1	2014	Male	51	Diabetic Ketoacidosis	Headache, unresponsive	Cerebral edema, Pneumocephalus	Not available	Dead	Blood	[1]
2	2020	Female	56	Diabetes Mellitus, Septic Shock	Pneumocephalus, Septic shock	Extensive pneumocephalus	Ceftazidime, Polymyxin B	Dead	CSF, Blood	[5]
3	2001	Male	58	Diabetes Mellitus, Liver Cirrhosis	Headache, brain abscess	Pneumocephalus, brain abscess	Cefotaxime	Dead	CSF, Blood	[10]

4	2008	Male	59	Diabetes Mellitus, Liver Cirrhosis	Headache, comatose	Pneumocephalus, cerebral edema	Cephalosporin	Dead	Blood	[3]
5	2006	Female	86	Diabetes Mellitus	Fever, unconsciousness	Pneumocephalus, brain abscess	Not available	Dead	CSF	[12]
6	2003	Male	55	Tuberculous Spondylitis	Fever, back pain	Pneumocephalus, cerebral edema	Imipenem	Dead	CSF, Blood	[7]
7	1999	Male	66	Diabetes Mellitus	Dizziness, hemiplegia	Pneumocephalus, brain abscess	Craniotomy	Cured	CSF	[9]
8	2008	Male	26	Otitis Media	Headache, fever, vomiting	Pneumocephalus	Amikacin, Meropenem	Cured	CSF	[11]
9	2021	Male	38	Diabetic Ketoacidosis	Fever, unconsciousness	Pneumocephalus, cerebral ede	Imipenem, Ceftriaxone	Dead	CSF, Blood	This study

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Note: "Not available" (NA) indicates information not explicitly detailed in the cited reference regarding that specific aspect. "Cured" implies survival and resolution of the acute infection.

This table provides a crucial backdrop, illustrating that while K. pneumoniae-associated pneumocephalus is rare, it is disproportionately observed in patients with underlying conditions such as diabetes, and tragically, often leads to fatal outcomes. The case presented in this article adds to this limited but critical body of knowledge, providing further insights into the clinical presentation, microbiological characteristics, and devastating course of this rare and aggressive infection. It serves as a compelling reminder of the need for heightened clinical suspicion and rapid, comprehensive management in vulnerable patient populations.

This article aims to provide a detailed and comprehensive account of this fatal case, illuminating the complex interplay between host susceptibility and bacterial virulence. By emphasizing the diagnostic challenges and therapeutic considerations, we hope to contribute to a better understanding of this rare and aggressive infection, ultimately improving recognition and management strategies for future patients.

METHODS

To understand what happened in this tragic case, we carefully reviewed all the medical records of a single patient who came to our hospital with severe brain problems and diabetic ketoacidosis. Our approach involved a thorough look back at every piece of information available: from the patient's personal details and health history to their symptoms, lab test results, detailed brain scans, and the specific tests done on the bacteria that caused the infection. We also meticulously documented every treatment given during their hospital stay. To ensure everything was handled ethically, our study received approval from the Institutional Review Board of [Institution Name, e.g., The Fifth Affiliated Hospital of Wenzhou Medical University], and we obtained permission from the patient's family to share this story, making sure to keep their identity private.

Patient Selection and Data Collection

We found this patient by looking through hospital admissions for individuals who had sudden severe brain issues and were also diagnosed with diabetic ketoacidosis complicated by a serious infection. To make sure this report was focused and relevant, we set strict criteria: the patient had to have confirmed pneumocephalus on brain scans, Klebsiella pneumoniae had to be found in a sterile body site (like blood or spinal fluid), they had to have DKA, and sadly, the infection had to be the direct cause of their death.

Two researchers, both with medical backgrounds, independently gathered all the data to ensure accuracy and reduce any bias. We used a standard form to collect all the important details. If there were any differences in the information collected, a senior doctor or an infectious disease specialist helped us reach an agreement. The extensive information we gathered included:

- Patient Background: Their age, gender, ethnicity, any existing health conditions (especially how long they had diabetes, how well it was controlled, and any complications), past hospital stays, recent antibiotic use, and if their immune system was weakened for any other reason.

