








# Emphysematous pyometra and emphysematous hepatitis caused by *Klebsiella pneumoniae* infection in a diabetic dog

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## Abstract

A 14-year-old intact female diabetic dog presented with seizures and hyperglycemic hyperosmolar syndrome. Radiographs revealed gas-filled tubular structures in the right and left caudal abdomen, raising concerns of emphysematous pyometra or small intestinal ileus. Ultrasonography played a pivotal role in confirming emphysematous pyometra, a technique previously documented only once in veterinary practice. This report also presents the first documented case of emphysematous pyometra in a diabetic dog attributed to *Klebsiella pneumoniae* and complicated by emphysematous hepatitis.

## KEYWORDS

canine, diabetes, gas, liver, uterus

## 1 | SIGNALMENT, HISTORY AND CLINICAL FINDINGS

A 14-year-old intact female Samoyed dog, previously diagnosed with diabetes mellitus, presented with generalized tonic-clonic seizures. No prior episodes of seizures had been documented in the medical history. Physical examination showed depressed mental status, dehydration, and a rectal temperature of 37.6°C. Neither vaginal discharge nor gastrointestinal signs were reported by the owners or detected on physical examination. The last estrus cycle occurred 1 month before the presentation.

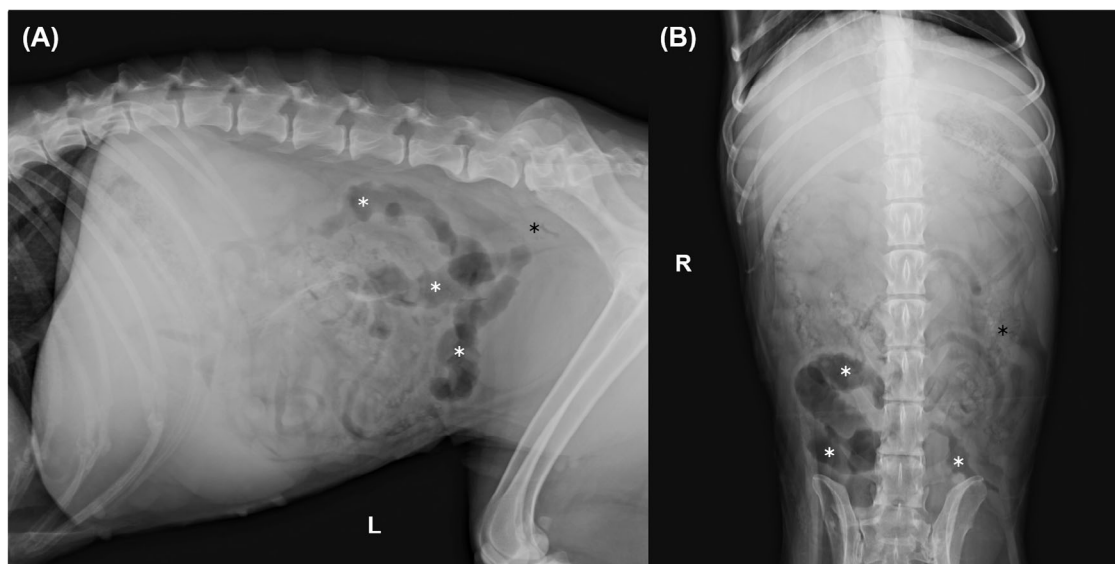
The complete blood count showed nonregenerative anemia (hematocrit 25.9%; reference interval [RI] 37.3–61.7%), marked leukocytosis ( $49.95 \times 10^9/L$ , RI  $5\text{--}16.8 \times 10^9/L$ ) with mature neutrophilia ( $43 \times 10^9/L$ , RI  $3\text{--}11.6 \times 10^9/L$ ), mild monocytosis ( $2.9 \times 10^9/L$ , RI  $0.15\text{--}1.3 \times 10^9/L$ ) and thrombocytosis ( $681 \times 10^9/L$ , RI

$148\text{--}484 \times 10^9/L$ ). Serum biochemistry revealed markedly increased glucose (1195 mg/dL, RI 60–110 mg/dL) and mildly increased alkaline phosphatase (436 U/L, RI 23–212 U/L), alanine aminotransferase (138 U/L, RI 10–125 U/L) and cholesterol (431 mg/dL, RI 110–320 mg/dL). The effective serum osmolality was 364.9 mOsm/kg (RI 290–310 mOsm/kg). Urinalysis collected by cystocentesis revealed a urine-specific gravity of 1.028 and glucosuria (4+) with negative urine ketones. The sediment was negative for bacteria. A diagnosis of hyperglycemic hyperosmolar syndrome was made.

