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## Postirradiation *Klebsiella pneumoniae*-Associated Necrotizing Fasciitis in the Western Hemisphere: A Rare but Life-Threatening Clinical Entity

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### Abstract

Necrotizing fasciitis (NF) caused by *Klebsiella* spp. is a unique entity, particularly, in Asia, where virulent strains of *Klebsiella* predominate. It is now clear that *Klebsiella* spp. are capable of causing NF either isolated or in the context of disseminated disease. We present a unique case of NF caused by *Klebsiella pneumoniae* in the Western hemisphere after radiotherapy in a hospitalized patient with significant comorbidities. Physicians should be aware of nosocomially acquired *K. pneumoniae* fasciitis after radiotherapy in the setting of chronic comorbidities, such as diabetes and malignancy. Early diagnosis, surgical intervention, and appropriate empirical antibiotics are essential for a favorable outcome in such rare but life-threatening cases of NF.

### Keywords

Necrotizing fasciitis; *Klebsiella pneumoniae*; Radiotherapy; Soft tissue infection; Gram negative bacteria

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Necrotizing fasciitis (NF) is a life-threatening soft tissue infection.<sup>1–3</sup> Although single-organism NF is usually caused by invasive streptococci,<sup>1–3</sup> other organisms have been implicated in the pathogenesis of this entity,<sup>3,4</sup> including *Klebsiella* spp. NF is increasingly recognized as a potential manifestation of disseminated *Klebsiella* infections and is strongly associated with predisposing conditions, such as diabetes mellitus.<sup>5,6</sup> Awareness of the potential for multiorgan involvement should prompt a thorough investigation of patients for metastatic foci of infection. We describe a unique case of NF caused by *Klebsiella* spp. in a patient who had recently received radiotherapy and we summarize the available literature.

### CASE REPORT

We describe the case of a 77-year-old man with a medical history significant for adult onset diabetes mellitus for 30 years, metastatic follicular thyroid cancer with metastasis to the spine, and a pathologic fracture of the left hip necessitating a total hip replacement 1 year

ago. He had received treatment with radioactive iodine 4 months before admission. He was a native American who lived in Massachusetts and had never traveled outside the United States. Because of worsening back and left hip pain, he was admitted to the hospital, and on the eighth day of hospitalization he was initiated on radiation therapy targeting the left hip and lumbar spine with significant improvement of his pain. On the 15th day of hospitalization, he developed hypotension, fever, and signs of septic shock and was transferred to the intensive care unit. He required inotropic support with vasopressors and was initially administered intravenous vancomycin and levofloxacin. The following day he was noted to have erythema and increased warmth of both thighs. At that time, his temperature was 38°C and there was erythema and tenderness over the left inner thigh and right lateral thigh. Pertinent laboratory data included a white cell count of  $2.8 \times 10^9/L$ , lactic acid of 5.4 mg/dL, and a serum creatinine of 1.6 mg/dL. His antimicrobials were changed to clindamycin, vancomycin, and cefepime for rapidly progressive cellulitis and concern for NF. He was taken to the operating room for fasciotomy that revealed NF and wide debridement of both thighs was performed. *Klebsiella pneumoniae* sensitive to all antimicrobials tested was isolated from blood, urine, and tissue cultures from the left thigh. The patient continued to deteriorate, but the family decided not to proceed with another surgery and to keep the patient comfortable. He died on the 18th day of hospitalization.

## DISCUSSION

### Necrotizing Fasciitis

NF is a life-threatening soft tissue infection that involves subcutaneous tissue, superficial fascia and results in rapidly spreading necrosis of the skin and underlying structures.<sup>7</sup> Despite advances in the management of this entity, mortality remains high.<sup>8</sup> In most NF cases, the causative organism cannot be isolated and, although polymicrobial infection is more common, single bacterial species can be isolated in up to 29% of culture-positive wounds.<sup>9</sup> Gram-negative enteric bacilli and Gram-positive cocci have been identified in the majority of patients.<sup>9–12</sup>

Generally, NF is a synergistic polymicrobial infection.<sup>3</sup> Although most reported cases of NF occur in a community-acquired setting,<sup>13</sup> NF can result from nosocomial infection and can be a devastating complication for patients who have undergone invasive procedures or recent surgery, especially in patients with morbid obesity or who have undergone chemotherapy. Postprocedural NF tends to be polymicrobial, and the diversity of organisms is probably the result of manipulation of areas that are contaminated (eg, gastrointestinal tract).<sup>14</sup> However, the epidemiology of NF varies according to geographical settings and the affected host. In 2 studies of NF in cirrhotic patients in Taiwan, NF was mainly monomicrobial, often caused by Gram-negative bacilli,<sup>15,16</sup> which is probably related to the variable distribution of these Gram-negative pathogens in aquatic environments in Taiwan and also to the predisposition of this subgroup of patients to infections associated with these pathogens.

