Emphysematous Cystitis: A Review of the Literature

Masayuki Amano¹ and Taro Shimizu²

Abstract

Emphysematous cystitis (EC) is a rare form of complicated urinary tract infection, its characteristic feature being gas within the bladder wall and lumen. Patients with EC present with variable clinical manifestations ranging from asymptomatic to severe sepsis. EC is typically observed in elderly women with severe diabetes mellitus. Escherichia coli and Klebsiella pneumoniae are often isolated from urine cultures. Imaging methods, such as plain conventional abdominal radiography and computed tomography, are pivotal for obtaining a definitive diagnosis of EC. Most cases can be treated with a combination of antibiotics, bladder drainage and glycemic control. EC is potentially life-threatening, with a mortality rate of 7%. Early medical intervention can contribute to achieving a favorable prognosis without the need for surgical intervention. In this review, we provide a comprehensive description of the clinical characteristics of EC.

Key words: emphysematous cystitis, review, urinary tract infection, diabetes mellitus

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Introduction

Emphysematous cystitis (EC) is a rare form of complicated urinary tract infection (UTI), with its characteristic feature being gas within the bladder wall and lumen. The occurrence of air within the urinary tract was first reported in 1671 in the case of a man presenting with pneumaturia. Infectious emphysema of the bladder was first reported at autopsy by Eisenlohr in the late 1800s; it was later defined as “cystitis emphysematosa” by Bailey in 1961 (1). We herein review the epidemiology, microbiology, symptomatology, diagnosis, treatment, prognosis and prevention of EC.

Epidemiology

Emphysematous cystitis is a relatively rare disease caused by gas-forming microbes, with only 135 cases reported in the English-language literature prior to 2006 (1). We searched PubMed and Ichushi-Web (the Japan Medical Abstracts Society) for articles of EC cases written in English or Japanese between 2007 and 2013. Although EC continues to be a rare condition, an increasing numbers of cases has been reported in recent years alongside advances in medical equipment and the wider use of imaging studies. We found 72 cases reported outside Japan and 30 cases reported in Japan. All cases were reviewed for patient age and sex, history of diabetes mellitus (DM), pathogens identified on culture, treatment and outcomes (Table). EC is a less severe condition than any other gas-forming infection of the urinary tract, with an overall mortality rate of 3-12%. However, when EC occurs in concert with another gas-forming disease within the upper UT, emphysematous pyelonephritis (EP), the mortality rate increases by up to 14-20% (2, 3). EC is typically observed in elderly women (60-70 years of age) with severe diabetes mellitus (1, 2, 4), with cases reported approximately twice as often in women as in men. Traditional risk factors for UTIs, such as DM, neurogenic bladder, recurrent UTI and urinary stasis secondary to bladder outlet obstruction (BOO), are also risk factors for EC because EC is considered to be a form of complicated UTI (1). Among the risk factors for EC, DM appears to be the strongest: almost 70% of patients with EC have DM, and women with EC are more likely to have DM than men (70% vs. 60%). One report shows that EC patients have poorly controlled DM, with a median serum glucose level of 293 mg/dL and an HbA1c level of 9.9% (2). The UT of diabetic patients can be damaged by conditions such as diabetic nephropathy, bladder dysfunction due to diabetic neuropathy and renal artery stenosis. Furthermore, a high glucose concentration within the UT plays a pivotal role in the development of EC, as glucose is one of the key substrates for natu-
Various microbes can cause emphysematous UTIs, *Escherichia coli* (60%) and *Klebsiella pneumoniae* (10-20%) being the two major organisms isolated in urine cultures. These species can ferment glucose and lactate to yield various gases, such as nitrogen, hydrogen, oxygen and carbon dioxide (2, 6). Other reported organisms include *Enterobacter aerogenes*, *Proteus mirabilis* and *Streptococcus* spp., which cause 5-8% of UTI episodes in total. The presence of other organisms, such as *Pseudomonas aeruginosa*, *Candida albicans*, *Clostridium perfringens*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Clostridium welchii*, *Candida tropicalis* and *Aspergillus fumigatus*, has also been reported, although these cases appear to be rare (1). The results of urine cultures in EC patients with non-gas-producing organisms, such as Enterococci, suggest the possibility of mixed infections (6).

