Case Report

Sepsis-associated purpura fulminans caused by emphysematous cystitis

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Abbreviations & Acronyms
CK = creatine phosphokinase
CRP = C-reactive protein
CT = computed tomography
DIC = disseminated intravascular coagulation
DM = diabetes mellitus
EC = emphysematous cystitis
PF = purpura fulminans
UTI = urinary tract infection
WBC = white blood cell

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Introduction: Emphysematous cystitis is a rare pathology characterized by gas bubbles within the bladder wall and lumen from gas-producing bacteria. Sepsis-associated purpura fulminans is also rare and shows poor clinical outcomes.
Case presentation: A 73-year-old man was hospitalized at a nearby hospital due to chronic subdural hematoma, symptomatic epilepsy, and diabetes mellitus. He was transferred to our hospital with fever, low blood pressure, and cyanosis of the legs, and was diagnosed with septic shock due to emphysematous cystitis with purpura fulminans. He underwent intensive treatment, including retroperitoneal drainage. Urine culture was positive for *Citrobacter freundii*. His general condition gradually improved and diffuse air decreased after surgery, but progressive purpuric skin necrosis became evident on the legs, which could not be salvaged. He died on the 25th hospital day.
Conclusion: Sepsis-associated purpura fulminans caused by emphysematous cystitis shows a very poor prognosis irrespective of intensive treatment, including retroperitoneal drainage.

Key words: emphysematous cystitis, purpura fulminans, retroperitoneal drainage, septic shock.

Keynote message

Sepsis-associated purpura fulminans carries a very poor prognosis. This report may be the first report of sepsis-associated purpura fulminans caused by emphysematous cystitis. When we see a patient with septic shock and purpura, we should consider sepsis-associated purpura fulminans.

Introduction

EC is a rare disease caused by gas-producing bacteria and characterized by air bubbles within the bladder wall and lumen on CT. Patients with DM, neurogenic bladder, urethral catheter placement, or recurrent UTI are at higher risk of EC.[1] PF is a rare and severe complication of sepsis, characterized by rapidly progressive development of purple skin lesions secondary to DIC and microvascular thrombosis.[2] PF is a life-threatening syndrome, with a mortality rate over 50%.[3] Sepsis-associated PF caused by EC is very rare, and no previous reports have been established. We describe a case of sepsis-associated PF caused by EC.

Case presentation

A 73-year-old man was hospitalized at a nearby hospital for 4 years due to chronic subdural hematoma, symptomatic epilepsy, and DM. He was transferred to our hospital with fever for 2 days, low blood pressure, and cyanosis of the legs. Physical examination revealed consciousness disorder (Glasgow coma scale 7; E2V1M4), a temperature of 38.0 , a blood pressure of 94/55 mmHg, a pulse rate of 150 bpm, a respiratory rate of 32/min, and an oxygen

