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【 CASE REPORT 】

Emphysematous Osteomyelitis of the Spine: A Case Report and Literature Review

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Abstract:
Emphysematous osteomyelitis is a rare but potentially fatal infection. It is caused by gas-forming organisms and is characterized by the presence of intraosseous gas. A 75-year-old woman with untreated diabetes mellitus presented with difficulty in moving and anorexia. Laboratory studies revealed inflammation, a urinary infection, and diabetic ketoacidosis. *Klebsiella pneumoniae* was detected in both urine and blood cultures. Computed tomography and magnetic resonance imaging revealed emphysematous lesions in the paravertebral soft tissue, spinal canal, and iliopsoas muscle, with intraosseous gas at L1 and L2. These findings led to a diagnosis of emphysematous osteomyelitis. We herein review 35 reported cases of emphysematous osteomyelitis including our case.

Key words: diabetes mellitus, emphysematous osteomyelitis, gas-forming organisms, intraosseous gas, *Klebsiella pneumoniae*, review of the literature

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Introduction

Emphysematous osteomyelitis is a rare but serious condition that may also be fatal. The presence of intraosseous gas is generally reported after trauma, biopsy, penetrating wounds, and fractures (1). However, the formation of intraosseous gas in the extra-axial skeleton in the absence of the above conditions is suggestive of emphysematous osteomyelitis, especially in patients with infections due to gas-producing organisms (2, 3). Ram et al. first described intraosseous gas as a sign of emphysematous osteomyelitis in 1981, and to date, only 34 emphysematous osteomyelitis cases have been reported in the English literature (1-27). We herein describe the case of a 75-year-old woman with diabetes mellitus who presented with combined diabetic ketoacidosis and emphysematous osteomyelitis caused by *Klebsiella pneumoniae* due to thehematogenous spread of a urinary tract infection. In addition, we reviewed all the pertinent literature on emphysematous osteomyelitis and summarized the characteristics.

Case Report

A 75-year-old Japanese woman presented to the emergency department with a 5-day history of difficulty in moving and anorexia. She had no remarkable medical or family history, and was not taking any medication because she had never visited a medical facility. However, she had developed polydipsia and polyuria for the past 1 year. Her eyesight had worsened 2 months previously and she had simultaneously developed difficulty in walking, although she denied experiencing any trauma or pain.

On arrival, the patient was slightly drowsy, but her Glasgow Coma Score was 15 and body mass index was 25.1 kg/m^2. Physical examination revealed percussion pain in the vertebrae and dryness in the tongue and armpits, but no tenderness on her back, with stable vital signs (blood pressure=107/75 mmHg; pulse=95/min; body temperature=35.8℃; respiratory rate=18/min; oxygen saturation=100%). Laboratory studies indicated pyuria on urinalysis, leukocytosis (white blood cell count=21,500/μL), an increased level of C-reactive protein (22.20 mg/dL), hyperglycemia (glucose=800 mg/dL), and an increased level of glycated hemoglobin

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Table 1. Summary of Laboratory Data on Admission.

<Hematology>		<Blood chemistry>		<Venous blood gas>	
WBC	215×10^2 /μL	TP	6.3 g/dL	pH	7.239
Neutro	93.5 %	Alb	2.1 g/dL	pCO_2	35.7 mmHg
Lym	4.0 %	AST	27 U/L	HCO_3	14.9 mEq/L
Mono	2.4 %	ALT	31 U/L	Anion gap	31.9 mEq/L
RBC	421×10^4 /μL	LDH	336 U/L		
Hb	11.7 g/dL	γ-GTP	29 U/L	<Urinalysis>	
Ht	34.1 %	ALP	565 U/L	Protein	1+
Plt	15.2×10^4 /μL	T-Bil	0.6 mg/dL	Blood	2+
		BUN	84.7 mg/dL	Glucose	4+
<Coagulation profile>		Cre	1.94 mg/dL	Ketone	1+
PT%	90 %	Na	136 mEq/L	RBC	10-19 /HPF
PT-INR	1.05	K	4.2 mEq/L	WBC	>100 /HPF
APTT	29.2 s	Cl	91 mEq/L	Bacteria	3+
		Ca	8.5 mg/dL		
		Glu	800 mg/dL		
		HbA1c	15.0 %		
		plasma osmolality	316 mOsm/kg		
		Ketones	(+)		
		CRP	22.2 mg/dL		