**Clinical manifestations**

The clinical signs of EC are highly variable, ranging from asymptomatic to severe sepsis (1). The most common symptom is abdominal pain, occurring in 80% of patients (7). Gross hematuria is also common (60%), as is ischuria (10%) (4). Fever is suggestive of pyelonephritis, although approximately 30-50% of patients can be febrile without having EP (2, 7, 8). Although pneumaturia appears to be a highly specific symptom, it is a rare patient complaint. Pneumaturia is observed in 70% of patients with bladder catheterization (7, 9). Other symptoms of acute cystitis (dysuria, urinary frequency and urinary urgency) occur in approximately 50% of patients. However, these symptoms are nonspecific and usually mild, if they exist. For this reason, no significant clinical features strongly suggestive of the presence of EC have been reported (10, 11), and up to 7% of patients may be asymptomatic. Such patients are incidentally diagnosed on abdominal imaging planned to evaluate other medical conditions (1). Being cognizant of such a background, physicians should be aware of subtle symptoms suggesting EC, such as abdominal pain, fever and hematuria. Patients with EC can develop ascending emphysematous infections, such as EP. Although the mortality rate of patients with EP is higher than that of patients with EC alone, early detection and optimal medical management can lower mortality and prevent the need for surgical intervention (2).

**Diagnosis**

Vital signs should be carefully observed for the possibility of upper UTIs and sepsis (1, 2). Fever may be observed in approximately 30-50% of patients, a sign usually absent in those with acute cystitis. In addition, the following risk factors for EC should be queried during medical interviews: DM and its severity; history of neurogenic bladder; and history of recurrent UTI, BOO or any other risk factors (1). A history of DM must be evaluated because other types of complicated UTIs, such as renal and perirenal abscesses, fungal infections, xanthogranulomatous pyelonephritis and EP, are more likely to occur in diabetic patients than in otherwise healthy individuals (12). It should be noted that the presence of chills, flank pain and percussion tenderness at the costovertebral angle is more common in patients with EP and of great significance (11). Performing urinalyses, Gram staining of the urine and urine cultures is essential for detecting the responsible pathogen and helps to select the appropriate antibiotic regimen. The presence of hematuria and pyuria with positive urine cultures is usually revealed in this process. With respect to blood analyses, there are no specific data suggesting the presence of EC, and although the C-reactive protein level is slightly lower in EC patients than in EP patients, this finding is insufficient to distinguish these conditions (11). Both urine and blood should be cultured, as it has been reported that 50% of patients with EC have bacteremia (7). The use of imaging is pivotal for obtaining a definitive diagnosis of EC, with plain conventional abdominal radiography being the most common imaging method. The characteristic radiographic feature involves curvilinear areas of increased radiolucency delineating the bladder wall, separated from the more posterior rectal gas. The occurrence of intraluminal gas can be detected as an air-fluid level that is not static. The presence of air in the bladder wall is characterized by a cobblestoned or “beaded necklace” appearance, reflecting irregular thickening of the non-dependent mucosal surface due to submucosal blebs (13). Computed tomography (CT) is also commonly used and is necessary for diagnosis, being more sensitive than plain abdominal films (Figure). CT also reveals the severity of the

### Table. Demographics, Outcomes and Isolated Urinary Pathogens in the Reviewed Population

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Reported cases outside Japan</th>
<th>Reported cases in Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E.coli</em></td>
<td>23/41 (56)</td>
<td>16/25 (64)</td>
</tr>
<tr>
<td><em>K.pneumonia</em></td>
<td>4/41 (10)</td>
<td>5/25 (20)</td>
</tr>
<tr>
<td><em>Enterobacter spp.</em></td>
<td>2/41 (5)</td>
<td>0/25 (0)</td>
</tr>
<tr>
<td><em>Proteus spp.</em></td>
<td>2/41 (5)</td>
<td>0/25 (0)</td>
</tr>
<tr>
<td><em>Streptococcus spp.</em></td>
<td>0/41 (0)</td>
<td>2/25 (8)</td>
</tr>
<tr>
<td>Others</td>
<td>10/41 (7)</td>
<td>2/25 (8)</td>
</tr>
</tbody>
</table>

Mean age, years 68 ± 7.2

Male 19/61 (31)  9/30 (30)

Female 42/61 (69) 21/30 (70)

Diabetic 38/58 (66) 21/30 (70)

Surgical intervention 3/58 (5)  2/30 (7)

Pathogens

- *E.coli*  23/41 (56)  16/25 (64)
- *K.pneumonia*  4/41 (10)  5/25 (20)
- *Enterobacter spp.*  2/41 (5)  0/25 (0)
- *Proteus spp.*  2/41 (5)  0/25 (0)
- *Streptococcus spp.*  0/41 (0)  2/25 (8)
- Others  10/41 (7)  2/25 (8)
condition (e.g., ascending emphysematous infections, intra-abdominal abscesses or adjacent neoplastic disease). Furthermore, other sources of pelvic air can be detected, such as vesicocolic or vesicovaginal fistulas, trauma, pneumatoasis cystoides intestinalis, gas gangrene of the uterus and vaginitis emphysematosa (12-14). Other imaging methods, including cystoscopy and bladder ultrasonography (US) can add information to confirm the diagnosis. Cystoscopy may reveal the presence of BOO, whereas US shows diffuse wall thickening and focally high-echoic regions with dirty acoustic shadowing (12, 15, 16).