- How They Presented to the Hospital: A detailed description of their initial symptoms – when they started, how long they lasted, and how they progressed. This included specifics about their headache, changes in mental state, seizures, any weakness or numbness on one side of their body, problems with facial movements or vision, fever patterns, and other signs of infection. We also noted their initial vital signs (temperature, heart rate, breathing rate, blood pressure, oxygen levels) and their Glasgow Coma Scale (GCS) score, which tells us about their level of consciousness.

- Ongoing Lab Tests: We tracked important blood and other lab values over time. This involved:

  - Metabolic Health: Blood sugar levels, blood gas analysis (pH, carbon dioxide, bicarbonate), ketone levels in blood and urine, and lactate levels.

  - Inflammation Markers: C-reactive protein (CRP), procalcitonin (PCT), and erythrocyte sedimentation rate (ESR), all of which indicate how much inflammation is in the body.

  - Blood Cell Counts: A full blood count, including white blood cells (which fight infection), the percentage of neutrophils (a type of white blood cell), lymphocyte counts, hemoglobin (for anemia), and platelet counts (for clotting).

  - Kidney and Liver Function: Levels of creatinine, BUN, liver enzymes (ALT, AST), and bilirubin.

  - Electrolytes: Sodium, potassium, chloride, phosphate, and magnesium, which are crucial for body function.

  - Long-Term Diabetes Control: Hemoglobin A1c (HbA1c) to see how well their blood sugar had been controlled over the past few months.

  - Immune System Health: If available, we looked at specific immune cell counts (CD4+, CD8+ lymphocytes) to

understand the extent of their weakened immune system.

● Brain Scans: We thoroughly reviewed all the reports and digital images from their brain scans. This included:

○ CT Scans: The initial non-contrast CT scan was done quickly to spot any air, bleeding, or major structural problems in the brain. We looked at slice thickness and different viewing "windows" to see brain tissue, bone, and air clearly. We specifically looked for:

■ Pneumocephalus: Where the air was (e.g., around the brain, under the skull, inside the brain tissue or fluid-filled spaces), how much there was, and if it was causing pressure, sometimes seen as the "Mount Fuji sign" (where the front parts of the brain separate due to air).

■ Pressure Effects: If the brain's normal folds were flattened, if the fluid-filled spaces (ventricles) were squeezed, or if the brain had shifted from its normal position.

■ Brain Swelling (Edema): Areas that looked darker than normal, indicating fluid buildup.

■ Bleeding (Hemorrhage): Bright areas indicating fresh blood.

■ Fluid Buildup: Enlarged ventricles (hydrocephalus).

■ Bone Breaks: Especially in the base of the skull or sinuses, which could be entry points for air.

○ MRI Scans: After the initial CT, a contrast-enhanced MRI was performed to get a much more detailed picture of the soft tissues. This involved different types of sequences:

■ T1-weighted (before and after contrast): For clear anatomical detail and to see areas that lit up after the contrast dye was given.

■ T2-weighted: Sensitive to swelling and fluid collections.

■ FLAIR (Fluid-Attenuated Inversion Recovery): This sequence suppresses the signal from spinal fluid, making it easier to see lesions near the ventricles or cortex.

■ DWI (Diffusion-Weighted Imaging) with ADC maps: Absolutely vital for diagnosing brain abscesses, which typically show restricted diffusion (appearing bright on DWI and dark on ADC maps) due to their thick, pus-filled centers.

■ SWI (Susceptibility-Weighted Imaging) or GRE (Gradient Echo) sequences: Sensitive to blood and other substances.

■ Post-contrast T1-weighted: After injecting a special dye, these images show areas where the blood-brain barrier is broken down, appearing as bright rings (characteristic of abscesses) or diffuse enhancement (in meningitis).

■ Our focus was on: Confirming brain abscesses, identifying meningitis or inflammation of the brain's lining, and understanding how the air collections related to these infections.

● Microbiology Details: We looked at all the results from cultures and advanced genetic tests.

○ Where We Took Samples: Blood, cerebrospinal fluid (CSF – the fluid around the brain and spinal cord), sputum (phlegm), and any other relevant samples (like urine or fluid from wounds).

○ Identifying the Bacteria: We confirmed Klebsiella pneumoniae using standard lab methods and advanced automated systems.

○ Antibiotic Sensitivity: We tested how sensitive the bacteria were to a wide range of antibiotics. This was done using specific lab methods, and the results were interpreted according to international guidelines (CLSI) to help doctors choose the best antibiotic.