WBC: white blood cells, Neutro: neutrophils, Lym: lymphocytes, Mono: monocytes, RBC: red blood cells, Hb: hemoglobin, Ht: hematocrit, Plt: platelet counts, PT %: prothrombin time %, PT-INR: prothrombin time-international normalized ratio, APTT: activated partial thromboplastin time, 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, Glu: glucose, CRP: c-reactive protein, pH: potential of hydrogen, pCO2: carbon dioxide partial pressure

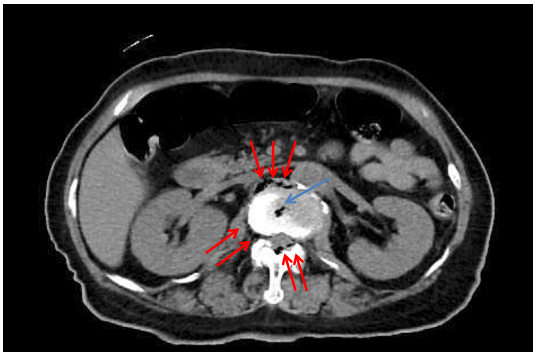

Figure 1. Computed tomography image of the abdomen showing emphysematous lesions around the spine (red arrows) as well as the presence of intraosseous air (blue arrows).

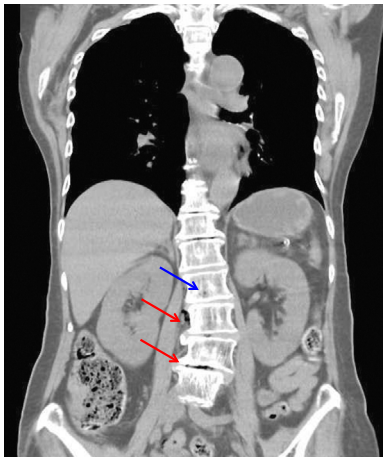

Figure 2. Computed tomography image of the abdomen showing emphysematous lesions around the spine (red arrows) as well as the presence of intraosseous gas (blue arrows).

(15.0%), which indicated uncontrolled diabetes mellitus. Other laboratory tests demonstrated ketones in the urine and serum, an effective plasma osmolality of 316 mOsm/kg, an arterial pH of 7.239, a serum bicarbonate level of 14.9 mEq/L, and an anion gap of 30.1 mEq/L (Table 1). We diagnosed a urinary infection due to neurogenic bladder dysfunction which was associated with diabetes mellitus and diabetic ketoacidosis.

Shortly after hospital admission, the patient developed a fever and thereafter became comatose. Urine and blood cultures were positive for *K. pneumoniae*, which both showed the same sensitivity. We did not perform a string test; therefore, we could not determine whether *K. pneumoniae* was hypervirulent. Head computed tomography (CT) revealed no bleeding, masses, or edema. A plain CT of the abdomen revealed emphysematous lesions in the paravertebral soft tissue, spinal canal, and iliopsoas muscle without abscess or fracture from Th12 to L2. In addition, the presence of intraosseous gas at L1 and L2 was observed, and a small amount of air in the disks from Th11 to L4 (Fig. 1, 2). We then conducted magnetic resonance imaging (MRI), where the