Treatment

With respect to management, 90% of patients are treated with initial intravenous antibiotics, whereas 9% are successfully treated with oral antibiotics alone. Several patients are managed as inpatients (1). Approximately 90% of cases are treated with medical therapy alone, whereas 10% require combined surgical and medical intervention (1, 7). Medical therapy consists of antibiotics, bladder drainage and treatment of predisposing conditions. Although published data regarding the selection of antibiotics in EC patients are limited, regimens for complicated UTIs appear to be favorable based on the observations of previous reports (4, 6, 7). Gram staining of the urine can also be helpful for determining the choice of empiric therapy. The initial parenteral therapy for complicated cystitis can be fluoroquinolone, ceftriaxone, carbapenem or an aminoglycoside (17), these antibiotics being similar to those chosen in reported cases of EC (4, 6). When Gram-positive cocci are identified, ampicillin or amoxicillin are required based on their usefulness against Enterococci. The initially selected antibiotics should be tailored to sensitivity according to the results of the culture. After a clinical improvement is obtained, the parenteral therapy can be switched to oral therapy (17, 18). With respect to bladder drainage, the use of early Foley catheter drainage is warranted to rest the bladder. Catheter placement also enables the clinician to monitor the urinary status (i.e., output and characteristics). In the presence of a significant amount of blood clots or difficulty voiding, bladder irrigation may be required to prevent bladder tamponade (7). Management without drainage should be considered only in mild cases on an outpatient basis (2). Regarding the treatment of predisposing conditions, controlling the glycemic level is effective and has been found to be successful in reported cases; subcutaneous (or even intravenous) insulin injections are required (1, 4). In patients with coexistent EC and EP, early percutaneous renal drainage must be considered, as it can result in a favorable prognosis without the need for surgical intervention (2). Surgery is required in patients exhibiting a poor response to initial medical management or those with severe necrotizing infections. Among the reviewed cases, five patients were treated with surgical intervention. All patients had peritonitis with the collection of extravesical gas. The severity of the disease determines the surgical method, i.e., surgical debridement, partial cystectomy, total cystectomy or even nephrectomy in combined EC/EP cases (1). Another modality, hyperbaric oxygen therapy, was reportedly used in a patient with EC and gas within the femoral vein (19).

Prognosis

EC can be successfully treated with appropriate antibiotics, bladder drainage and glycemic control, reserving surgical intervention for severe cases. The overall death rate among patients with EC has been reported to be approximately 7% (1, 2). Among the reviewed cases, the incidence was 12% outside Japan and 3% in Japan. EC can affect the upper UT in an ascending manner and may subsequently develop into EP (the reported mortality rate of EP is 14-20%) (2, 3). A delayed diagnosis can also result in bladder rupture, overwhelming infection and death (20). Among the reviewed cases, eight patients in total die, three of whom were reported to die from septic shock due to EC; one death was the result of a late presentation, one patient refused surgical intervention despite having perforation of the bladder and the remaining patient was a nonresponder to medical therapy. Making an early diagnosis of EC and providing early treatment is essential to achieving a good prognosis.

Prevention

Preventive measures for managing EC have not been established to date, and there are few ways to prevent even asymptomatic UTIs in diabetic patients with asymptomatic bacteruria (21). Considering the low morbidity of EC, placing an emphasis on secondary prevention is recommended to achieve better outcomes. Hence, the most effective strategy for preventing EC is to educate both health care providers and patients and encourage vigilance regarding this potentially life-threatening condition.

Conclusion

Emphysematous cystitis is a relatively rare form of com-
plicated UTI characterized by the presence of gas within the bladder wall and lumen. The predisposing risk factors and conditions include an older age, female gender and severe DM. No significant clinical features strongly suggestive of EC have been reported to date; hence, physicians should be aware of subtle symptoms indicating this condition (e.g., abdominal pain, fever and hematuria). Although EC is potentially life-threatening, providing early medical intervention, including antibiotic therapy, bladder drainage and glycemic control, can contribute to achieving a favorable prognosis without the need for surgical intervention.

The authors state that they have no Conflict of Interest (COI).

References


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