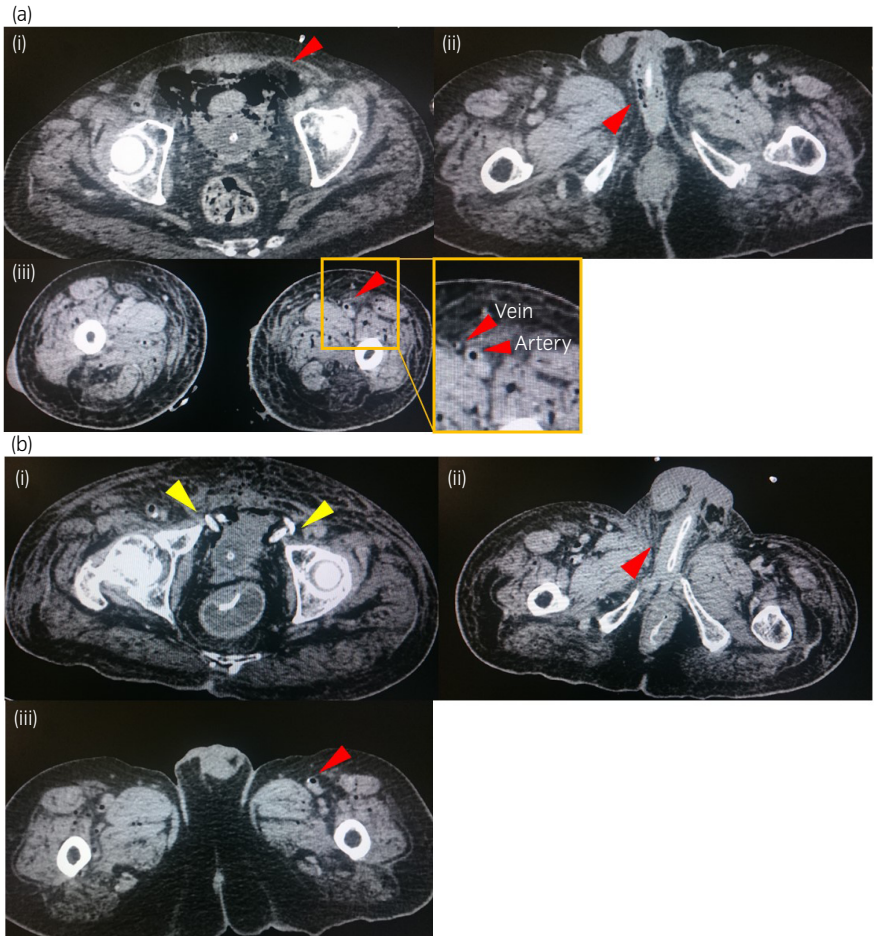


Fig. 1 Image findings before and after retroperitoneal drainage. (a) CT of the abdomen and pelvis shows diffuse air within the bladder wall and extending into the retroperitoneal space (i), cavernous body of the penis (ii), muscles of the lower legs and femoral artery and vein (iii). (b) We placed two drainage tubes (yellow triangles) in the retroperitoneal space. Diffuse air decreased postoperatively, but air bubbles in vessels remained (i–iii).

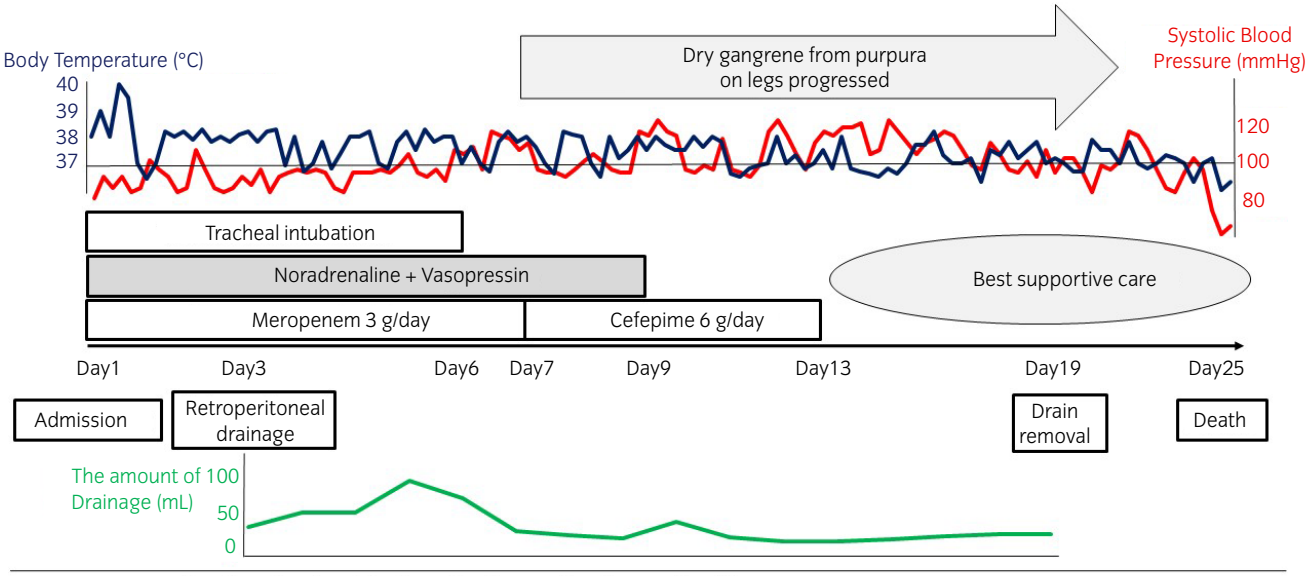
saturation of 99% (oxygen reservoir mask at 10 L/min). CT showed diffuse air bubbles within the bladder wall extending into the retroperitoneal space, cavernous body of the penis, muscles of the lower legs and femoral arteries and veins in spite of under urethral catheter placement (Fig. 1a). Laboratory data showed peripheral leukocytosis (WBC count, 15 400/mm^3, 85.9% segmented forms) and rhabdomyolysis (CK 14 340 U/L) and elevated CRP (22.8 mg/dL) (Table 1). Sequential organ failure assessment score was 14 and Japanese Association for Acute Medicine sepsis-induced DIC score was 8 (where a score ≥4 is defined as DIC). Urine culture revealed positive results for *Citrobacter freundii*, otherwise blood cultures from peripheral artery and vein revealed negative. Therefore, septic shock due to EC was diagnosed. We also suspected PF because purpura appeared different from purpura due to DIC, which reflect bruising and the formation of small dots on the skin (petechiae). He was admitted to our hospital and taken to the intensive care unit. His clinical course is shown in Figure 2. Tracheal intubation was performed under general anesthesia for respiratory management, an indwelling urethral catheter was replaced, and administration of antibiotics and vasopressors was initiated. However, his general condition did not improve, so retroperitoneal drainage was performed on the third hospital day. The amount of drainage was 35 mL and the culture was negative.