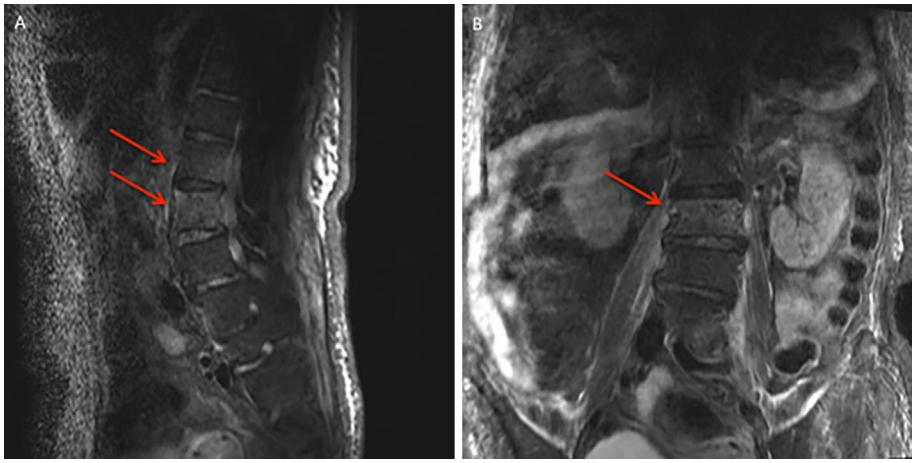

Figure 3. **A STIR sequence in the MRI image showing a high signal at L1 and L2: (A) Sagittal view. (B) Coronal view. STIR: short TI inversion recovery**

short TI inversion recovery (STIR) sequence demonstrated high signals at L1 and L2 (Fig. 3). The findings from a blood culture, CT, and MRI led to the diagnosis of emphysematous osteomyelitis. In addition, infective endocarditis was also suspected; however, the patient could not undergo transesophageal echocardiography due to her general poor condition. Transthoracic echocardiography demonstrated no vegetation or regurgitation.

Initially, the patient was admitted to the intensive care unit and treated for sepsis and diabetic ketoacidosis. A Foley catheter was inserted into her bladder and broad-spectrum antibiotics (meropenem) and intravenous fluid therapy were initiated. The patient's blood sugar level was strictly controlled with an insulin drip. However, the patient did not respond to these treatments. Blood culture tests were repeated but no bacteremia was detected. On day 4, we repeated the CT scan to check for any abscess, but none was detected. Surgical treatment was also considered, but it was not indicated because she did not have an abscess. The patient died 10 days after hospital admission due to multi-organ failure including disseminated intravascular coagulation.

Discussion

Emphysematous osteomyelitis should be considered as one of the possible diagnoses if intraosseous gas is detected, especially in the extra-axial skeleton (22). The differential diagnosis of intraosseous gas includes trauma, post-surgical change, lymphangiomatosis of the bone, degenerative disease, osteonecrosis, and neoplasm (19, 24). To date, there have only been 34 cases of emphysematous osteomyelitis reported in the English literature. We reviewed all 34 cases as well as our case (Table 2).

The characteristics these cases showed no sex deviation, with 17 of the 35 cases reported in women. The median age at presentation was 52 years of age among women (range 14-78 years) and 51 years of age among men (range 23-72 years). Remarkable predisposing factors were diabetes mellitus (n=12), malignant tumors (n=5), alcohol abuse (n=4), enteritis (n=3), and sickle cell anemia (n=2). No predisposing factors were observed in seven cases (Fig. 4). Diabetic ketoacidosis was a complication in the present case; to the best of our knowledge, this is the first case to report the presence of diabetic ketoacidosis as a complication. Emphysematous osteomyelitis and non-emphysematous osteomyelitis are not remarkably different in terms of their symptoms. The most common symptoms include fever and pain at the infected site. It is difficult to distinguish between emphysematous osteomyelitis and non-emphysematous osteomyelitis based on only the symptoms or physical assessment; therefore, we suggest that imaging should be performed.

To date, most reported emphysematous osteomyelitis cases including our case have been monomicrobial. Among the 35 reported cases, 24 were monomicrobial, 10 were polymicrobial, and one was an unknown infection. These infections were located in the vertebrae (n=17), pelvis (n=10), femur (n=8), tibia/fibula (n=3), and sternum (n=2) (Fig. 4). The causative organisms of emphysematous osteomyelitis are similar to those reported for other gas-forming infections, such as *Escherichia coli*, (n=10), *K. pneumoniae* (n=7), *Bacteroides spp.* (n=7), and *Fusobacterium* (n=5) (Fig. 4). In contrast, the most common causative agent of vertebral osteomyelitis is *Staphylococcus aureus* (28). Therefore, when diagnosing osteomyelitis caused by gas-forming organisms, emphysematous osteomyelitis should always be considered in the differential diagnosis. Vertebral infectionsare most commonly observed in patients with emphysematous osteomyelitis caused by *K. pneumoniae*. The rate of *K. pneumoniae* infection increases in individuals with impaired host defenses. Diabetes was an underlying condition in 36% of the cases and malignancy in 26% of the cases in a report of 101 patients with *Klebsiella* bacteremia, which is similar to that reported among emphysematous osteomyelitis cases (29).

