

Necrotizing Soft Tissue Infection Caused by *Klebsiella pneumoniae* After Intra-Articular Injection: A Case Report and Literature Review

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Background: Necrotizing soft tissue infection is a fulminant, life-threatening condition causing sepsis along with multiorgan failure, with *Klebsiella pneumoniae* -induced cases rising, especially in diabetics. Intra-articular injection-related *Klebsiella pneumoniae* -induced necrotizing soft tissue infection has not been reported previously; only 35 *Klebsiella pneumoniae* -induced extremity necrotizing soft tissue infection cases exist in English literature.

Case Presentation: A 67-year-old diabetic woman with hypertension developed right lower extremity *Klebsiella pneumoniae* -induced necrotizing soft tissue infection post-intra-articular glucocorticoid/anesthetic injection. She had swelling, pain, confusion; computed tomography showed soft tissue swelling/gas, blood culture confirmed *Klebsiella pneumoniae*, Laboratory Risk Indicator for Necrotizing Fasciitis score was 9 (out of 13). Family refused debridement; despite antibiotics, Continuous Renal Replacement Therapy, and glucose control, she died of multiorgan failure 18 hours post-admission.

Conclusion: *Klebsiella pneumoniae* -induced cases rising, especially in diabetics is highly lethal (38.9% mortality in 36 reviewed cases), with diabetes as the main risk factor. Early diagnosis (computed tomography, Laboratory Risk Indicator for Necrotizing Fasciitis) and aggressive debridement are critical. Intra-articular injection infection prevention and timely etiological exams are essential.

Keywords: intra-articular injection, diabetes mellitus, necrotizing soft tissue infection, *Klebsiella pneumoniae*

Background

Necrotizing soft tissue infection (NSTI) is a fulminant infectious condition capable of affecting any layer within the skin and soft tissue.¹ It is characterized by several key features: the presence of toxin-secreting bacteria, localized tissue damage, rapid and fulminant progression of the inflammatory response, and early-onset systemic toxic manifestations—all of which can culminate in sepsis, multiple organ failure, and even death.¹ Soft-tissue infections arising from subcutaneous, intravenous, or intramuscular injections using contaminated needles differ in severity and encompass conditions such as cellulitis, abscess, myositis, and necrotizing fasciitis.² The microorganisms associated with these infections are typically diverse, with *Staphylococcus aureus* and *Streptococcus pyogenes* being the most common.² Monomicrobial NSTI triggered by *Klebsiella pneumoniae* (Kp) has now emerged as an infectious disease, particularly among patients with diabetes.³ It is the first report of a case of extensive Kp-induced NSTI in the right lower limb after intra-articular injection of glucocorticoids and local anesthetics. The publication of the case details has been approved by the Ethics Review Committee of Tongxiang First People's Hospital. We also review here 36 cases of Kp-induced NSTI of extremities including this case.

Case Presentation

A 67-year-old woman with uncontrolled type 2 diabetes as well as hypertension was admitted to the Emergency Department of Tongxiang First People's Hospital, Jiaxing City, Zhejiang Province, People's Republic of China on

August 10, 2023, due to swelling and pain in the right thigh, right knee, and right calf area for 1 day, accompanied by confusion for 3 hours. The patient had a 16-year history of diabetes mellitus, was diagnosed with type 2 diabetes mellitus complicated with retinopathy 5 years ago, and had a 10-year history of hypertension. Her recent glycated hemoglobin (HbA1c) level was 11.3%, indicating poor glycemic control, which necessitated long-term subcutaneous injection of insulin aspart and insulin glargine for glycemic management. For blood pressure control, she was prescribed valsartan, hydrochlorothiazide tablets, and levamlodipine besylate tablets. The patient was asked about her medical history. Three days ago, she underwent anteroposterior and lateral X-ray examination of the right knee joint at a local health center because of right knee pain that lasted for 3 days (Figure 1). Subsequently, she received intra-articular injection of glucocorticoids (triamcinolone acetonide acetate injection 20 mg) and local anesthetics (lidocaine hydrochloride injection 0.1 g) in the right knee joint.

On admission, the patient had a normal body temperature but presented with confusion, with Glasgow Coma Scale (GCS) score of 13 and the body mass index (BMI) of 18.7 kg/m². Physical examination revealed diffuse swelling involving the right thigh, right knee region, and proximal right lower leg, with ill-defined boundaries extending proximally to the upper thigh and distally to the lower leg. Associated findings included tenderness and palpable crepitus; however, no obvious skin erythema, skin lesions, or blisters were observed. Vital signs were stable: blood pressure 117/99 mmHg, pulse 114 beats per minute, temperature 36.2°C, respiratory rate 28 breaths per minute, and oxygen saturation 95%.

Abdominal computed tomography (CT) showed extensive swelling and pneumatosis of the right perihip, buttock, and iliac internal and external muscles (Figure 2).

