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Case Report

Monomicrobial *Klebsiella pneumoniae* necrotizing fasciitis with diabetic ketoacidosis: a case report and review of literature

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Abstract: Background: Monomicrobial *Klebsiella pneumoniae* necrotizing fasciitis (KP-NF) is a rare and fatal infectious disease with a high mortality rate, which is strongly associated with diabetes. Herein is reported a case of KP-NF in a patient complicated with diabetic ketoacidosis (DKA) and the report includes a systematic review of the available literature on this condition. Case summary: A 56-year-old woman complained of forearm swelling one day after an injury and was referred to our emergency center. The patient, had a 20-year history of poorly controlled diabetes. Drowsiness was present on admission and the presence of forearm erythema and swelling occurred on the first night. Laboratory examinations and intraoperative exploration suggested the diagnosis of necrotizing fasciitis, comorbid withDKA. Blood and pus bacteriology confirmed monomicrobial *Klebsiella pneumoniae*. Two timely surgical debridements and sustained combined antibiotics did not stop the disease from progressing. The patient developed serious septic shock and disseminated intravascular coagulation (DIC) 7 days after transfer to EICU. Finally, the patient then succumbed one day after transferring back home. Conclusion: Though KP-NF is a fatal infectious disease with high mortality, it frequently lurks in early stages and can be resistant to complete debridement and sustained antibiotic therapy. DKA is an extreme and fatal metabolic state of uncontrolled diabetes and may have been the catalyst for rapid progression in the early stages of KP-NF in this case. Reciprocally, KP-NF may also trigger and promote the occurrence of DKA. Clinicians, especially in East Asia, should pay more attention to the interactions between the two rare but fatal diseases.

Keywords: *Klebsiella pneumoniae* necrotizing fasciitis, diabetic ketoacidosis, thrombosis, sepsis, case report

Introduction

Monomicrobial *Klebsiella pneumoniae* necrotizing fasciitis is a rare, progressive, and life-threatening disease caused by *Klebsiella pneumonia* (*K. pneumonia*, KP-NF) [1, 2]. It frequently occurs latently in the fascia in early stages and develops into the inflammation and necrosis of subcutaneous soft tissue and skin, which disseminates quickly. Due to the lack of specific characteristics in the early stages, KP-NF often gets both delayed diagnosis and management resulting in a poor prognosis. Sepsis shock and multiple organ dysfunction syndrome (MODS) are the most common causes of death as a result [3, 4]. Existing reports suggest that KP-NF is prevalent mostly in East Asia and is significantly associated with diabetes [5]. Urgent surgical debridement and complete fasciotomies with broad-spectrum antimicrobials are considered key therapies for KP-NF.

As a diabetic acute complication, diabetic ketoacidosis (DKA) is an extreme and fatal metabolic state of uncontrolled diabetes [6]. It has been shown to cause metabolic acidosis, drowsiness, and shock in patients, and infection is one of the most common causes of DKA. This is a report of a case of KP-NF in a patient complicated with DKA.

Materials and methods

A 56-year-old woman was referred to our emergency center with right forearm swelling. Her