Predisposing factors for the development of NF caused by *Streptococcus pyogenes* include penetrating injuries, blunt trauma, minor cuts, burns, surgical procedures, varicella infection, and muscle strain.<sup>17,18</sup> NF may also occur as a nosocomial or postoperative infection.<sup>19</sup> It may also occur spontaneously in immunocompromised patients<sup>7</sup> and can also affect

previously healthy and young persons. Primary or idiopathic NF is a different clinical entity characterized by the absence of an external port of entry of bacteria. This type of infection occurs in patients with chronic debilitating diseases and has been postulated to be the result of either hematogenous spread of bacteria or bacterial invasion through small unrecognized breaks in the epidermis.<sup>20</sup> Diabetes mellitus is the most common underlying disease<sup>7,21</sup> associated with the development of NF, whereas other systemic host debilitating disorders include advanced age, peripheral vascular disease, cancer, human immunodeficiency virus, malnutrition, alcohol abuse, or obesity.<sup>7,11,21–23</sup> NF has also been reported in renal transplant patients who receive immunosuppressive agents.<sup>24</sup> Patients with cirrhosis are more susceptible to necrotizing soft tissue infections caused by Gram-negative pathogens.<sup>15</sup> Mortality seems to be higher with comorbidities. In 1 study, mortality was significantly increased in patients with 2 or more comorbidities, such as diabetes mellitus combined with liver cirrhosis.<sup>25</sup>

### Radiotherapy as a Risk Factor for NF

Acute infections secondary to mucositis during concurrent chemotherapy and radiation are common.<sup>26</sup> Potential causes for the increased incidence of infectious complications are related to alterations on the mucosa and soft tissue, lymphatic vascular injury leading to lymphedema, vascular damage caused by radiation with impairment of oxygen delivery, and immunologic function. Thus, the inflammatory response and the reparative process of local tissues are impaired after radiotherapy.<sup>27</sup> Thus, bacteria introduced into these tissues may lead to an aggressive soft tissue infection.

Daly et al<sup>28</sup> reported 5 patients with slightly progressive mixed polymicrobial necrotic wound infections of the subcutaneous tissue and skin around surgical incisions that traversed fields of pelvic irradiation. The authors concluded that the local obliterative endarteritis and poor collagen formation caused by radiation favor the development and spread of necrotizing infection.<sup>28</sup> Only 8 cases reports of NF have described the association of this infection with NF (Table 1).<sup>29–34</sup> Maluf et al<sup>29</sup> were the first to report the potential association between chemoradiation therapy and NF caused by *S. pyogenes*. Most authors suggested that radiation therapy could be a risk factor for NF in combination with other risk factors, such as diabetes,<sup>31</sup> chemotherapy,<sup>30</sup> advanced age, vascular disease, and malignancy<sup>31</sup> and that the cumulative effects of these risk factors could favor the development, progression, and persistence of NF.<sup>31</sup> Radiation-induced noninfectious myofasciitis has also been described in the literature.<sup>35,36</sup> Our patient is the ninth case described and also had advanced age and significant comorbidities, such as diabetes mellitus, vascular disease, and malignancy, as risk factors. Although more data is necessary, radiotherapy seems to be a risk factor for the development of NF.