Laboratory test results revealed that: C-reactive protein (CRP) 251.5 mg/L, creatinine 123 µmol/L, lactate 10.1 mmol/L, creatine kinase (CK) 436 U/L, and blood glucose 30.58 mmol/L were significantly increased. Other tests showed no ketones in urine or serum, with an effective plasma osmolality of 305.3 mOsm/L, arterial blood pH of 7.402 (within normal range), serum bicarbonate (HCO₃⁻) of 14.1 mmol/L, and anion gap (AG) of 12.7 mmol/L (Table 1).

The initial clinical diagnosis was NSTI. Emergency surgical incision and debridement of the right hip and gluteal region are recommended. However, the patient's family has reservations and requests conservative medical management instead.

After admission, the patient was transferred to the Emergency Intensive Care Unit (EICU), where she was administered intravenous infusions of imipenem-cilastatin sodium and linezolid. Shortly thereafter, the patient developed

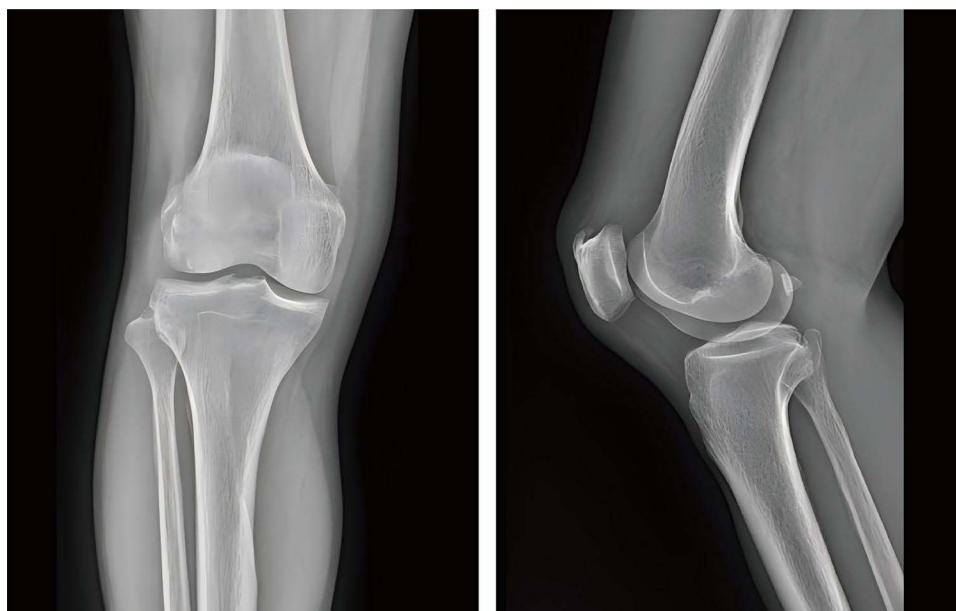


Figure 1 Right knee joint radiograph reveals no surrounding soft tissue swelling or gas shadows.

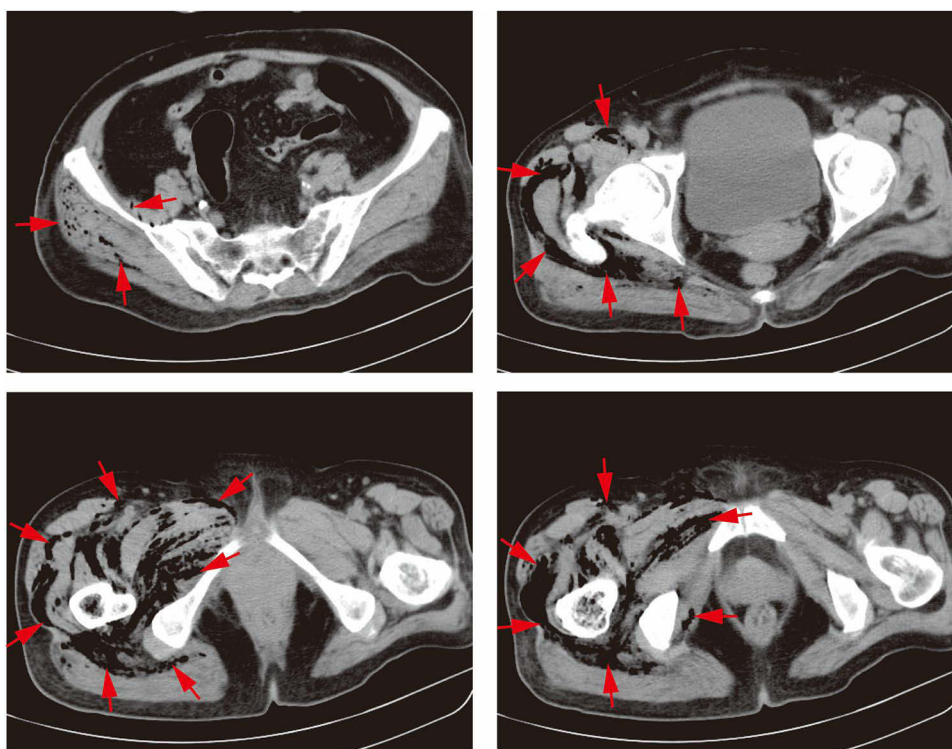


Figure 2 Abdominal computed tomography (CT) demonstrates extensive gas accumulation within the right Hip, buttock, and internal/external iliac musculature (red arrows).

fever, hypoxemia, and decreased blood pressure, followed by coma. Microbiological analysis revealed that Kp was the only pathogen isolated from the blood cultures and was susceptible to the aforementioned antibiotics. (Table 2). Tissue and pus cultures were not obtained because the patient's family refused debridement. The patient's typical signs, hypotension, Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score (Table 3), blood culture, and CT findings were consistent with the diagnosis of NSTI.