Luey et al. (3) reviewed the literature on approximately 25 previous emphysematous osteomyelitis cases. However,

Table 2. Patients with Emphysematous Osteomyelitis Reported in the English Literature.

Patient	1	2	3	4	5
References	1	2	3	4	5
Age	14	54	15	21	57
Sex	F	F	F	F	F
Predisposing factor	Diabetes mellitus	Non-SCLC, typhlitis	None	None	Diabetes mellitus, hypertension
Location	Left femoral neck	Left femoral neck	S1 and ilium	Left iliac crest	Right femoral head
Bacteriologic results	*Bacteroides fragils*	*Clostridium septicum*	*Fusobacterium necrophorum*	*Fusobacterium necrophorum*	*Fusobacterium necrophorum*
Antibiotics treatment	ND	ND	4 weeks IV+4 weeks oral	16 days	ND
Surgical treatment	None	None	Surgery 4 times	Surgery 1 time	Surgery 2 times
Abscess	None	None	Epidural abscess	Liver abscess	None
Outcome	ND	Cure	Cure	Died day 16	Cure
Follow up	None	None	18 months	-	9 months

Patient	6	7	8	9	10
References	6	7	8	9	10
Age	78	60	64	65	70
Sex	F	M	F	F	M
Predisposing factor	None	Metastatic SCLC, alcohol abuse	Hemolytic anemia, receiving prednisone	Diabetes mellitus	Diabetes mellitus
Location	L5 and S1 vertebrae	Pelvis, and T5, T6, L1, L4 and L5 vertebrae	L1 vertebra	L3 vertebra	T12–L5 vertebrae
Bacteriologic results	*Fusobacterium necrophorum*	*Peptococcus indolicus*	*Escherichia coli*	*Escherichia coli*	*Escherichia coli*
Antibiotics treatment	4 weeks IV+8 weeks oral	34 days	ND	7 days	16 days
Surgical treatment	None	None	None	None	L3/4 laminectomy and drainage
Abscess	None	Iliopsoas abscess	None	None	Epidural abscess
Outcome	Cure	Died day 34	Cure	Died day 7	Died day 16
Follow up	24 months	None	-	-	-

Patient	11	12	13	14	15
References	9	11	12	13	14
Age	50	59	36	51	66
Sex	M	F	F	M	M
Predisposing factor	Diabetes mellitus, hypertension	None	Sickle cell anemia	Non-Hodgkin lymphoma	Addison's disease
Location	L2 vertebra	Pelvis and vertebrae	Bilateral distal femurs and proximal tibias	Bilateral femoral heads	T7 and T8 vertebrae
Bacteriologic results	*Klebsiella pneumoniae*	*Klebsiella pneumoniae*	*Proteus mirabilis*	*Salmonella* serogroup D	*Mycobacterium tuberculosis*
Antibiotics treatment	9 days	ND	ND	ND	ND
Surgical treatment	None	Surgery multiple times	Multiple surgeries with eventual bilateral above knee amputations	Surgery 1 time	None
Abscess	Liver abscess and psoas abscess	Abscess (unkown site)	Abscess of the distal ends of the femora	Abscess in the subcutaneous tissue of both thighs	None
Outcome	Died day 9	Wounds still draining 6 months later. Died 2 years later from brain hemorrhage	ND	Died day 56	ND
Follow up		24 months	None	-	None

Table 2. Patients with Emphysematous Osteomyelitis Reported in the English Literature. (continued)

Patient	16	17	18	19	20
References	15	16	16	16	17
Age	29	30	35	57	66
Sex	M	M	M	F	F
Predisposing factor	None	Crohn's disease	Crohn's disease	Cervical cancer treated with radiotherapy	None
Location	L3 and L4 vertebrae	Sacrum	Sacrum	Sacrum	*Pelvic girdle and right femoral head*
Bacteriologic results	*Escherichia coli, Klebsiella* spp, *Bacteroides* spp, Group D *Streptococcus*	*Escherichia coli, Bacteroides* spp	*Escherichia coli, Bacteroides fragilis*	*Peptostreptococcus* spp, *Vellionella* spp, *Staphylococcus epidermidis, Candida* spp	*Escherichia coli, Enterococcus* spp
Antibiotics treatment	ND	ND	ND	ND	ND
Surgical treatment	L3 and L4 resection and bone graft fusion	Surgery 1 time	Drainage	Surgery 1 time	None
Abscess	Paraspinal abscess	Presacral abscess	Presacral abscess	Pelvic abscess and right psoas abscess	None
Outcome	Cure	Cure	ND	ND	Died in hospital (unkown day)
Follow up	None	None	None	None	-