### K. pneumoniae Fasciitis

*Klebsiella* spp. are opportunistic human pathogens that cause severe diseases, such as septicemia, pneumonia, urinary tract infection, and soft tissue infection.<sup>37</sup> Although *K. pneumoniae* is a common co-pathogen in patients with polymicrobial NF,<sup>38–40</sup> monomicrobial NF caused by *Klebsiella* spp. is very rare. All previous cases included in our literature review were found using a Pubmed search (1980 to November, 2008) of the

English-language medical literature applying the term “*Klebsiella* fasciitis.” The references cited in these articles were examined to identify additional reports. We identified 38 cases of *K. pneumoniae* fasciitis in the literature.<sup>5,6,25,39,41–52</sup> One case of fasciitis caused by *K. oxytoca*<sup>53</sup> and 1 case of NF caused by *K. aeruginosa*<sup>52</sup> have also been reported. In a large series in China, *K. pneumoniae* was the most common pathogen isolated,<sup>25</sup> unlike the previous series, in which *Streptococcus* was the prevalent pathogen.<sup>11</sup> *K. pneumoniae* was the most common Gram-negative pathogen identified as cause of monomicrobial NF with 13 of 59 cases (22%).<sup>25</sup> In another study of patients with NF, *K. pneumoniae* (16%; 4 of 25 patients) and Group A streptococci (16%) were the most common microorganisms identified in microbiologic cultures.<sup>46</sup>

Most of the 38 cases occurred in Asian countries, with 14 (36.8%) cases being reported in China,<sup>25,44</sup> 8 cases (21%) in Taiwan,<sup>5,39,42,49</sup> 5 (13.2%) cases in Turkey,<sup>43,46</sup> 4 cases (10.5%) in Singapore,<sup>51</sup> 2 cases in Malaysia,<sup>47,50</sup> 1 case in Saudi Arabia,<sup>52</sup> 1 case in Hong Kong,<sup>41</sup> and 1 case in Japan.<sup>45</sup> One case in Canada occurred in a native of India who had recently traveled to Singapore.<sup>6</sup> Only 1 case has been reported in the United States of 1 native of Cambodia who had recently traveled to Cambodia.<sup>48</sup> We report the first case, to our knowledge, of *K. pneumoniae* causing NF in a native American who did not have any travel history.

In Table 2, we present data on 15 cases of monomicrobial NF caused by *Klebsiella* spp., in which the organism was cultured from tissue specimens taken during surgical debridement and in which details on clinical presentation and the treatment administered were available.<sup>5,6,41–43,47–52</sup>

With the exception of a 10-day-old neonatal infant in Turkey,<sup>43</sup> the age of 15 patients with NF caused by *K. pneumoniae*, where data were available, varied from 7 to 76 years with a median age of 52 years.<sup>5,6,42–44,47–52</sup> Eleven of 15 (73.3%) of these patients<sup>6,41–44,47–49,52</sup> were men with 4 of 15 (26.6%) being women.<sup>5,45,50,51</sup>

Significant comorbidities were present in these patients with *K. pneumoniae* fasciitis. Twelve (80%) of these patients had diabetes,<sup>5,6,41,42,44,49–52</sup> 3 patients (20%) had cirrhosis,<sup>41,48,51</sup> 1 had chronic renal failure,<sup>52</sup> 1 had malignancy,<sup>47</sup> and 1 had no identified comorbidity,<sup>43</sup> whereas 2 comorbidities were noticed in 3 patients.<sup>41,51,52</sup> In the large series of *K. pneumoniae* fasciitis from China, all patients had underlying disease, including diabetes mellitus in 13 patients and both diabetes and cirrhosis in 3 patients.<sup>25</sup> NF was not the initial presentation in 2 of these diabetic patients who had metastatic infection with *K. pneumoniae* bacteremia.<sup>25</sup> One of the patients had in addition acute pyelonephritis and the other had a liver abscess. Data from the small number of reported cases, thus, suggest that monomicrobial *K. pneumoniae* is strongly associated with diabetes mellitus and chronic liver disease. Most of the previously reported cases of *Klebsiella* NF were associated with other septic foci of infection, commonly liver abscesses, urinary tract infections, and endogenous endophthalmitis.<sup>5,6,41</sup> When *K. pneumoniae* bacteremia occurs in these patients, clinicians should be vigilant about metastatic soft tissue infections. In 10 cases,<sup>5,6,41,44,48,51</sup> at least one other organ was involved, ie, liver,<sup>5,6,44,51</sup> eyes,<sup>5</sup> urinary tract,<sup>49,51</sup> kidneys,<sup>5,51</sup> pancreas,<sup>5</sup> peritoneum,<sup>41</sup> and knee.<sup>48</sup> Consistent with the literature, the commonest site of

associated pathology was the liver (5 cases, 50%) followed by the urinary tract in 4 cases (40%).<sup>49,51</sup>