The patient received targeted treatment for septic shock, hyperglycemia, and acidosis. Broad-spectrum antibiotics (imipenem-cilastatin sodium and linezolid) were given as initial anti-infection therapy, followed by intravenous infusion of cefoperazone sodium-sulbactam sodium and metronidazole. Continuous intravenous insulin infusion was used to strictly

Table 1 Summary of the Laboratory Data on Admission

Hematology		Biochemistry		Arterials Blood Gas		Coagulation Profile	
WBC	$3.6 \times 10^9/L$	TP	66.5g/L ↓	pH	7.402	PT	14.5s ↑
Neu	88.3%	Alb	27.1g/L ↓	pCO ₂	23.1mmHg ↓	INR	1.31 ↑
Lym	7.2% ↓	AST	37U/L ↑	HCO ₃	14.1mmol/L ↓	APTT	33.9 s
Mono	4.3%	ALT	25U/L	Anion gap	12.7mmol/L	TT	18.5 s
Eosino	0.1% ↓	LDH	206.1U/L	LAC	10.1mmol/L ↑	FIB	8.34g/L ↑
Baso	0.1%	γ-GTP	58U/L ↑			D-D	2519μg/L ↑
RBC	$4.29 \times 10^{12}/L$	ALP	205U/L ↑				
Hb	107g/L ↓	T-Bil	12.6μmol/L				
Ht	32.2% ↓	BUN	14.4mmol/L ↑				
PLT	$81.0 \times 10^9/L$ ↓	Cre	123μmol/L ↑				
		Na	126.9mmol/L ↓				
		K	3.26mmol/L ↓				

(Continued)

Table 1 (Continued).

Hematology		Biochemistry		Arterials Blood Gas		Coagulation Profile	
		Cl	90mmol/L ↓				
		Ca	2.23mmol/L				
		Glu	30.58mmol/L ↑				
		Ketones	(-)				
		CRP	251.5mg/L ↑				
		CK	436U/L ↑				
		UA	496μmol/L ↑				

Notes: Increased (↑) and decreased (↓) values are indicated by upward and downward arrows, respectively.

Abbreviations: WBC, white blood cells; Neu, neutrophils; Lym, lymphocytes; Mono, monocytes; Eosino, eosinophil; Baso, basophils; RBC, red blood cells; Hb, hemoglobin; Ht, hematocrit; PLT, platelet counts; TP, total protein; Alb, albumin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; γGTP, γ-glutamyl transpeptase; ALP, alkaline phosphatase; T-Bil, total bilirubin; BUN, blood-urea-nitrogen; Cre, creatinine; Na, sodium; K, potassium; Cl, chlorine; Ca, calcium; Glu, glucose; CRP, c-reactive protein; CK, creatine kinase; UA, uric acid; pH, potential of hydrogen; pCO₂, carbon dioxide partial pressure; HCO₃, bicarbonate ion; LAC, lactic acid; PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; TT, thrombin time; FIB, fibrinogen; D-D, D-dimer.

Table 2 Antimicrobial Resistance Profiles and Minimum Inhibitory Concentrations of Kp (Isolated from Blood Cultures)

Antibiotic	Drug Sensitivity	MIC (μg/mL)
Cefazolin	S	UD
Meropenem	S	UD
Cefoperazone/sulbactam	S	UD
Cefepime	S	≤ 1
Ciprofloxacin	S	≤ 0.25
Cefotetan	S	≤ 4
Gentamycin	S	≤ 1
Cotrimoxazole	S	≤ 20
Tobramycin	S	≤ 1
Piperacillin/tazobactam	S	≤ 4
Ceftazidime	S	≤ 1
Ceftriaxone	S	≤ 1
Levofloxacin	S	≤ 0.25
Ampicillin-sulbactam	S	4
Aztreonam	S	≤ 1
Ertapenem	S	≤ 0.5
Imipenem	S	≤ 1
Amikacin	S	≤ 2

Abbreviations: MIC, minimum inhibitory concentration; R, resistant; S, sensitive; UD, undetected.

control blood glucose, and Continuous Renal Replacement Therapy (CRRT) was used to correct acidosis and reduce serum creatinine. Despite the aforementioned comprehensive treatment, the patient's condition did not significantly improve, and she finally died of multiple organ failure including disseminated intravascular coagulation 18 hours after admission.

Dynamic monitoring of the patient's white blood cell count, C-reactive protein, and procalcitonin during hospitalization showed that these three indicators closely related to infection exhibited a significant upward trend during the patient's hospitalization (Figure 3).