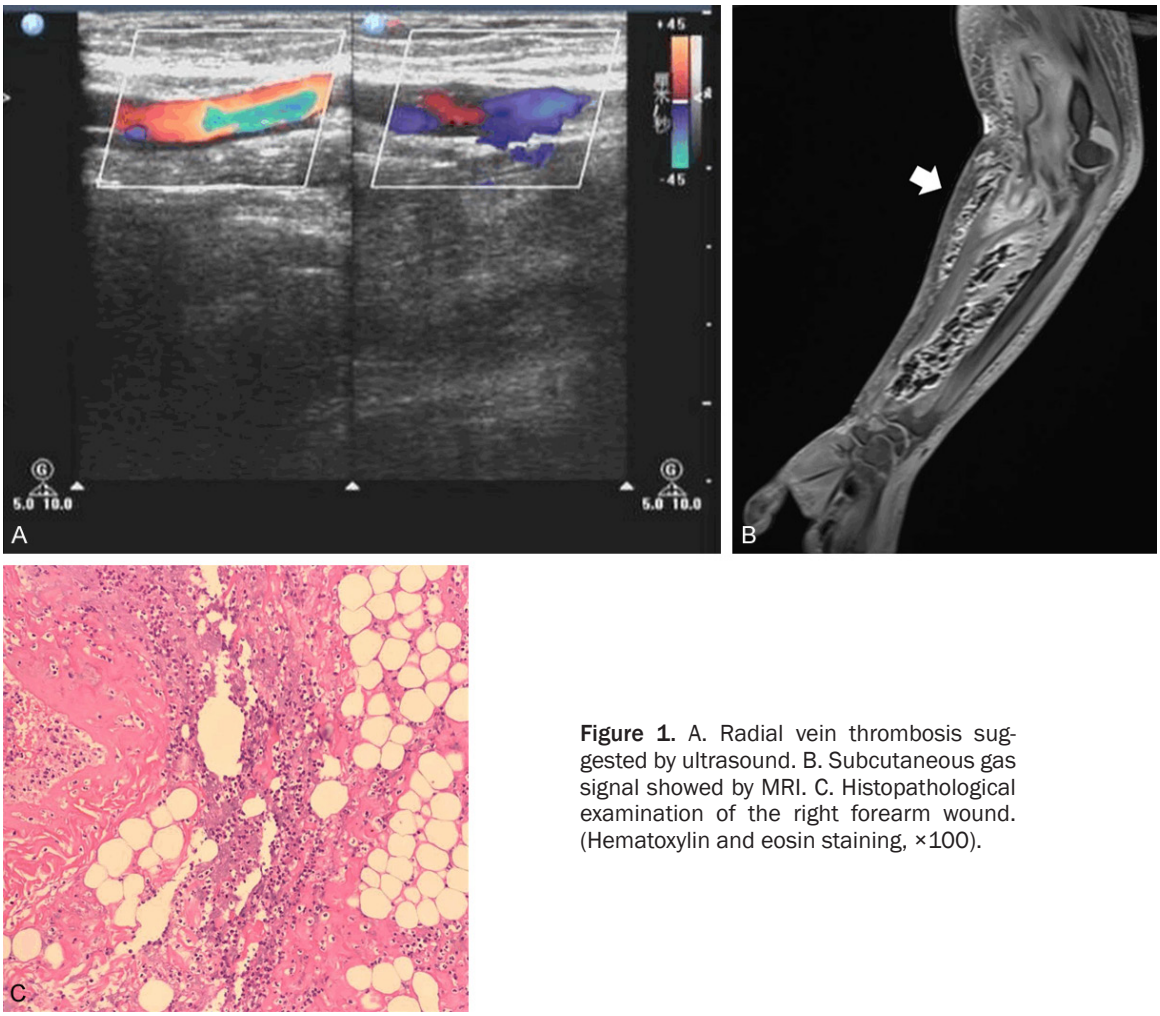

Figure 1. A. Radial vein thrombosis suggested by ultrasound. B. Subcutaneous gas signal showed by MRI. C. Histopathological examination of the right forearm wound. (Hematoxylin and eosin staining, ×100).

right forearm incurred swelling after a closed injury by bracelet compression one day prior. She had a 20-year history of poorly controlled diabetes and denied a medical history of liver or lung disease. On admission, symptoms included an altered mental state and swelling and warmness of the right forearm. Drowsiness was found during the night of admission. Laboratory tests revealed a blood glucose of 19.6 mmol/L, positive blood ketone body (KB) and an AG level of 25.27 on admission. pH of arterial blood was 7.285. Diagnosis of DKA was established. Insulin and other treatments were applied.

Erythema and extreme swelling soon presented at the forearm on day 1. Laboratory tests revealed the white blood cell (WBC) count was $16.93*10^9$/L. Also, at day 1, while there was a decreased glucose level there was a positive KB and lactic acid of 2.8 mmol/L. Closed infection was considered. Emergency ultrasound suggested radial vein thrombosis, and magnetic resonance imaging (MRI) revealed a subcutaneous gas signal (**Figure 1A** and **1B**). Urgent surgical intervention was performed at once and necrotizing fascia and muscle were found. Histopathological examination confirmed diagnosis of necrotizing fasciitis and blood and pus bacteriology suggested monomicrobial K. pneumoniae (**Figure 1C**). The patient was transferred into EICU and received broad-spectrum antimicrobials treatments with high-level life support.