○ Understanding What Made the Bacteria Virulent:

■ Hypermucoviscous Test (String Test): We performed a simple test where we touched a lab loop to a bacterial colony. If a sticky "string" longer than 5 mm formed as we lifted the loop, it meant the bacteria had a thick, slimy capsule – a sign of hypervirulence.

■ Gas Production: We checked if the K. pneumoniae could produce gas by growing it in special broths with inverted tubes to trap any gas bubbles. If the lab had the capability, we also analyzed the gas composition (e.g., hydrogen, carbon dioxide) using gas chromatography.

■ Genetic Fingerprinting (Capsular Genotyping): We used advanced molecular techniques like PCR to identify the specific type of capsule the bacteria had (e.g., K63). We also used Multilocus Sequence Typing (MLST) to determine its genetic lineage. If available, we used Pulse Field Gel Electrophoresis (PFGE) to see if the bacteria found in different body sites (sputum, blood, CSF) were genetically identical, confirming they came from the same source.

■ Virulence Genes: We looked for specific genes (like magA, rmpA, iucABCD-iutA, iroN, kfu) that are known to make K. pneumoniae more dangerous. Finding these genes further supported the hypervirulent nature of the K63 strain.

● Treatment and Monitoring: We documented all the treatments the patient received.

○ DKA Management: This included giving intravenous fluids quickly to rehydrate them, a continuous insulin drip to lower blood sugar and correct the acid buildup, and carefully replacing electrolytes like potassium and phosphate.

- Antibiotic Treatment: We started broad-spectrum intravenous antibiotics immediately after taking samples, choosing ones that could get into the brain well. Once we knew what the bacteria were and what they were sensitive to, we adjusted the antibiotics to be more specific. Brain infections often need long courses of antibiotics, sometimes 4-8 weeks or more.

- Brain Surgery Consultation: Brain surgeons were consulted to see if any surgical procedures were needed, such as draining fluid from the brain (EVD), making small holes to relieve pressure or drain abscesses (burr holes), or larger surgery to remove abscesses (craniotomy). The decision was always made carefully, weighing the risks of surgery against the potential benefits, especially since the gas and abscesses were so widespread in this case.

- Supportive Care: This involved putting the patient on a breathing machine if needed, giving medications to raise blood pressure if they were in shock, monitoring brain pressure (if possible), giving anti-seizure medications, providing nutrition, and managing their body temperature.

- Patient's Journey and Outcome: We kept detailed daily notes on their progress, including how their brain function changed, their vital signs, fluid balance, and how their lab tests responded to treatment. We also repeated brain scans when necessary to see if the infection was getting better or worse. Ultimately, we recorded whether the patient survived and what the direct cause of death was.

How We Looked at the Information

Since this was a report about a single patient, we didn't use complex statistical analysis. Instead, we described everything in detail, focusing on the timeline of their symptoms, lab results, scan findings, and how they responded to treatment. We compared our findings to other reported cases of K. pneumoniae brain infections in diabetic patients to see what was unique about this case and what common patterns emerged. Our goal was to paint a clear picture of the challenging interaction between this aggressive germ and a vulnerable patient.

Results

Our patient, a 38-year-old man with a long history of poorly managed type 2 diabetes, arrived at the emergency department in a critical state. He was rapidly losing consciousness, had a high fever (39.5°C), and complained of a severe, unyielding headache. His body was clearly fighting a major battle, as indicated by his fast heart rate and rapid breathing. When we first examined him neurologically, he was deeply drowsy, his neck was stiff (a classic sign of irritation around the brain and spinal cord), and he had clear signs of weakness and numbness on his right side. His Glasgow Coma Scale (GCS) score, which measures consciousness, was very low at E2V3M4, indicating significant brain impairment.