To present a more comprehensive view of the timelines for key physiological indicators and therapeutic interventions throughout the patient's course from admission, disease progression to deterioration, and ultimately death, we have

Table 3 LRINEC Score

Variables	Units	Day 1		
		00:58	03:28	13:13
CRP	mg/L	251.5	239	310.17
WBC	$\times 10^9/L$	3.6	4.0	6.4
Hb	g/L	107	101	113
Na	mmol/L	126.9	133.1	140.8
Glu	mmol/L	30.58	22.39	13.74
Cre	$\mu\text{mol/L}$	123	110	88
Score		9	9	6

Notes: Total LRINEC score out of 13. Once the score ≥ 6 , NF may be suspected; once the score ≥ 8 , the diagnosis would be strongly suspected.

Abbreviations: CRP, c-reactive protein; WBC, white blood cells; Hb, hemoglobin; Na, sodium; Glu, glucose; Cre, creatinine.

developed a timeline chart (Figure 4). This chart details the changes in the patient's vital signs (eg, blood oxygen saturation), laboratory test indicators (eg, hemoglobin, platelet count, C-reactive protein, lactic acid, albumin, creatinine, potassium, sodium, blood glucose, procalcitonin) at different time points, as well as the therapeutic measures administered.

Discussion and Conclusion

NSTIs are a group of life-threatening skin and soft tissue infectious diseases characterized by extensive tissue necrosis.^{4,5} The disease is usually critical and progresses rapidly and is often complicated with sepsis and multiple organ failure. NSTI is capable of affecting any part of the body, though its most common sites are the limbs, perineum, and genitals; a subset of cases also occur in the chest or abdomen. The disease usually occurs when the epithelial or mucosal surface is

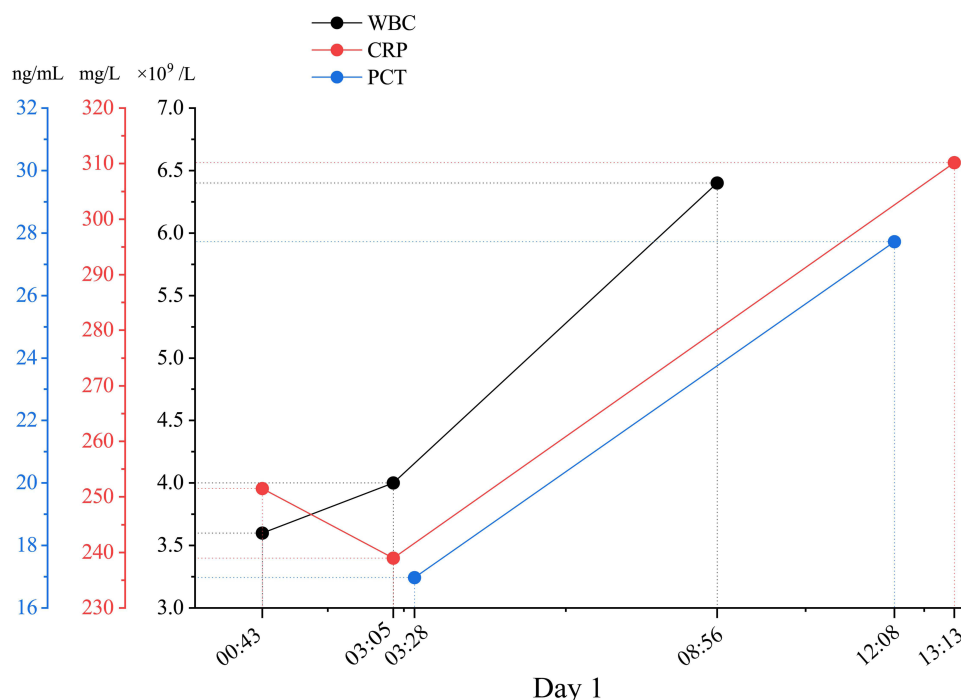


Figure 3 Serial changes in white blood cell count, C-reactive protein, and procalcitonin during the patient's hospitalization.

Abbreviations: WBC, white blood cells; CRP, C-reactive protein; PCT, procalcitonin.