In our review of 15 cases of *K. pneumoniae* with available data, risk factors that could be related with the development of NF caused by this pathogen were identified in 9 patients (60%). These included recent travel to Asia,<sup>6,48</sup> previous infectious process due to *K. pneumoniae*, such as emphysematous cystitis,<sup>49</sup> spontaneous bacterial peritonitis,<sup>41</sup> and liver abscess,<sup>44</sup> previous worsening of edema in the area of NF,<sup>50,51</sup> biopsy,<sup>47</sup> or repeated manipulation near the site of NF.<sup>43</sup> No obvious risk factor was identified in 6 cases (40%).<sup>5,42,51,52</sup> Bacteremia was documented in 11 of 15 cases (73.3%).<sup>5,6,41,44,47–49,51</sup>

Capsular serotyping was performed in only 2 of the previously reported cases of *Klebsiella* spp. Fasciitis, and, in that case, the capsular serotype was K1.<sup>5,48</sup> Virulent strains of *K. pneumoniae* (K1 and K2 serotype) seem to be predominant in the syndrome of disseminated *Klebsiella* infection with multiple metastatic septic foci in the East.<sup>54</sup> One study demonstrated that cluster A plays an important role in the high incidence of *K. pneumoniae* liver abscess in Taiwan and metastatic infections, including NF.<sup>55</sup> Pulsed-field gel electrophoresis, a useful method for the detection of genetic diversity, was performed in only 1 case that revealed that bacterial translocation from the gastrointestinal tract of *K. oxytoca* caused a fatal episode of NF.<sup>53</sup>

In our review of 15 cases of patients with NF, data regarding mortality were available in 13 cases, whereas in 2 cases no data were reported.<sup>25,47</sup> Four of 13 (30.8%) patients died, <sup>41,42,48,51</sup> whereas 9 of 13 (69.2%) survived.<sup>5,6,43,44,49–52</sup> One patient with *K. oxytoca* NF also died.<sup>53</sup> A review of *K. pneumoniae* fasciitis by Wong et al<sup>51</sup> showed a mortality rate of 18%, with almost all patients requiring extensive debridement.

The clinical features of NF caused by *Klebsiella* spp. are similar to those of NF caused by other organisms.<sup>1–3</sup> In NF caused by other organisms, the initiating event is usually direct inoculation from a superficial site.<sup>1–3</sup> However, *Klebsiella* spp. have the unique potential for multifocal infection and may cause NF by either direct entry from undetected trauma of the affected site or, more commonly, hematogenous spread from other septic foci. Hematogenous spread from another site in our case is supported by the simultaneous multifocal NF (eg, both lower limbs) similar to other cases<sup>6,41</sup> and the presence of a separate septic focus (urinary tract infection). Our patient had bacteremia from *K. pneumoniae* and it is unclear if the urinary tract infection preceded the fasciitis or vice versa. In 1 report, 2 of 4 patients who had bacteremia developed urinary tract infections with a *Klebsiella* strain after the onset of fasciitis.<sup>51</sup> Regardless of the mode of entry, once established, NF caused by *Klebsiella* spp. has a propensity to spread and to involve other organ systems and this underscores the invasive character of virulent strains of *Klebsiella* and the propensity for multiorgan involvement, once a septic site has been established.

Another possible pathogenetic mechanism of *Klebsiella* spp. NF in humans is via bacterial translocation that might explain how enteric bacteria become the source of infection in other organs, such as in soft tissues.<sup>53</sup> In 1 study of patients with cirrhosis and NF, the authors suggested that Gram-negative bacteria in the intestines translocate to the bloodstream and

then cause soft tissue infections in unilateral or bilateral extremities. In this study, involvement of 2 extremities was noted in 13 (28%) patients and concurrent Gram-negative bacteremia in 17 (53%) of 32 patients with Gram-negative bacillary NF. Our patient developed bilateral NF in the lower extremities without any obvious portal of entry. This could be related to the previous radiotherapy, which had been initiated during hospitalization and could have caused alterations on the mucosa of the intestine or urinary tract, thus, facilitating bacteremia and bacterial translocation.