Generalized tonic-clonic seizures were presumed to be secondary to hyperglycemic hyperosmolar syndrome, as hyperosmolarity leads to cellular dehydration, with the nervous system being the principal organ affected by this shift.<sup>1</sup> The differential diagnosis for the clinicopathologic abnormalities described above included infectious, inflammatory, and neoplastic causes. However, a primary suspicion leaned toward an infectious or inflammatory process, given the marked mature

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**FIGURE 1** Left lateral (A) and ventrodorsal (B) abdominal radiographs. A, Three gas-filled tubular structures (white asterisks) are located dorsal, ventral, and superimposed with the descending colon (black asterisk). At the pelvic entrance, they are located ventral to the colon and dorsal to the urinary bladder. The hepatic silhouette is mildly enlarged, extending beyond the costal arch. B, The previously described three gas-filled structures (white asterisks) are identified in the right and left caudal abdomen.

neutrophilic leukocytosis combined with monocytosis and thrombocytosis. An increase in liver enzymes suggested mild intrahepatic cholestasis and hepatocellular damage, which could be secondary to previously diagnosed diabetes mellitus or concomitant hepatic disease such as hepatitis. Considering these abnormalities, thoracic and abdominal imaging was indicated for further investigation.

## 2 | IMAGING, DIAGNOSIS, AND OUTCOME

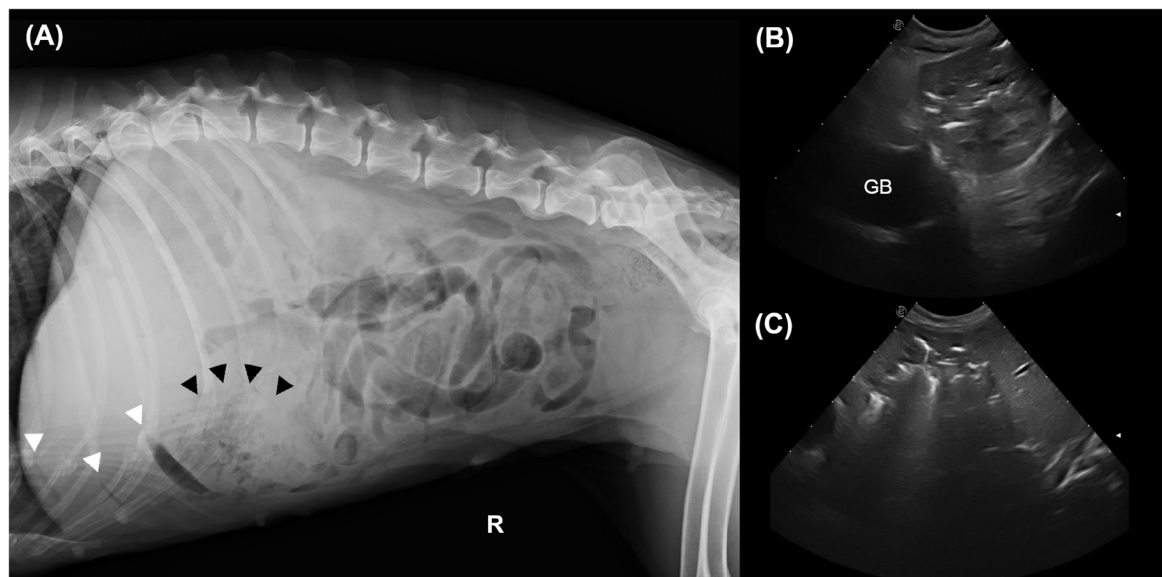
Thoracic and abdominal radiographs were performed using a digital radiography unit (AeroDR NS, Konika Minolta). The left lateral abdominal radiograph showed three gas-filled mildly tortuous tubular structures in the caudal abdomen, located dorsal, ventral, and superimposed with the descending colon (Figure 1A). At the pelvic entrance, these structures were located ventral to the colon and dorsal to the urinary bladder. The maximum diameter of these structures was twice the height of the body of the fifth lumbar vertebra. In the ventrodorsal projection, two of the gas-filled structures were in the right caudal abdomen and the other one was in the left caudal abdomen (Figure 1B). In both radiographs, the small intestine was normal in diameter with mixed opacity content. There was mild hepatomegaly. The thoracic radiographs were unremarkable. In the absence of clinical signs supportive of mechanical small bowel obstruction, the presence of bloodwork abnormalities supporting infection, and considering the location and appearance of the gas-containing tubular organs, a top differential of emphysematous pyometra was provided. The possibility of a clinically silent small bowel obstruction was offered as an unlikely alternative.