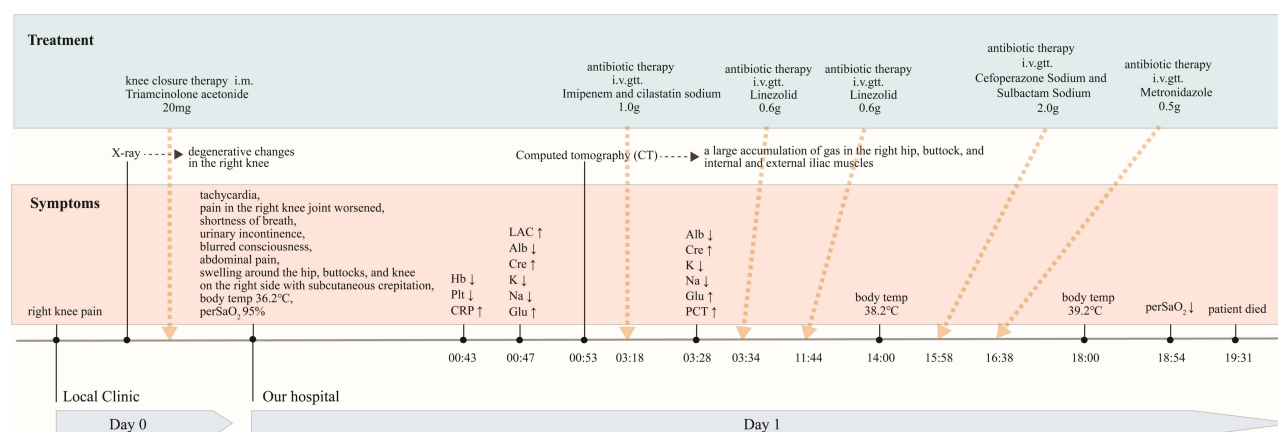


Figure 4 Timeline. Black solid lines: Used to connect timeline nodes to corresponding clinical examination methods (eg, linking specific time points to X-ray and CT examinations); • Horizontal black dashed arrows: Point to the results derived from the corresponding examinations (eg, pointing to “degenerative changes in the right knee joint” as identified by X-ray, and “massive gas accumulation in the right Hip, buttock, and internal/external iliac muscles” as detected by CT); • Light Orange dashed arrows: Used to connect timeline nodes to key medication information corresponding to each time point; • Upward/downward arrows: The upward arrow (↑) indicates an elevation in the value of the relevant clinical indicator, while the downward arrow (↓) indicates a reduction.

Abbreviations: perSaO₂, peripheral capillary oxygen saturation; Hb, hemoglobin; Plt, platelet counts; CRP, C-reactive protein; LAC, lactic acid; Alb, albumin; Cre, creatinine; K, potassium; Na, sodium; Glu, glucose; PCT, procalcitonin.

damaged, allowing the pathogen to invade the subcutaneous tissue. A variety of etiologies have been reported, including trauma, intravenous drug use and insulin, skin infection and ulcers, animal and insect bites, visceral-skin fistula, surgical complications, percutaneous catheter placement, abscess and idiopathic causes.⁶ Soh et al reported a case of NSTI after intravenous injection of non-steroidal anti-inflammatory drugs, and the diabetic patient developed NSTI in the left shoulder and upper limb after receiving intravenous diclofenac for flu-like symptoms, which required multiple wound debridement.⁷ However, there have been no reported cases of NSTI after intra-articular injection. To date, only 35 cases of Kp-induced extremity NSTI have been described in the English medical literature. On the basis of reviewing the above 35 reported cases, the clinical data of this patient were further included for analysis.

Early differentiation of NSTI from other types of soft tissue infections remains one of the major challenges in managing this potentially life-threatening condition. Therefore, numerous studies have attempted to aid in its early and accurate diagnosis through the analysis of imaging features and laboratory parameters. Fernando et al conducted a systematic review and meta-analysis to evaluate the accuracy of physical examination findings, imaging studies, and LRINEC scores in diagnosing NSTI in patients with suspected NSTI.⁸ They found that the sensitivity of CT for NSTI diagnosis was 88.5% and the specificity was 93.3%.⁸ The LRINEC score is a validated clinical decision tool used to distinguish NSTI from other soft tissue infections.⁹ It includes six predictors: (1) C-reactive protein (mg/L), (2) white blood cell count ($\times 10^9/L$), (3) hemoglobin (g/L), (4) sodium (mmol/L), (5) creatinine ($\mu\text{mol/L}$), and (6) glucose (mmol/L). In their study, Fernando et al showed that an LRINEC score ≥ 6 had a sensitivity of 68.2% and a specificity of 84.8% for NSTI diagnosis, while a score ≥ 8 had a sensitivity of 40.8% and a specificity of 94.9%.⁸ In the case of our patient, the clinical manifestations and computed tomography results not only strongly indicated NSTI, but her LRINEC score of 9 also further validated the early diagnosis. NSTI can be caused by a variety of pathogens, either mixed infection or single pathogen infection. There is a high incidence of NSTI in patients with diabetes mellitus, especially the proportion of single pathogen infection with Kp is increasing year by year. To date, most reported cases of Kp causing NSTI in the extremities, including our case, have been mono-microbial. Of the 36 cases reported, 34 were mono-microbial and 3 were polymicrobial. These infections were located in the left lower limb ($n = 7$), right lower limb ($n = 7$), both lower limbs ($n = 6$), left thigh ($n = 4$), left upper limb ($n = 3$), right thigh ($n = 4$), right forearm ($n = 2$), left calf ($n = 2$), left knee ($n = 2$), right forearm ($n = 1$), right upper limb ($n = 1$), both thighs ($n = 1$), right knee ($n = 1$), right lower leg ($n = 1$), and both lower legs ($n = 1$) (Table 4).