Initial comprehensive lab tests confirmed he was in severe diabetic ketoacidosis (DKA). His blood sugar was alarmingly high at 22.07 mmol/L (far above the normal range of 3.90-6.10 mmol/L), and his blood was very acidic with a pH of 7.198 (normal is 7.350-7.450). His body was trying to compensate by breathing rapidly, which was reflected in his low carbon dioxide level (PCO2 of 21.5 mmHg). Both his blood and urine showed strong positive results for ketones, confirming the DKA. Signs of severe inflammation were everywhere: his C-reactive protein (CRP) was sky-high at 325 mg/L (normal is less than 8.0 mg/L), and procalcitonin (PCT), another infection marker, was 13.65 ng/mL (normal is less than 0.05 ng/mL). His white blood cell count, a key indicator of infection, was very high at 21.1 x 10^9 cells/L, with most of them being neutrophils, the first responders to bacterial infections. His long-term diabetes control was clearly very poor, as his HbA1c was 15.4% (normal is 4.0-6.0%). He also showed signs of general systemic weakness, with low albumin (a protein in the blood) and low levels of complement proteins (C3 and C4), which are part of the immune system. Further tests on his immune cells showed significantly low CD4+ and CD8+ T-cell counts, indicating his cellular immunity was severely compromised.

Table 2: Detailed Laboratory Examination Results of the Patient

Test Category	Parameter	Result (Day 1)	Reference Value	Unit	Deviation	Result (Day 2)
Blood	Glucose (GLU)	22.07	3.90-6.10	mmol/L	↑	Not specified
	Total Protein (TP)	46.7	65.0-80.0	g/L	↓	Not specified
	Albumin (ALB)	24	40-55	g/L	↓	Not specified

	Complement C3	0.50	0.90-1.80	g/L	↓	Not specified
	Complement C4	0.05	0.10-0.40	g/L	↓	Not specified
	C-reactive protein (CRP)	325	<8.0	mg/L	↑	Not specified
	Procalcitonin (PCT)	13.65	<0.05	ng/mL	↑	56.61
	Hemoglobin A1c (HbA1c)	15.4	4.0-6.0	%	↑	Not specified
	White Blood Cell (WBC)	21.1	3.5-9.5	10^9/L	↑	Not specified
	Neutrophil % (NEU%)	89.1	40.0-75.0	%	↑	Not specified
	CD4+ T-cells	178	432-1341	cells/µL	↓	Not specified
	CD8+ T-cells	100	238-1075	cells/µL	↓	Not specified
	pH	7.198	7.350-7.450	-	↓	7.069
	PCO2	21.5	35.0-45.0	mmHg	↓	Not specified
	BNP	Not specified	<100.0	pg/mL	-	944.3
Urine	Glucose (GLU)	+++	Negative	-	↑	Not specified
	Ketone bodies (KET)	+++	Negative	-	↑	Not specified
	Protein (TP)	++++	Negative	-	↑	Not specified
	Occult	+++	Negative	-	↑	Not

	blood (OB)					specified

Note: ↑ indicates above reference value; ↓ indicates below reference value; +++ or ++++ indicates strong positive. Some values were only available for specific days as indicated.

Given his rapid neurological decline, an urgent non-contrast CT scan of his brain was performed. The images were alarming: they showed extensive air trapped everywhere inside his skull – in the spaces around the brain, within the fluid-filled ventricles, and even directly within the brain tissue itself, appearing as multiple gas-filled pockets. This was a clear sign of severe pneumocephalus. The air was under so much pressure that it was pushing his brain, causing significant swelling, flattening of the normal brain folds, squeezing of the ventricles, and a noticeable shift of his brain structures by about 8 mm to the left. A subsequent contrast-enhanced MRI scan provided even more disturbing details. It confirmed the widespread air and clearly showed multiple ring-enhancing lesions, ranging from 1 to 3 cm in size, which were consistent with active brain abscesses. These abscesses were not confined to one area but were scattered throughout both sides of his brain, extending into the brainstem and even the cerebellum. Special MRI sequences (DWI) showed restricted diffusion in the center of these abscesses, a definitive sign of thick, pus-filled bacterial infections. The MRI also revealed diffuse enhancement of the thin membranes surrounding his brain (leptomeningeal enhancement), confirming that he also had bacterial meningitis.

Lab cultures from both his blood and cerebrospinal fluid (CSF) – the fluid surrounding his brain and spinal cord – grew pure colonies of Klebsiella pneumoniae. The CSF analysis further supported the diagnosis of bacterial meningitis: it was teeming with white blood cells (71,298 cells/μL, mostly neutrophils), had low glucose (which bacteria consume), and very high protein levels. The K. pneumoniae strain isolated from both his blood and CSF was remarkable: it passed the "string test" with flying colors, confirming its hypermucoviscous (super-sticky) nature. Genetic tests identified its capsular genotype as K63, a known highly virulent type. Further lab tests, including analyzing the gas produced in cultures, confirmed that this strain was a potent producer of hydrogen gas, along with nitrogen, carbon dioxide, and carbon monoxide. To confirm that all the infections came from the same source, we performed a "fingerprinting" test (Pulse-Field Gel Electrophoresis, PFGE) on bacteria from his sputum, blood, and CSF. All samples showed identical patterns, proving they were from a single, aggressive bacterial clone.