Patient	21	22	23	24	25
References	18	19	8	17	17
Age	23	49	58	37	51
Sex	M	M	M	F	M
Predisposing factor	Sickle cell anemia, stroke	Diabetes mellitus, infective endocarditis	Alcohol abuse	Chondrosarcoma	None
Location	Right femur	Left femoral head	T6 vertebra	Right tibia	Right fibula
Bacteriologic results	*Bacteroides melaningenicus, Propionibacterium* spp, *alpha-hemolytic Streptococcus*	*Bacteroides stercoris,* group *C streptococcus*	*Bacteroides* spp, *Streptococcus milleri, Streptococcus mitis*	*Pseudomonas* spp, *Enterococcus* spp, *Staphylococcus aureus, non hemolytic Streptococcus*	*Enterococcus* spp, *Streptococcus intermedius*
Antibiotics treatment	6 weeks IV	ND	ND	ND	ND
Surgical treatment	Surgery 1 time	Femoral head resection and abscess drainage	Debridement 1 time	Surgery 1 time	Surgery 1 time
Abscess	None	Left iliopsoas abscess	Paraspinal abscess	Tibia acscess	Right calf abscess
Outcome	Cure	Cure	Died day 56	ND	ND
Follow up	None	None	-	None	None

Patient	26	27	28	29	30
References	20	21	22	22	23
Age	60	58	53	45	72
Sex	M	M	F	M	M
Predisposing factor	None	Diabetes mellitus, hypertension, alcohol abuse, splenectomy, right transmetatarsal amputation	Diabetes mellitus	Diabetes mellitus	Diabetes mellitus
Location	L5 vertebra	Metatarsals remnants, midtarsal bones, and head of the talus	L2 and L3 vertebrae	L4 and L5 vertebrae	Pelvis and vertebrae
Bacteriologic results	*Klebsiella* spp	Group G *Streptococcus*	*Klebsiella pneumoniae*	Unkown	*Escherichia coli*
Antibiotics treatment	4 weeks IV+2 weeks oral	ND	4 weeks IV+2 weeks oral	ND	ND
Surgical treatment	None	Right below-knee amputation	None	None	None
Abscess	None	Necrotizing fasciitis	None	None	None
Outcome	Cure	Cure	Cure	Died in hospital (unkown day)	Died in hospital (unkown day)
Follow up	2 months	6 weeks	6 weeks	None	-

Table 2. Patients with Emphysematous Osteomyelitis Reported in the English Literature. (continued)

Patient	31	32	33	34	35
References	24	25	26	27	This case
Age	46	62	74	58	76
Sex	M	M	F	F	F
Predisposing factor	Alcohol abuse	Arthroscopy of the knee	Multiple myeloma	Diabetes mellitus, hypertension	Diabetes mellitus
Location	Lumbar vertebrae	Sacrum	Sternum and T6 vertebrae	Sternum and left clavicle	L1 and L2 vertebrae
Bacteriologic results	*Klebsiella pneumoniae*	*Fusobacterium necrophorum*	*Escherichia coli*	*Escherichia coli*	*Klebsiella pneumoniae*
Antibiotics treatment	2 days	16 days	20 days	13 weeks IV	10 days
Surgical treatment	Debridement 1 time	None	None	Debridement 1 time	None
Abscess	None	Piriformis muscle abscess	None	Iliopsoas abscess	None
Outcome	Died day 2	Died day 16	Cure	Cure	Died day 10
Follow up	-	-	None	13 weeks	-