An abdominal ultrasound was performed using a 3–10 MHz micro-convex transducer (Esaote MyLab Eight XP, Esaote). Two tubular



**FIGURE 2** Ultrasound image of the uterus in the longitudinal plane. The uterine horns appear as moderately gas-distended tubular structures with mildly thickened hypoechoic walls, without evidence of intestinal wall layering. Luminal fluid was also identified (not shown). Multiple regions of apparent wall thinning with rounded foci of reverberating gas were observed within the uterine wall (white arrowheads). A clear intramural linear distribution of these features was noted in the recorded clips (not shown).

structures with a hypoechoic wall, no evidence of wall layering, and multiple intramural hyperechoic foci with reverberation artifacts could be detected (Figure 2). These structures extended from the caudal abdomen, bifurcating cranial to the uterine body and reaching the ovaries. These were identified as the uterine horns and also contained intraluminal gas and fluid. No gastrointestinal abnormalities were detected. The liver appeared mildly to moderately enlarged with diffusely heterogeneous parenchyma having ill-defined



**FIGURE 3** A, Right lateral abdominal radiograph. There is an irregularly circumscribed soft tissue opacity mass located in the ventral aspect of the cranial abdomen, confluent with the hepatic silhouette (black arrowheads). Few free peritoneal small gas bubbles can be identified cranial to the lesion described (white arrowheads). B, Ultrasound image of the mass described in the radiographic study. Multiple ill-defined hypoechoic areas and hyperechoic foci with reverberation artifacts can be observed in the mass. C, The presence of multiple reverberation artifacts, indicating the presence of intraparenchymal gas, were identified within the mass and extended through the left hepatic division. GB, gallbladder.

hypo- and hyperechoic areas. Neither pneumoperitoneum nor peritoneal effusion was present.

These findings were consistent with an emphysematous pyometra. For the heterogeneous hepatomegaly, potential diagnoses included vacuolar hepatopathy, nodular hyperplasia, or, less likely, hepatitis or neoplastic infiltration.

After stabilization of the hyperglycemic hyperosmolar syndrome with fluid therapy and insulin, an ovariohysterectomy was performed. In order to rule out neoplasia, a liver biopsy of the edge of the left medial hepatic lobe was performed using a “guillotine” biopsy technique.<sup>2</sup> The uterus was submitted for culture and sensitivity testing and the liver sample was submitted for histopathology. Upon discharge, the dog received porcine lente type insulin (0.5 IU/kg) twice daily, a diabetic diet twice a day, analgesia, and empiric antibiotic treatment with amoxicillin-clavulanic (22 mg/kg) twice daily. Four days later, the culture revealed *Klebsiella pneumoniae* growth resistant to amoxicillin-clavulanic, prompting a change to cefalexin (20 mg/kg) and metronidazole (15 mg/kg) two times a day.