Despite our intensive efforts to manage his DKA with continuous insulin and fluids, and initiating strong intravenous antibiotics (starting with ceftriaxone and then switching to imipenem based on his worsening condition and lab results), the patient's neurological state continued to decline rapidly. On his second day in the hospital, his condition worsened dramatically: his blood pH dropped further to 7.069, and his procalcitonin soared to 56.61 ng/mL, indicating a worsening infection. His heart was also under severe strain, shown by a high BNP level of 944.3 pg/mL. Tragically, his pupils stopped reacting to light, and he became completely unresponsive. Repeat CT scans on his sixth day revealed a grim picture: his lung infection was worse, brain swelling had progressed, the pneumocephalus had increased even further, and he had developed massive bleeding under the brain's membranes (subarachnoid hemorrhage), with clear signs that his brain was being pushed downwards (herniation). Given the widespread nature of the gas and multiple abscesses, combined with his critical and rapidly deteriorating state, brain surgery to drain the gas or abscesses was deemed too risky and simply not feasible. The pressure inside his skull became uncontrollable, and he ultimately passed away from the overwhelming brain infection and its complications on the ninth day after his symptoms began.

DISCUSSION

This case sadly illustrates a rare and devastating consequence of Klebsiella pneumoniae infection: fatal pneumocephalus in a patient already struggling with severe diabetic ketoacidosis. The speed at which his brain function deteriorated, the sheer amount of air trapped inside his skull, and the ultimate tragic outcome truly highlight how incredibly aggressive this particular bacterium can be, especially when it encounters a vulnerable host.

Pneumocephalus, while not common, usually happens after head injuries or brain surgery, or sometimes when air leaks in from sinuses [4]. But when it's caused by an infection, especially by bacteria that produce gas, it's a whole different, much more dangerous story [3, 9, 12]. When gas builds up in the confined space of the skull, it can put immense pressure on the brain, cutting off blood flow and causing severe damage [4]. Our patient's scans clearly showed extensive air, not just around the brain but inside the ventricles and brain tissue itself, which immediately told us this was a gas-producing infection. We know from past reports that gas-forming brain abscesses due to K. pneumoniae often have a very poor prognosis [3, 9, 12]. For example, similar cases have been reported where K. pneumoniae caused rapid gas formation in brain abscesses, showing just how aggressive these infections can be [9, 12].

The specific Klebsiella pneumoniae strain we found in our patient was particularly concerning. It was "hypermucoviscous" (super-sticky) and had a specific capsular genotype, K63. Think of the hypermucoviscous

capsule as a thick, slimy shield that helps the bacteria evade our immune system's attacks, allowing it to spread more easily and cause severe infections, even in people who are otherwise healthy [6]. The K63 capsule type, like K1 and K2, is strongly linked to this hypervirulent behavior. What made this strain especially deadly in our patient was its proven ability to produce hydrogen gas through sugar fermentation [8]. This gas production directly contributed to the rapid and dangerous buildup of air inside his skull, leading to immense pressure on his brain and rapid neurological collapse. So, we had a perfect storm: a super-aggressive, gas-producing bacterium combined with a highly virulent capsule type, overwhelming the patient's defenses and causing widespread brain damage.

Our patient's underlying diabetic ketoacidosis (DKA) was a critical factor that set the stage for this catastrophe. Uncontrolled diabetes essentially weakens the body's entire immune system. It impairs how our white blood cells (like neutrophils) fight infection, reduces the number of key immune cells (like the low CD4+ and CD8+ counts we saw), and generally throws the body's inflammatory response out of whack [2]. The high sugar and acidic environment of DKA also create a perfect breeding ground for bacteria and can make them even more aggressive. On top of that, chronic diabetes can damage the blood-brain barrier, which is supposed to protect the brain from harmful substances in the blood [2]. This damage allowed the bacteria, likely from a primary infection elsewhere (perhaps his lungs, as suggested by initial scans), to easily cross into his brain and spinal fluid, explaining the rapid development of widespread brain abscesses and meningitis. We've seen similar tragic outcomes in other diabetic patients with K. pneumoniae brain infections, highlighting their increased vulnerability [10]. The combination of this highly virulent, gas-producing K. pneumoniae and the severe immune suppression from DKA created an unstoppable force that quickly overwhelmed our patient.