Gas-forming necrotizing soft tissue infection (GNSI) is one of the important subtypes of NSTIs. It is an acute, life-threatening infection caused by gas-forming pathogens, characterized by soft tissue necrosis accompanied by gas

Table 4 Kp-Induced Extremity NSTI: a Review of Cases Reported in the English Literature

Case	Age/ Gender	Comorbidity	Location	Bacteriologic Results	Treatment	Outcome	References
1	16/ND	Chondromalacia; Chronic left patella subluxation	Left knee;	<i>Klebsiella</i> <i>ozaenae</i> ; <i>Staphylococcus</i> <i>epidermidis</i> ; <i>Corynebacterium</i> <i>species</i>	ND	ND	[10]
2	51/M	DM	Both legs	Kp	Antibiotics &Surgical drainage	Discharged	[11]
3	24/F	—	Right forearm	hvKp	Antibiotics &Debridement	Discharged	[12]
4	47/M	—	Left lower leg	hvKp	Antibiotics &Surgical drainage	Discharged	[13]
5	72/F	DM; CRF; Obstructive arteriosclerosis	Both lower legs	hvKp	ND	Discharged	[13]
6	29/M	CML;DVT; Compartment syndrome	Right thigh	<i>Multidrug-</i> <i>resistant (MDR)</i> <i>K. pneumoniae</i>	Antibiotics &Fasciotomy &Debridement	Discharged	[14]
7	60/M	Decompensated hepatitis C cirrhosis; Liver transplantation	Both thighs	Kp	Antibiotics &Debridement	Died	[15]
8	59/F	Hepatitis C cirrhosis; Liver-kidney transplant; Recurrent hepatitis C and renal failure; Bacteremia; Perinephric abscess	Both legs	<i>Pan-susceptible</i> <i>K. pneumoniae</i>	Antibiotics alone	Died	[15]
9	64/F	ALF; Liver transplantation	Left upper extremity; right lower extremity	CRKp	Antibiotics alone	Died	[15]
10	50/F	Autoimmune hepatitis; Subfulminant hepatic failure; Liver transplantation	Left lower extremity	CRKp	Antibiotics alone	Died	[15]
11	40/M	Hemophilia type A;SBP; HIV infection; Hepatitis C cirrhosis; Bacteremia; Liver transplantation	Right lower extremity	CRKp	Antibiotics &Debridement	Died	[15]
12	62/M	Hepatitis C cirrhosis; Renal failure; Worsening hepatic function; Underwent 2 Liver transplantation	Left lower extremity	CRKp	Antibiotics &Debridement	Died	[15]
13	46/M	—	Left lower extremity	Kp	Antibiotics alone	Discharged	[16]
14	75/M	DM	Left forearm	Kp	Fasciotomy; Antibiotics;ND	Discharged	[3]
15	50/M	Chronic hepatitis B infection and advanced cirrhosis	Left knee and thigh	<i>K. pneumoniae</i> <i>KI</i>	Antibiotics &Debridement	Died	[17]

(Continued)

Table 4 (Continued).

Case	Age/ Gender	Comorbidity	Location	Bacteriologic Results	Treatment	Outcome	References
16	52/M	DM; Hepatitis B-related liver cirrhosis	Left lower extremity	Kp	Antibiotics & Debridement	Died	[18]
17	92/F	Hypertension; AF; DLB	Right lower extremity	<i>K. pneumoniae</i> K2	Antibiotics & Debridement	Died	[19]
18	68/M	DM; Hypertension	Right lower extremity	CRKp	Debridement & NPWT; Antibiotics: ND	Discharged	[20]
19	75/M	DM	Left forearm	Kp	Antibiotics & Fasciotomy	Discharged	[21]
20	75/M	DM	Left lower extremity	Kp	Antibiotics & Fasciotomy & Percutaneous drainage	Discharged	[22]
21	40/M	DM	Left lower extremity	Kp	Antibiotics & Fasciotomy	Discharged	[22]
22	60S/M	COPD; Obesity; AF; Hypertension; Pulmonary edema; Crohn's disease; Urethral stricture; Bilateral hip prostheses; Acute heart and kidney failure	Both legs	Kp; <i>Staphylococcus epidermidis</i>	Antibiotics & Debridement	Died	
23	37/M	DM	Left upper extremity; left lower leg	Kp	Antibiotics & Fasciotomy	Discharged	[23]
24	77/M	DM; Metastatic follicular thyroid cancer with metastasis to the spine; Treatment with radioactive iodine; Pathologic fracture of the left hip; A total hip replacement	Left thigh; right thigh	Kp	Antibiotics & Debridement & Fasciotomy	Died	[24]
25	74/M	DVT and atherosclerosis in the left low extremities	Both lower extremities	Kp	Antibiotics alone	Discharged	[25]
26	70/M	DM; Hypertension; Strokes	Right lower extremity	<i>Acinetobacter baumannii</i> ; <i>Pseudomonas aeruginosa</i> ; NDM and OXA-48-producing <i>K. pneumoniae</i>	Antibiotics & Debridement	Discharged	[26]
27	72/F	Decompensated liver cirrhosis; Gas gangrene of the lower limbs	Both lower extremities	CS-hvKp	Antibiotics; Surgical treatment: ND	Discharged	[27]
28	29/M	DM	Right lower extremity	Kp	Antibiotics & Fasciotomy	Discharged	[28]

(Continued)

Table 4 (Continued).