Seven days after discharge the dog presented for fever (103.82°F). Anemia had worsened (19.7%, RI 37.3–61.7%) and mild leukocytosis persisted ( $17.9 \times 10^9/L$ , RI  $5\text{--}16.8 \times 10^9/L$ ). Serum glucose remained high (588 g/dL, RI 60–110 mg/dL) and alanine aminotransferase was significantly increased (585 U/L, RI 10–125 U/L). Histopathology from the liver biopsy was available at the time and was consistent with nodular hyperplasia.

Abdominal radiographs revealed an irregularly circumscribed soft tissue opaque mass with coalescing gas bubbles, creating a vesicular-like gas pattern, located in the ventral aspect of the cranial abdomen (Figure 3A), possibly involving the liver. There was a generalized

decrease in serosal detail and a few free peritoneal small gas bubbles could be identified cranial to the described lesion. A hepatic abscess was the primary clinical suspicion. Other causes of emphysematous hepatitis such as liver lobe torsion or necrotic-suppurative neoplasm could not be excluded but were considered less likely, particularly neoplasia based on previous biopsy results. Emphysematous splenitis affecting the splenic tail could also be compatible with the imaging findings<sup>3</sup>; however, it was considered less likely given the significant increase in liver enzymes compared with prior bloodwork. A mesenteric origin was considered highly unlikely.

On abdominal ultrasound, an irregularly defined round structure of approximately  $4 \times 3$  cm in diameter was observed within the liver. This structure exhibited multiple ill-defined hypoechoic areas and hyperechoic foci with reverberation artifacts, indicating the presence of intraparenchymal gas (Figure 3B). The gas extended primarily through the left hepatic division (Figure 3C). Doppler examination revealed normal vascularization in the liver. A mild to moderate amount of anechoic free peritoneal fluid with echogenic particles and pneumoperitoneum were detected. The uterine stump was normal in appearance.

Abdominal ultrasound confirmed emphysematous hepatitis, with the primary differential diagnosis being an abscess, possibly of hematogenous or iatrogenic origin. The pneumoperitoneum was considered to be either secondary to the rupture of the hepatic abscess or secondary to the recent laparotomy. Fluid analysis was consistent with a septic exudate and its culture yielded *Klebsiella pneumoniae* growth. Laparotomy was recommended but declined due to financial constraints. The dog was discharged with previous medical treatment. Five days later the dog was euthanized due to septic shock. Necropsy was performed with the owner's consent.

On postmortem examination, the liver showed a moderate enlargement and diffuse lobular pattern. A poorly defined cavity with purulent content measuring 1 cm was found in the caudoventral margin of the left medial hepatic lobe, close to the previous biopsy site. No suture material was identified. Upon sectioning, the lesion extended 8 cm into the left hepatic division, presenting necrotic and purulent content. Histologically, it was identified as necrotizing-suppurative hepatitis with severe hydropic degeneration. Postmortem bacterial culture of the uterine stump and affected liver both yielded a *Klebsiella pneumoniae* growth.

### 3 | DISCUSSION

Emphysematous pyometra is a rare uterine infection in dogs characterized by gas and fluid accumulation within the uterine lumen with or without associated endometrial pneumatosis due to gas-producing bacteria. Only six cases have been previously reported, involving various bacteria.<sup>4–9</sup> This report presents the first described case of emphysematous pyometra linked to *Klebsiella pneumoniae*, a facultatively anaerobic Gram-negative bacterium. This pathogen, known for causing pneumonia, urinary tract infections, nonemphysematous pyometra, and bloodstream infection in companion animals,<sup>10</sup> can develop antibiotic resistance and increase the potential severity of a zoonotic infection.<sup>11</sup>

The radiographic findings of emphysematous pyometra have been described in previous reports.<sup>4–9</sup> This condition is characterized by the presence of tubular structures with gas-opaque content commonly located in the right and/or left abdomen, where the uterine horns are found, and in the caudal abdomen near the cervix. These gas-filled structures may not always be symmetrically distributed and can be mistaken for dilated bowels. Radiography alone may not yield a definitive diagnosis, although it can strongly suggest a presumptive diagnosis. Ultrasound may be employed to confirm the findings; however, there is limited literature on the use of ultrasound to diagnose emphysematous pyometra, with a single case report describing its use.<sup>9</sup> In that report, ultrasound revealed two tubular structures with hyperechoic speckles in the wall, along with gas and fluid intraluminal content, connecting to the ovaries and uterine body. While a previous study noted limitations due to excessive gas in the uterus,<sup>6</sup> the present case demonstrated successful ultrasound evaluation, allowing the diagnosis of emphysematous pyometra.