Getting a quick diagnosis was absolutely vital. CT scans were crucial for immediately spotting the extensive air in his brain, and then MRI provided even more detailed information, showing the multiple brain abscesses and inflammation of the brain's lining. The widespread gas and multiple abscesses on the scans immediately pointed towards a gas-forming bacterial infection. It's important to distinguish this from other types of air in the brain, like an air bubble from a distant blood clot; in our case, the abscesses confirmed the infectious origin [1].

Treating gas-forming brain infections is incredibly difficult. While strong antibiotics are the first line of defense, surgery to remove the source of infection and relieve pressure is often essential. However, in our patient's case, the gas was so widespread, and the abscesses were so numerous and scattered, that surgery was simply too risky and impractical. This highlights a heartbreaking dilemma: even with the best antibiotics, if the physical damage from the gas and lesions is too extensive, it might not be enough. Although his initial response to antibiotics seemed positive, with inflammatory markers decreasing and blood cultures turning negative, the continued increase in air on follow-up scans showed that the brain infection was still progressing, eventually leading to fatal brain swelling and pressure. This reminds us that even if the systemic infection is controlled, the localized damage within the brain can continue to worsen with devastating results.

This case adds an important, albeit somber, entry to the limited medical literature on fatal pneumocephalus caused by hypervirulent, gas-producing K. pneumoniae in diabetic patients. It reinforces what we've learned from previous reports: these infections are rare but have an extremely high death rate, often despite appropriate antibiotic treatment [5, 10, 11]. The fact that our patient was relatively young (38 years old) compared to many previously reported cases (often over 50) underscores just how aggressive this particular hvKp strain can be, even in a susceptible host. The unusual observation that the K. pneumoniae strain grew only at the edges of the CSF culture plate, but not in the center (as seen in the original PDF's Figure 1C), is a fascinating microbiological detail. It might suggest something unique about how this hypermucoviscous, gas-producing strain grows in a lab setting, which could potentially affect how we detect it with standard culture methods.

In summary, this case is a powerful reminder for doctors to be highly suspicious of gas-forming bacterial brain infections, especially in diabetic patients who suddenly develop severe neurological problems and show signs of air in their brain. A quick and thorough diagnostic workup, including advanced brain imaging and detailed lab tests to identify the specific germ, is absolutely essential. While we must start strong antibiotics right away, the unique challenges posed by extensive gas buildup and widespread brain involvement can limit how effective even targeted treatments are. This case highlights the urgent need for new ways to fight these deadly infections, perhaps by targeting the bacteria's virulence factors or finding better ways to manage the gas accumulation, to give these vulnerable patients a fighting chance.

CONCLUSION

In closing, we've shared the unfortunate story of a patient who succumbed to pneumocephalus caused by a K. pneumoniae brain infection, complicated by diabetes. This case serves as a stark example of the severe and often irreversible damage that can occur when highly virulent, gas-producing Klebsiella pneumoniae strains infect the central nervous system, particularly in individuals whose immune systems are severely weakened by conditions like diabetic ketoacidosis. Even though the K. pneumoniae strain was sensitive to the antibiotics we used, the sheer volume of gas and sticky mucus it produced, combined with the patient's compromised defenses, led to a rapid and ultimately fatal increase in pressure inside his skull.

This tragic outcome is consistent with what we've seen in other reports of similar infections in diabetic patients, underscoring the grim prognosis [10]. Therefore, it's incredibly important for medical professionals to pay close attention to the unique ways these hypermucoviscous and gas-producing K. pneumoniae strains behave, especially when they appear in diabetic patients. Early recognition, aggressive supportive care, and a team-based approach are critical. However, the ongoing challenge of managing the physical effects of gas trapped inside the brain remains a significant hurdle to improving patient outcomes. We hope that future research will explore new therapies that can specifically target the bacteria's dangerous virulence factors or find better ways to reduce gas accumulation, offering a glimmer of hope for patients facing these devastating infections.

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