Case	Age/ Gender	Comorbidity	Location	Bacteriologic Results	Treatment	Outcome	References
29	50/F	DM;DKA	Both legs	Kp	Antibiotics & Debridement &Fasciotomy	Died	[29]
30	58/M	Osteomyelitis of the left tibia	Left thigh	Kp	Antibiotics & Debridement	Died	[30]
31	57/M	DM;Hypertension	Right upper arm	Kp	Antibiotics & Debridement	Discharged	[31]
32	61/M	DM	Left upper extremity; right lower extremity	<i>K. pneumoniae</i> K2	Antibiotics & Debridement & Surgical drainage	Discharged	[32]
33	66/M	DM;Hypertension; Ankylosing spondylitis; Hypercholesterola-emia	Left lower extremity	<i>K. pneumoniae</i> K2	Antibiotics & Fasciotomy	Discharged	[33]
34	ND/F	Heroin Addict with DM	Left thigh	Kp	ND	ND	[34]
35	38/M	DM	Right thigh	hvKp	Antibiotics & Debridement & Surgical drainage	Discharged	[35]
36	67/F	DM;Hypertension	Right knee and thigh; right lower leg	CSKp	Antibiotics alone	Died	Our case

Abbreviations: DM, Diabetes mellitus; CRF, Chronic renal failure; CML, Chronic myeloid Leukaemia; DVT, Deep vein thrombosis; ALF, Acute liver failure; HIV, Human Immunodeficiency Virus; SBP, Spontaneous bacterial peritonitis; DLB, Dementia with Lewy bodies; AF, Atrial fibrillation; COPD, Chronic obstructive pulmonary disease; DKA, Diabetic ketoacidosis; ND, No data; Kp and *K. pneumoniae*, *Klebsiella pneumoniae*; hvKp, Hypervirulent *Klebsiella pneumoniae*; CRKp, Carbapenem-resistant *Klebsiella pneumoniae*; CS-hvKp, Carbapenem-susceptible hypervirulent *Klebsiella pneumoniae*; CSKp, carbapenem-sensitive *Klebsiella pneumoniae*; —, None.

production. The most typical pathogenic bacteria in clinical practice are anaerobes such as *Clostridium perfringens* (*C. perfringens*). However, in recent times, the number of reported cases of gas-forming soft tissue infections resulting from non-anaerobic bacteria has gradually increased. In particular, cases caused by Kp as a single pathogen have attracted extensive attention and discussion in the scientific community. Kp is a gram-negative bacteria that often exists in the human respiratory tract and intestinal tract. As an opportunistic pathogen, Kp can invade soft tissues and cause infection when the immunity is compromised or there is trauma. Wu et al reported a case of gas gangrene combined with sepsis caused by a single Kp (ST412/K57) infection.²⁷ Hypervirulent *Klebsiella pneumoniae* (hvKp) was isolated from the knee joint pus and blood of the patient, which was confirmed to be homologous by whole genome analysis.²⁷ This case report not only ruled out the involvement of other anaerobic bacteria but also confirmed the high ability of gas production and pathogenicity of the strain through a live infection model. Additionally, whole-genome analysis suggested that the strain has genetic characteristics of enhanced gas production, strong biofilm and high capsule formation ability, which greatly enhanced its tissue invasiveness and drug resistance. Furthermore, Das et al reported a case of non-*Clostridium* gas gangrene after intramuscular injection.³⁶ Kp was isolated from the patient's blood culture and autopsy, and no other anaerobic bacteria were detected during antemortem and postmortem, and typical gas foam was observed in gross and histopathological findings, which confirmed that Kp could be the main pathogenic factor causing gas gangrene.³⁶ Sookdee et al reported a rare case of deep head and neck abscess complicated with gas gangrene caused by Kp.³⁷ This patient was a diabetic patient who had obvious gas overflow from the incision during emergency surgery. The results of tissue and blood culture only detected Kp, and no anaerobic bacteria were isolated by multiple microbiological tests, further emphasizing that Kp can independently cause deep soft tissue gas-producing infection.³⁷

In this case, the patient was infected after intra-articular injection, and the blood culture was positive, combined with the rapid progress of infection and soft tissue necrosis, which was consistent with the clinical features of Kp infection.

As a fatal infectious disease, NSTI caused by Kp is more common in patients with diabetes, chronic liver disease or immunocompromised status.⁶ To further clarify the clinical characteristics of NSTI of the extremities caused by Kp, a statistical analysis was performed on 36 enrolled cases (including this case) (Figure 5). In terms of age distribution, patients with this type of infection were mainly concentrated in the 50–80 years age group. This may be associated with factors such as the gradual decline in immune function and the higher incidence of underlying diseases in the middle-aged and elderly population. Regarding comorbidities, diabetes mellitus was the most common comorbidity, accounting for as high as 52.8%, followed by liver diseases (25.0%). Only 8.3% of patients had no definite comorbidities (Figure 5). This further confirms that underlying diseases such as diabetes mellitus and liver diseases are important risk factors for extremity NSTI caused by Kp, which is consistent with the case characteristics described earlier and the conclusions of previous studies.