After surgery, his general condition gradually improved and diffuse air decreased on CT (Fig. 1b), but purpuric skin necrosis and epidermal peeling gradually progressed to the lower legs on the 7th hospital day and dry gangrene from purpura on the legs showed rapid progression on the 13th hospital day (Fig. 3a). Skin biopsy findings indicated extensive red blood cell extravasation with gangrenous dermal necrosis (Fig. 3b). He required amputation of dry gangrene, but this could not be performed because his general condition

Table 1 Laboratory data

WBC	15.4 × 10^4/μL	ALP	189 U/L	Blood gas analysis†	
RBC	428 × 10^4/μL	T-Bil	1.4 mg/dL	pH	7.476
Hb	13.4 g/dL	D-Bil	0.6 mg/dL	$PaCO_2$	21.7 Torr
Ht	40.6%	CK	14 340 U/L	PaO_2	356 Torr
Plt	7.4 × 10^4/μL	BUN	33.7 mg/dL	HCO_3^-	15.8 mEq/L
PT	15.9 s	Cre	0.96 mg/dL	BE	−5.4 mEq/L
PT-INR	1.33	Na	138 mEq/L	Lac	3.5 mg/dL
APTT	43.6 s	K	4.3 mEq/L		
Fib	293 mg/dL	Cl	104 mEq/L		
FDP	668.5 μg/mL	CRP	22.8 mg/dL		
AST	74 U/L	Glucose	273 mg/dL	SOFA	14
ALT	15 U/L	HbA1c	6.6%	DIC	8
LDH	1001 U/L				

On transfer to our hospital, blood examination showed leukocytosis and an increased inflammatory reaction. Arterial blood gas analysis showed metabolic acidosis. †Arterial blood and 100% oxygen reservoir mask at 10 L/min.



	Day3	Day4	Day5	Day6	Day8	Day10
WBC (/mm^3)	15,400	19,600	17,900	17,200	13,300	12,500
CRP (mg/dL)	22.4	22.0	15.6	14.1	16.9	19.9
CK (IU/L)	19,430	15,100	17,590	13,210	8,420	4,610

Fig. 2 Clinical course of the patient with sepsis-associated PF caused by EC. Postoperatively, respiratory and circulatory dynamics were gradually stable, but fever and inflammatory findings remained.

was considered inadequate to tolerate the additional surgery. He died on the 25th hospital day due to multiple organ dysfunction syndromes.

Discussion

EC is a rare disease and typically presents as pneumaturia, hematuria, storage symptoms, and abdominal pain with sepsis.[4] Since Bailey first described EC in 1961,[5] the reports have been increasing with the increased use of CT and a greater awareness of such diseases. Mortality rate of EC is 3–12%, but 90% of all EC cases improve under conservative treatment.[1,6] The most common pathogen from urinary cultures is *Escherichia coli*, followed by *Klebsiella pneumoniae* and *Enterobacter aerogenes*.[1]

PF is a rare and severe complication of sepsis caused by bacterial infection. This condition is defined as simultaneous ischemic necrosis of more than two affected distal limbs without obstruction of the proximal arteries.[2] The main pathogens are *Neisseria meningitides*, *Streptococcus pneumoniae,* and *Haemophilus influenzae*.[7] In contrast, *E. coli* and *Enterococcus faecalis* are rare causative organisms.[8] According to these pathogens, PF caused by a UTI is rare.

In this case, he had risk factors for EC; DM, neurogenic bladder, and urethral catheter placement and the first CT showed severe EC findings. We attributed the gas bubbles across an extensive area to increased intravesical pressure due to obstruction of urethral catheter and bacterial injury to the bladder wall allowing translocation of the gas into surrounding vessels. The gas bubbles within vessels and the state of septic shock may have led to severe PF and rhabdomyolysis. We should consider appropriate management of urethral catheter for preventing UTI. His urine culture detected *C. freundii*, a Gram-negative rod that produces carbon dioxide from glucose fermentation. According to the previous report, positive blood cultures could be accounted for 50% of the EC cases.[9] The reason why blood cultures revealed negative was insufficient volume due to hypovolemia.