Signs and symptoms of systematic infection intensified and an additional complete debridement was performed on day 3. Subsequent blood and pus bacteriology again showed the presence of monomicrobial K. pneumoniae. Sepsis shock developed according to laboratory tests on day 4. On day 4, pH of arterial blood

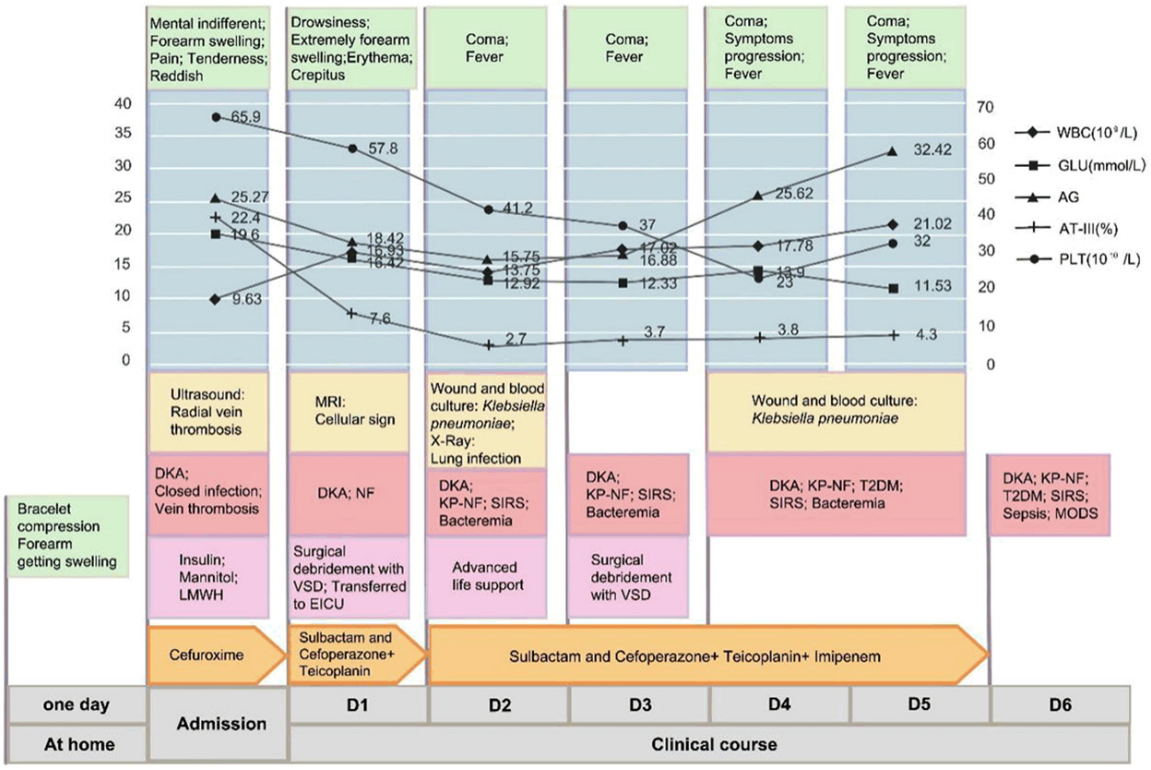

Figure 2. Summary of the clinical course.

was 7.205, lactic acid was 3.8 mmol/L, and KB was positive. Diagnosis of DIC was established on day 5, with aggravated infectious indicators and acidosis. Unfortunately, the family asked to transfer the patient home and she succumbed one day after discharge on day 6. A summary of the clinical course of this disease is illustrated in **Figure 2**.

Results and discussion

Monomicrobial KP-NF was first reported in 1996 and accounts for 16% of all NF, and has the highest mortality rate at 60% [7]. It is strongly associated with diabetes, and has a predilection for East Asian countries. Trauma is often not the main cause of KP-NF. Injuries to deep tissues and hematogenous infections makes KP-NF less identifiable at the early stages of infection [8]. Compared with other forms of NF, KP-NF presents a more severe and complicated progression with very rapid development in late stages of diabetic patients. As such, KP-NF is usually detected in the middle and late stages of pathological progression [9]. Urgent interventions with broad-spectrum antimicrobials therapy according to current clinical guidelines holds the key for recovery during a KP-NF infection.

Despite appropriate treatment, the patient in this case progressed rapidly in early stages compared to the typical time interval. The patient deteriorated systemically in only 5.45 days, despite timely management being performed [5, 10]. This may be due to mutual progression of DKA, a serious metabolic disorder complication of diabetes.