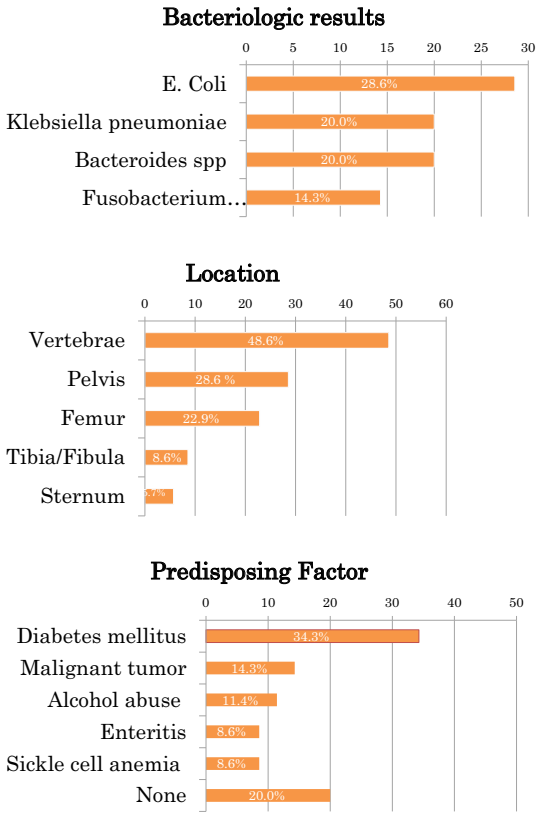

Figure 4. Characteristics of emphysematous osteomyelitis.

we would like to emphasize the characteristics of the most recent 10 cases (20-27). Among these 10 cases, diabetes mellitus was present in 60% of the cases and *Klebsiella* species were the causative organisms in four cases. Half of these cases were fatal. Three of four emphysematous osteomyelitis cases caused by *Klebsiella* species were reported in Asian countries (India, Taiwan, and Japan). Invasive syndromes caused by *K. pneumoniae* have been particularly detected in Asia over the past two decades (28). Diabetes mellitus predisposes a patient to an invasive syndrome caused by *K. pneumoniae*. The syndrome is associated with the hypermucoviscous phenotype of *K. pneumoniae* strains, which cause bacteremic dissemination, including endophthalmitis, meningitis, and necrotizing fasciitis. The invasive nature of some *K. pneumoniae* strains includes a hypermucoviscous phenotype associated with serotypes K1 and K2 and a regulator of the mucoid phenotype A gene. Definite invasive syndrome is defined as a *K. pneumonia*e infection caused by the K1 or K2 serotype. Furthermore, invasive syndrome is defined as the hypermucoviscous phenotype confirmed by a string test, which monitors the formation of a viscous string >0.5 cm in length which is stretched by the inoculation loop. We assume that this invasive syndrome includes emphysematous osteomyelitis. We did not test for this phenotype in our case; however, an invasive *K. pneumoniae* infection may occur. Further studies are needed to evaluate the emphysematous osteomyelitis caused by *Klebsiella* species.

Empiric treatment should include antibiotics with activities against the causal microbe. Unfortunately, the details regarding the optimal duration for administering antibiotics for the treatment of emphysematous osteomyelitis cases has not been elucidated in the pertinent literature, and thus no definitive conclusions can be made. However, the high level of surgical intervention and high mortality rate associated with emphysematous osteomyelitis are clearly evident (17). Surgical intervention should be considered for the treatment of acute osteomyelitis if abscess formation or radiologic evidence of necrosis is detected (26). Among the reported 35 cases, at least 19 cases (54%) required surgical intervention and four cases (11%) required multiple surgeries. There were 19 cases with abscesses. Our case did not have any abscess; therefore, no surgery was required. However, surgery was performed in three cases without any abscess for infectious source control, which led to a good prognosis. In contrast, surgery performed in three cases with abscesses resulted in a fatal outcome. Compared with vertebral osteomyelitis, with a mortality rate of 6% to 11%, emphysematous osteomyelitis was associated with a higher mortality rate (37%; 13 patients emphysematous osteomyelitis died in the hospital 56 days after diagnosis) (30-32).

Therefore, our findings suggest that an early diagnosis

and immediate treatment, including effective antibiotics and surgical intervention, when indicated, are essential for preventing the potentially fatal consequences associated with emphysematous osteomyelitis.

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

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