If conservative therapy proves ineffective for EC, surgical treatment should be considered. Sasaki *et al*. reported successful use of retroperitoneal drainage for severe EC.[10] We performed a similar intervention and his condition was improved, but we could not salvage. Since he could not explain his symptoms due to consciousness disorder, severe EC and PF might have already been progressed markedly on admission to our hospital, contributing to poor clinical outcomes despite retroperitoneal drainage. We should perform surgical treatment immediately when encounter a patient with sepsis and severe complication such as PF.

PF is a life-threatening syndrome but the optimal treatment of PF is uncertain.[3] Patients who survive often require amputation of areas of dry gangrene that progress from purpura in distal lesions and the functional prognosis is poor. In this case, he was considered to require amputation of the legs to survive, but that surgery could not be performed because of his poor general condition. Supportive therapy such as anticoagulation and prostaglandin could not have prevented the progression of PF or even controlled severe EC. Because sepsis-associated PF has a high mortality rate and this patient required amputations to survive, detecting rapid progression

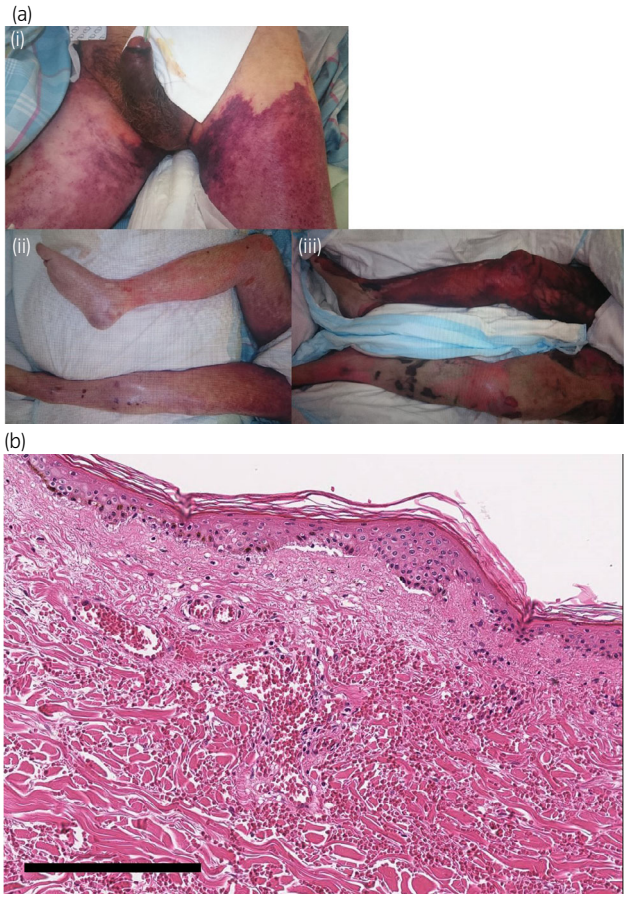


Fig. 3 Macroscopic appearance of the lesion and histological findings. (a) On admission to our hospital, purple discoloration of the skin is seen over both legs (i, ii). Purpura appear different from purpura due to DIC, which reflects bruising and the formation of small red dots on the skin (petechiae), so we suspected PF. Purpuric skin necrosis and epidermal peeling gradually progressed to the lower legs. On the 13th hospital day, dry gangrene from purpura on the legs shows rapid progression (iii). (b) Skin biopsy (hematoxylin and eosin staining). Interface vacuolar changes, dermal capillary dilatation, and congestion with red blood cells are evident. Extensive extravasation of red blood cells into the dermis and gangrenous dermal necrosis is also seen. Gram staining to exclude necrotizing fasciitis reveals no obvious bacteria in the lesion.

of systemic purpura is key to early diagnosis. To the best of our knowledge, this represents the first description of sepsis-associated PF caused by EC.

Conclusion

In conclusion, sepsis-associated PF caused by EC have a very poor prognosis, irrespective of intensive treatments including retroperitoneal drainage. When we encounter a patient with septic shock and rapidly progressing systemic purpura, sepsis-associated PF should be considered.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Obtained from his family.

Registry and the Registration No. of the study/trial

Not applicable.

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