Infection is a most common cause of DKA in diabetic patients. In our case, DKA induced by uncontrolled diabetes and infection may have accelerated vascular thrombosis and lead to trafficking of *K. pneumoniae* to the injured site. Both hypercoagulable and hyperglycemic states involve an increased activation of factor VIII and fibrinogen, which are responsible for the progression of blood coagulation [11-13]. Metabolic and pro-coagulant factor disorders caused by DKA disrupt the basal hemostatic mechanisms and can promote a pro-thrombotic state [14]. The accumulation of organisms results in local infection and stimulates vascular thrombosis by aggregating platelet-leuko-

Table 1. Summary of recent KP-NF cases with treatment strategies and outcomes

Age, sex	Diabetes	Liver disorders	Sight affected	Surgery done	Hospital stays	Outcome	District	Reference no.
84, M	+	-	Right upper limb	Fasciotomy	8 days	Death	Taiwan	[10]
90, F	+	-	Left lower limb	Amputation + debridement	16 days	Death		
58, M	+	+	Left lower limb	Fasciotomy + debridement	59 days	Death		
49, M	+	+	Right lower limb	Fasciotomy + skin graft	44 days	Survived		
55, M	+	+	Right upper limb	Fasciotomy + skin graft	26 days	Survived		
29, M	+	+	Right lower limb	Fasciectomy + debridement	40 days	Survived	Taiwan	[21]
75, M	+	-	Left upper limb	Fasciotomy	NA	NA	Taiwan	[22]
75, M	+	+	Left upper limb	Fasciotomy	50 days	Survived	Taiwan	[23]
53, F	+	+	Left upper eyelid	Debridement + flap transplantation	90 days	Survived	South Korea	[24]
48, M	+	-	Left foot and eye	Amputation + debridement	18 days	Survived	Philippines	[25]

cytes and activating clotting mechanisms. This can induce ischemic destruction of soft tissues in early stages of KP-NF [15, 16]. Additionally, hyperglycemia and acidosis also contribute to impaired blood flow and thrombogenesis [17].

Metabolic disorders caused by DKA result in the release of pro-inflammatory factors, leading to further disorders of the immune system and may induce septic shock [18]. Although timely insulin therapy reduced KB in this case, metabolic acidosis induced by DKA was aggravated and an increased lactic acid level was revealed. DKA caused by infection can also aggravate MODS through rapidly progressing sepsis and the systemic inflammatory response syndrome (SIRS), resulting in a poor prognosis. A study from Taiwan, China showed that infection-precipitated DKA in septic patients can quickly induce AKI and cause MODS [18].

There have been no cases reported of KP-NF complicated with DKA to provide management and treatment guidance. Herein is reviewed KP-NF cases from the most recent three years with treatment strategies and outcomes in **Table 1**. A case of *Streptococcus* necrotizing fasciitis precipitating a DKA coma was reported in 1986 and the patient recovered after 80 days of hospitalization and a large removal of soft tissues of the face [19]. A case of cervical necrotizing fasciitis with diabetic ketoacidosis was reported in 2013 [20]. In this case, NF was complicated and intensified by DKA and *Streptococcus sp.* and *Candida albicans* were isolated. The patient underwent aggressive surgical tissue removal and was discharged on day 75.

According to the literature review of recent cases, although limb amputation should be avoided whenever possible, aggressive surgical removals and even amputation surgeries are necessary to preserve life in some NF patients with DKA [19-21]. KP-NF cases in diabetic patients are more likely to receive limb amputation for infection control, which may actually decrease mortality rates according to current research [7]. It takes less time for the condition of patients with DKA to degrade clinically, as their wounds are difficult to treat with less intensive infection control. As such, amputation may happen more quickly in the infection progression, with a resultant increase in survival rates.

In summary, DKA may accelerate and aggravate the progression of KP-NF in early stages, which may imply a fulminate course and extremely poor prognosis. Control of DKA and an urgent aggressive debridement may be the key approach to improve prognosis. Clinicians should be particularly aware of the latent mutual progression between these two rare and fatal diseases.

Conclusion

In conclusion, KP-NF is a rare and fatal infectious disease that is strongly associated with diabetes in East Asia. DKA as an extreme and fatal metabolic state of uncontrolled diabetes and may be responsible for a rapid progression in the early stages of KP-NF. DKA induced in early stages of KP-NF may trigger systematic sepsis shock and DIC, which results in a subsequently diminished outcome. Control of DKA and aggressive surgical intervention may be key approaches in securing a positive prognosis. However, more explicit evidence and experience is needed to elucidate the most efficacious therapies for this combined condition.

Clinicians, especially in East Asia, should pay particular attention to the interactions between these two rare but fatal diseases.

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Disclosure of conflict of interest

None.

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