In recent years, reports of a variety of serious infections caused by Kp have been increasing, and its clinical characteristics are mainly characterized by poor response to antimicrobial therapy. These strains gradually evolved into hypervirulent or resistant strains by acquiring additional genetic properties.³⁸ Leukocyte chemotaxis, phagocytosis and bactericidal function in diabetic patients are significantly decreased, and local tissue ischemia facilitate the occurrence and progress of NSTI.³⁹ The cases reported in this study further confirm that diabetic patients infected with Kp are prone to develop a rapidly progressive NSTI with a trend of rapid deterioration in clinical course, ultimately leading to poor prognosis. To further clarify the clinical characteristics of NSTI of extremities caused by Kp, a total of 36 reported cases of Kp-induced NSTI of extremities were systematically analyzed. Among the 36 cases, hvKp infection accounted for 5 cases (13.9%), and Carbapenem-resistant *Klebsiella pneumoniae* (CRKp) infection accounted for 4 cases (11.1%). The overall case fatality rate in this group was as high as 38.9% (Figure 5). However, this study has certain limitations: no mucoid phenotype analysis, virulence gene detection, or capsular typing of the isolated Kp was performed.

The standard treatment of NSTI includes the application of broad-spectrum antibiotics, extensive surgical debridement and supportive care. The disease has significant morbidity and mortality, with a mortality rate of 25%–35%.⁶ Active surgical intervention is the cornerstone of NSTI treatment. Early and thorough removal of necrotic tissue is essential to control the disease, prevent disease progression, and prevent systemic complications.⁴⁰ Of the 36 reported cases, 28 (77.8%) cases, including our case, required surgical treatment. A key limitation of this case is that surgical intervention was not performed. As the recognized gold standard for the treatment of NSTI, early debridement can theoretically significantly improve the treatment effect and achieve a more ideal clinical outcome if it can be applied in time in this case.

Both Kp and *C. perfringens* are capable of causing gas-producing NSTI. CT images in this case revealed multiple gas shadows and soft tissue swelling (Figure 2). However, due to the lack of tissue and pus cultures, it was impossible to definitively distinguish between a monomicrobial Kp infection and a co-infection with other gas-forming bacteria such as *C. perfringens*. Considering the gas distribution pattern and the rapid progression of the disease, the possibility of co-infection with gas-producing bacteria (eg, *C. perfringens*) could not be absolutely ruled out. In this case, because the

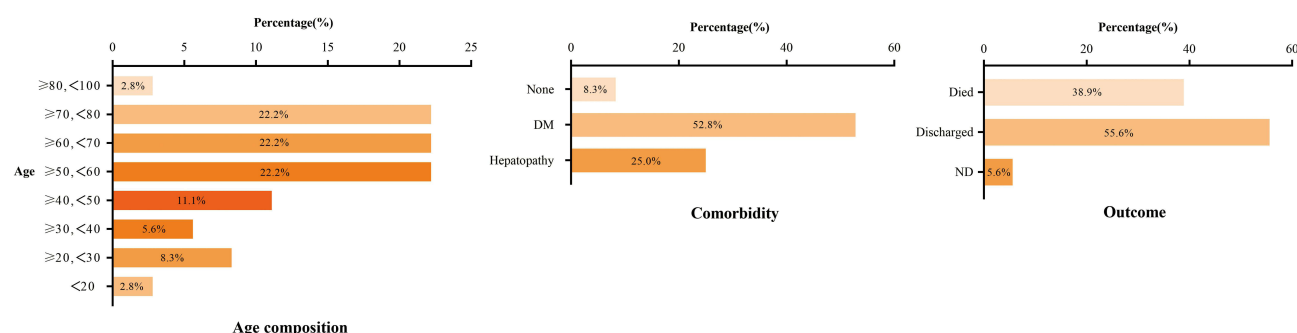


Figure 5 Characteristics of necrotizing soft tissue infections of the extremities caused by Kp.

patient's family refused debridement, the complete pathogen composition could not be identified, which represents a limitation in both diagnosis and management.

In conclusion, this case involves a Kp-induced NSTI following intra-articular injection. Due to the patient's family's refusal of critical invasive procedures, despite the identification of Kp in blood cultures, it was impossible to fully confirm whether there was a co-infection with other gas-producing bacteria such as *C. perfringens* through tissue/pus cultures or debridement, resulting in limitations in diagnosis and management. The patient's death within 18 hours of admission highlights the high lethality of NSTI and underscores the critical role of early accurate diagnosis and aggressive debridement intervention in improving prognosis. Clinically, emphasis should be placed on infection prevention and control during intra-articular injections. For similar cases, efforts should be made to promptly complete etiological examinations and seize the optimal timing for debridement.

Ethics Approval and Informed Consent

The study was approved by the ethics committee of Tongxiang First People's Hospital (ethical approval number: 2023-240-02). The consent for publication has been obtained from the patient's son since the patient died and cannot sign her own name.

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Disclosure

The authors report no conflicts of interest in this work.

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