Regarding antimicrobial susceptibility patterns, in our review of cases with available data, *Klebsiella* strains causing NF were susceptible to all cephalosporins and aminoglycosides in 8 cases.<sup>6,41,42,48,51,52</sup> Multiple antimicrobial resistance was detected in only 1 case.<sup>47</sup> In 6 cases, no data on antimicrobial susceptibility were available.<sup>5,43,44,49,50</sup> An antibiogram characteristic of invasive strains of *K. pneumoniae* in the Orient has been described and includes resistance to ampicillin but susceptibility to other antibiotics, including all cephalosporins and aminoglycosides tested (studies from Singapore, Taiwan, China, and Japan).<sup>42</sup>

Surgical debridement and fasciotomy are the cornerstones of NF treatment and are associated with improved survival, but the role of appropriate antimicrobial therapy should not be ignored.<sup>2,56</sup> The type of antimicrobial regimen and the duration of antibiotic treatment were not specified in most of the reports reviewed herein. Data regarding antimicrobial treatment of 12 cases of *K. pneumoniae* fasciitis indicated that third-generation cephalosporin was chosen as treatment in 9 cases,<sup>5,6,43,47,48,51,52</sup> parenteral extended-spectrum penicillin with beta-lactamase inhibitor was used in 2 cases,<sup>41,43</sup> and aminoglycosides were used in 7 cases (Table 1).<sup>5,42,43,47,51</sup> The antibiotic regimen was not specified in 3 cases.<sup>44,49,50</sup> The combination antimicrobial regimen that was most widely used included parenteral cephalosporin in combination with an aminoglycoside in 6 cases.<sup>5,42,43,47,51</sup> In 3 patients, who survived, oral cefuroxime was given for 2 to 3 more weeks after discharge from the hospital.<sup>51,52</sup> Surprisingly, no data on quinolone use were reported. Accurate early diagnosis and surgical intervention and appropriate empirical antibiotics according to the antibiogram (because resistance patterns of *Klebsiella* spp. evolved and multidrug-resistant strains emerged during the last few years) are essential for a favorable outcome in cases of NF.

## CONCLUSION

The patient described here represents a unique presentation of NF caused by *K. pneumoniae* in the Western hemisphere. Five cases of polymicrobial *K. pneumoniae* fasciitis have been described in the United States.<sup>14,57</sup> There is only 1 case of monomicrobial *K. pneumoniae* fasciitis described in the United States in a native Cambodian who had a recent travel to Cambodia.<sup>48</sup> The current report is the first case of monomicrobial *K. pneumoniae* fasciitis described in the Western hemisphere associated with radiotherapy in a native American who had never traveled to Asia, where these infections are becoming increasingly common. Patient developed this infection after 2 weeks of hospitalization and this represents a nosocomially acquired *K. pneumoniae* fasciitis. The bilateral NF in the lower limbs could be spontaneous or more likely a result of metastatic seeding during bacteremia. Data on the



seroepidemiology of *Klebsiella* in the United States are largely historical and the prevalence of the K1 capsular serotype in *Klebsiella* infections in the United States is not known.<sup>48</sup> Physicians should be aware of the risk of aggressive *K. pneumoniae* soft tissue infections in patients presenting with muscle pain, especially in the setting of a serious chronic comorbidity. This case of NF from *K. pneumoniae* in the Western hemisphere should prompt a renewed interest in the seroepidemiology of this potentially deadly pathogen.

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TABLE 1.