To the authors' knowledge, this is the first case of emphysematous pyometra in a diabetic dog. Emphysematous infections, including emphysematous cystitis, have been documented in diabetic dogs.<sup>12,13,14,15</sup> The exact mechanism behind emphysematous cystitis remains unclear, although it is hypothesized that there is gas formation due to the fermentation of urine glucose by gas-producing bacteria that, combined with an impaired immune system, results in emphysematous cystitis.<sup>16</sup> Other reported emphysematous infections in diabetic dogs include emphysematous pyelitis<sup>15</sup> or pyelonephritis<sup>17</sup> and gas-producing infective endocarditis,<sup>18</sup> all of them presumed to

be secondary to emphysematous cystitis. In this case, the absence of bacteria in the urine sediment and the lack of gas within the urinary bladder wall in both the initial and follow-up ultrasounds, make emphysematous cystitis an unlikely source of infection.

Generally, poorly controlled diabetes mellitus in humans is associated with an increased susceptibility to infectious diseases, including emphysematous infections, potentially due to altered tissue glycolysis and elevated glucose levels in interstitial fluid, which may support the growth of gas-producing bacteria.<sup>19,20</sup> Consequently, uncontrolled diabetes could be considered a predisposing factor for the development of emphysematous pyometra in veterinary medicine. Alternatively, infectious diseases themselves can predispose previously stable diabetic dogs to suffer from a diabetic crisis.<sup>21</sup> Pyometra has been associated with immune system suppression<sup>22</sup> and, although infrequent, hematogenous dissemination of bacteria originating from a uterine infection to distant sites of the body has also been described in dogs and cats.<sup>23,24</sup> There is a single case report describing an emphysematous hepatic abscess due to the hematogenous spread of bacteria from a uterine infection in a bitch, *Burkholderia cepacia* being the causative agent.<sup>25</sup> In the present case, the authors consider that the source of infection spreading to the liver could also be hematogenous. However, it is worth highlighting that, in this instance, the liver biopsy likely played a significant role in dissemination. Potentially, the biopsy procedure created a wound that was more susceptible to infection than other parts of the body. This susceptibility, combined with the probable bacteremia of the patient, might have led to the dissemination of the infection to the liver. However, an iatrogenic origin due to surgical contamination cannot be ruled out.

In conclusion, emphysematous pyometra and emphysematous hepatitis should both be considered as potential infectious diseases in poorly controlled diabetic dogs. Abdominal ultrasound complemented radiography and played a crucial role in the identification of both pathologies. Culture sensitivity testing should also be contemplated as different pathogens can produce this infection, including *Klebsiella pneumoniae*, which can develop antibiotic resistance and increase the potential severity of zoonotic infection.

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#### Category 1

- a) Conception and design: Palomares
- b) Acquisition of data: Palomares, Espada, Abarca, Martino, Viñeta
- c) Analysis and interpretation of data: Palomares, Espada, Tobón Restrepo, Torrente, Roura, Novellas

#### Category 2

- a) Drafting the article: Palomares
- b) Revising article for intellectual content: Espada, Tobón Restrepo, Abarca, Torrente, Martino, Viñeta, Roura, Novellas

#### Category 3

- a) Final approval of the completed article: Palomares, Espada, Tobón Restrepo, Abarca, Torrente, Martino, Viñeta, Roura, Novellas



## Category 4

- a) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: Palomares, Espada, Tobón Restrepo, Abarca, Torrente, Martino, Viñeta, Roura, Novellas

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## PREVIOUS PUBLICATION OR PRESENTATION DISCLOSURE

None.

## REPORTING CHECKLIST DISCLOSURE

No EQUATOR network checklist or other reporting checklist was used.

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