Cases of necrotizing fasciitis associated with external beam radiation therapy

Author	Year	Country	Location (necrotizing fasciitis within the irradiation fields)	Age(yr)	Sex	Risk factors	Time period between radiation and onset of fasciitis	Comorbidities	Microbiology (tissue culture)	Outcome
Maluf et al <sup>29</sup>	2007	Brazil	Neck	64	M	None	9 mo	Squamous cell carcinoma of the oropharynx chemotherapy and radiotherapy 9 mpreviously	<i>Streptococcus pyogenes</i>	Survived
Miyagawa et al <sup>30</sup>	2005	Japan	Penis and left upper limb	60	M	Mild and persistent edema of the penile and scrotal skin since radiotherapy	7 yr	Testicular cancer highdose chemotherapy (HDCT) andradiotherapy 7 yr previously	<i>S. pyogenes</i>	Died
Mortimore and Thorp <sup>32</sup>	1998	South Africa	Neck and chest	56	M	None	6 yr	Squamous cell carcinoma of the mouth	Group A p-haemolytic <i>Streptococcus</i>	Survived
Mortimore and Thorp <sup>32</sup>	1998	South Africa	Neck	52	M	Osteoradionecrosis of the mastoid portion of the temporal bone for 10 yr before presentation	10 yr	Squamous cell carcinoma of tongue, alcohol abuse	<i>Streptococcus milleri</i> and numerous anaerobic bacteria	Survived
Livengood et al <sup>31</sup>	1991	USA	Pelvis, inguinal area	51	F	Total abdominal hysterectomy and bilateral salpingo-oophorectomy36 d before onset of fasciitis	56 d	Obesity, diabetes, stage IV uterine mullerian tumor, radiotherapy	<i>Proteus mirabilis</i> and numerous anaerobic bacteria	Died
Livengood et al <sup>31</sup>	1991	USA	Pelvis	68	F	Radiation proctosigmoiditis	12 mo	Diabetes, stage III adenocarcinoma of cervix, advanced age	<i>Escherichia coli</i> , <i>Clostridium</i> spp.	Died
Husseinzadeh et al <sup>33</sup>	1984	USA	Buttock, pelvis	25	F	Radiation dermatitis	10 d	Invasive cervical cancer, radiotherapy, methotrexate	Anaerobic bacteria from wound culture	Survived
Krespi et al <sup>34</sup>	1981	USA	Neck	60	M	Osteoradionecrosis of the temporal bone	9 mo	Squamous cell carcinoma of the middle ear, radiotherapy 9 mpreviously	<i>P. mirabilis</i> , <i>Enterococcus</i> , and <i>E. coli</i>	Survived

**TABLE 2.** Cases of monomicrobial necrotizing fasciitis caused by *Klebsiella pneumoniae*, where detailed data were available

Author	Year	Country	Location	Age	Sex	Risk factors	Comorbidities	Microbiology	Management	Outcome
Oishi et al <sup>53</sup>	2008	Japan	Lower extremities	73	M	Ingestion of raw fish	Hepatocellular cell carcinoma, liver cirrhosis, and chronic renal failure	<i>Klebsiella oxytoca</i>	Palliative care	Died
Kohler et al <sup>48</sup>	2007	USA	Left groin, thigh, and knee	50	M	Cambodian, recent travel to Cambodia 6 m previously	Chronic hepatitis B infection, advanced cirrhosis, emphysema	Wound, blood culture, grew <i>K. pneumoniae</i> sensitive to cephalosporins, gentamicin identified as having KI capsular antigen	Ceftazidime, meropenem	Died
Chen et al <sup>49</sup>	2006	Taiwan	Iliac and gluteal muscles	74	M	Complicated emphysematous cystitis	Diabetes mellitus	<i>K. pneumoniae</i> was cultured from blood, urine, and pus	Intravenous antibiotics and surgical debridement of his left hip	Survived
Mazita et al <sup>50</sup>	2005	Malaysia	Neck	65	F	Indian, 1-mo history of increased neck swelling	Diabetes mellitus	<i>Klebsiella</i> spp. (tissue)	Surgical debridement, wide-spectrum antibiotics	Survived
Wong et al <sup>51</sup>	2004	Singapore	Left neck, chest wall, and urinary tract	43	M	None	Diabetes mellitus	<i>Klebsiella</i> strain susceptible to ceftriaxone, cephalixin, and gentamicin was isolated from blood, tissue, and fluid cultures and, subsequently, from urine, methicillin-resistant <i>Staphylococcus aureus</i> from tissue cultures	Two surgical debridements, parenteral ceftriaxone, metronidazole, and vancomycin, followed by oral cefturoxime (74 d)	Survived
Wong et al <sup>51</sup>	2004	Singapore	Left buttock and thigh and urinary tract	40	M	None	Diabetes mellitus	Tissue, blood, and urine cultures grew a <i>Klebsiella</i> strain susceptible to ceftriaxone, cephalixin, and gentamicin	Two debridements, ceftriaxone and gentamicin for 32 d, followed by oral cefturoxime for a total of 52 d	Survived
Wong et al <sup>51</sup>	2004	Singapore	Right popliteal fossa and right lower limb, right lobe of liver, and right kidney	56	M	Pain and swelling of right knee and calf for 2 d before admission	Diabetes mellitus, chronic liver disease, hepatitis B	Tissue, blood, and urine culture <i>Klebsiella</i> strain susceptible to ceftriaxone, cephalixin, and gentamicin	Two surgical debridements, ceftriaxone, gentamicin, and metronidazole for a total of 152 d	Survived
Wong et al <sup>51</sup>	2004	Singapore	Right posterior thigh	76	F	None	Diabetes mellitus	Tissue and blood cultures both grew a <i>Klebsiella</i> strain that was susceptible to ceftriaxone, cephalixin, and gentamicin	Surgical debridement. Parenteral penicillin, cloxacillin, and gentamicin (patient)	Died, toxic shock syndrome developed septic

Author	Year	Country	Location	Age	Sex	Risk factors	Comorbidities	Microbiology	Management	Outcome
Al-Ammar andMaqbool <sup>52</sup>	2004	Saudi Arabia	Left face and cervical area	50	M	NR	Diabetes mellitus, chronic renal failure	Tissue culture revealed a heavy growth of <i>Klebsiella aerogenosa</i> sensitive to many antimicrobial agents, including ceftriaxone and cefuroxime	succumbed within 48 hr) Two surgical debridements. Parenteral ceftriaxone, clindamycin for 3 wk, and oral cefuroxime for 10 d	shock,ARF and DIC Survived with residual permanent facial paralysis
Parasakthi et al <sup>47</sup>	2000	Malaysia	Perineum	7	M	Testicular biopsy	Acute myelogenous leukemia	Multidrug-resistant <i>K.pneumoniae</i> from blood and wound culture resistant to ceftazidime, sensitive to imipenem and ciprofloxacin, and confirmed to be extended-spectrum beta-lactamase producers	Debridement, ceftazidime, and amikacin	NR
Ho et al <sup>41</sup>	2000	Hong Kong	Both lower limbs, spontaneous bacterial peritonitis of ascitic fluid	52	M	Spontaneous bacterial peritonitis 4 d before admission	Diabetes mellitus, liver cirrhosis	Blood cultures, tissue cultures from the lower limb grew <i>K.pneumoniae</i> that was susceptible to ceftazidime, cefoperazone/sulbactam, amoxicillin/clavulanate, and ofloxacin	Surgical debridement, amoxicillin/clavulanate, and ofloxacin	Died
Hu et al <sup>5</sup>	1999	Taiwan	Left leg, left eye, abscesses in the liver, both kidneys and pancreas	71	F	None	Diabetes mellitus	<i>K. pneumoniae</i> tissue culture from the lower limb and pus from the liver abscess. The two isolates belonged to capsular serotype K1	Multiple debridements of the lower limb and evisceration of the left eye, ceftriaxone	Survived
Hu et al <sup>5</sup>	1999	Taiwan	Left lower limb, liver abscesses	40	M	None	Diabetes mellitus	<i>K. pneumoniae</i> tissue cultures of the left lower limb and bloodcultures	Cefazolin and gentamicin (37 d)	Survived
Dylewski andDylewski <sup>6</sup>	1998	Canada	Both lower limbs and liver abscess	47	M	Native of India, sailor, his ship with recent stops in Singapore, South Africa, and Morocco	Diabetes mellitus	<i>K. pneumoniae</i> tissue cultures from the left and right lower limb, pus from liver abscess (resistant to cephalothin but susceptible to ceftriaxone and ciprofloxacin) and blood cultures	Two surgical debridements, ciprofloxacin, ceftriaxone	Survived
Wang et al <sup>42</sup>	1998	Taiwan	Right leg	NR	NR	None	Diabetes mellitus	<i>K pneumoniae</i> resistant to ampicillin and ticarcillin/carbenicillin and susceptible to all other antibiotics	Surgical debridement, cefazolin, gentamicin	Died

Author	Year	Country	Location	Age	Sex	Risk factors	Comorbidities	Microbiology	Management	Outcome
Ozkan et al <sup>43</sup>	1997	Turkey	Perianal region	10 d	M	Repeated rectal temperature measurements	None	<i>K. pneumoniae</i> tissue culture from perianal area or wound. Negative blood cultures	Ampicillin-sulbactam, ceftazidime followed by imipenem and netilmicin (2 wk). Surgical debridement	Survived
Chou and Kou <sup>44</sup>	1996	China	Thigh	60	M	Liver abscess	Diabetes mellitus	<i>K. pneumoniae</i> liver aspirate, blood cultures	NR	Survived