Review Article

Emphysematous osteomyelitis of the spine: a case report and case based review of the literature

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Background/Objective: Emphysematous osteomyelitis (EO) of the spine is an uncommon type of osteomyelitis characterized by intraosseous gas-formation in the vertebrae. The objective of this report is to present a rare case of spine EO in a patient with emphysematous cystitis. A case-based review of the literature on spinal EO was also performed as an update to the relevant literature of this rare infection.

Case Description/Methods: A 55-year-old female with diabetes mellitus and peripheral vascular disease (PVD) presented to our institution with recurrent falls, fatigue, and low back pain. Computed tomography (CT) and magnetic resonance imaging (MRI) scans confirmed emphysematous cystitis and EO at L4. Given the diffuse involvement, surgical intervention was deferred for IV antibiotic therapy. A case-based review was also conducted by searching the SCOPUS and PubMed databases for the following terms: "emphysematous osteomyelitis", "gas", and "spine". Only publications in English were included in this review.

Key Content/Findings: Urine/blood cultures identified *Klebsiella pneumoniae*. After initial improvement with six weeks of broad-spectrum antibiotics, the patient re-presented with recurrent fevers and fatigue. Despite maximal medical therapy, the patient expired 2 months later due to multi-organ system failure. Including the present report, only 29 cases of spine EO have been described in the literature. Patients almost consistently presented with fever, elevated inflammatory markers, and localized pain. Most cases of spinal EO (89.7%) were monomicrobial. *Escherichia coli* (37.9%) and *Klebsiella pneumoniae* (27.6%) were the most causative organisms identified. Medical treatment universally consisted of broad-spectrum IV antibiotics prior to tailoring. Debridement and decompression, with or without fusion, were the main operative procedures performed for spine EO. Outcomes following spinal EO are varied with a 44.4% mortality rate.

Conclusions: We present a case of EO of the spine and concomitant emphysematous cystitis with *Klebsiella pneumoniae* and a case-based review of the literature. Appropriate work up for this rare infection should include inflammatory markers, cultures, and CT/MRI imaging. Treatment consists of IV antibiotics with anaerobic and gram-negative coverage. However, treatment guidelines and operative indications for spinal emphysematous osteomyelitis remain unclear.

Keywords: Emphysematous; osteomyelitis; spine; case report; review

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Introduction

Emphysematous osteomyelitis (EO) of the spine is a rare, rapidly progressive and potentially fatal variant of osteomyelitis caused by gas-forming bacteria. EO was first described in 1981 involving the appendicular skeleton with the pathognomonic radiologic finding being the presence of gas and the absence of any penetrating wounds, open fractures or biopsies (1-4). In 1986, Bielecki *et al.* described the first documented phenomenon involving the spine as a clinically distinct condition from other noted spine infections, like pyogenic vertebral osteomyelitis and granulomatous osteomyelitis (5-8). While current literature is limited on the role of surgical intervention versus medical management, a multidisciplinary approach to care with early detection is essential to prevent devastating outcomes. We present a case report of a 55-year-old female with EO of the lumbar spine caused by *Klebsiella pneumoniae* and review the literature of previously reported cases. To the author's knowledge, this is the first reported case of spine EO with concomitant emphysematous cystitis. The objective of the literature review was to review the patient demographics, comorbidities, symptoms, treatment provided, and outcomes when treating EO in the spine. We present the following article in accordance with the CARE and Narrative Review reporting checklists (available at https://jss.amegroups.com/article/view/10.21037/jss-22-6/rc).

Case presentation

A 55-year-old female arrived at the emergency room of a major urban Level 1 Trauma Center after two episodes of falls the week prior with primary complaints of overall weakness, low back pain, and left lower extremity pain. Her past medical history included insulin-dependent type II diabetes, obesity, hypertension, peripheral neuropathy, ischemic ulceration due to peripheral vascular disease (PVD), and bilateral retinopathy. Her BMI was 36 and her Charlson Comorbidity Index score was 4 (+1 for age 50–59 years, +1 for PVD, and +2 for end-organ damage diabetes mellitus) with an estimated 53% 10-year survival rate. Vitals on presentation were 37.3 Celsius, heart rate 70 beats/minute, blood pressure 141/100 mmHg. Physical exam was unremarkable except for abdominal flank bruising. She had tenderness to palpation over the low back. Neurological exam demonstrated full strength in the lower extremities bilaterally except for a chronic left extensor hallucis longus and left tibialis anterior weakness, unrelated to current presentation.

Notable laboratory values on admission included elevated glucose levels (203 mg/dL), normal white-blood cell count (WBC) (6.7×10^9/L), elevated C-reactive protein (CRP) (42.2 mg/dL), and elevated erythrocyte sedimentation rate (ESR) (137 mm/h). The patient also had an acute kidney injury as her creatinine levels on admission were elevated at 2.0, from 0.9 at a prior admission. Lactic acid levels were normal at 2.1 mmol/L. Initial lumbar radiographs obtained demonstrated mild compression deformity of the superior endplate of L4 and air projections in the retroperitoneum suggestive of a gas forming infection (*Figure 1*). Initial computed tomography (CT) scan of the patient's pelvis/abdomen demonstrated gas within the bladder wall. A small compression fracture of the L4 vertebral body without retropulsion was noted. Intraosseous gas was noted within the L4 vertebral, L3-L4/L4-L5 disc spaces, the adjacent spinal canal, retroperitoneum, prevertebral soft tissues, and bilateral iliopsoas muscles (*Figure 2*). Magnetic resonance imaging (MRI) obtained of the lumbar spine/pelvis confirmed emphysema in the aforementioned locations noted on CT scan. In addition, the small collections initially noted on the CT scan were confirmed in the prevertebral space and within the ventral epidural space on MRI as well. Hyperintense signals in the L4 vertebral body, paraspinal iliopsoas muscles, and posterior spinal elements were noted (*Figure 3*). These findings were concerning for EO of the spine and emphysematous cystitis with surrounding musculature and paraspinal involvement. The pumice stone appearance of the intramedullary gas on CT further supported a diagnosis of spine EO rather than degenerative changes or vacuum phenomenon in the spine. Further, the involvement of gas in the bladder walls and direct tracking of gas along the iliopsoas muscles on imaging to the levels in question (L4 vertebral body, L3-L4/L4-L5 disc spaces) made emphysematous infection more likely. Subsequent urine and blood cultures also tested positive for pan-sensitive *Klebsiella pneumoniae*, a known gas producing opportunistic pathogen. No other foci of infection were identified on whole body CT imaging and multiple echocardiogram exams.

Given the diffuse nature, surgical intervention was deferred and empiric intravenous (IV) clindamycin and vancomycin were initiated. Broad spectrum therapy was tailored to IV ceftriaxone following the positive pan-sensitive *Klebsiella pneumoniae* results. After initial improvement, hospital course was then complicated by worsening renal function necessitating hemodialysis, fever,

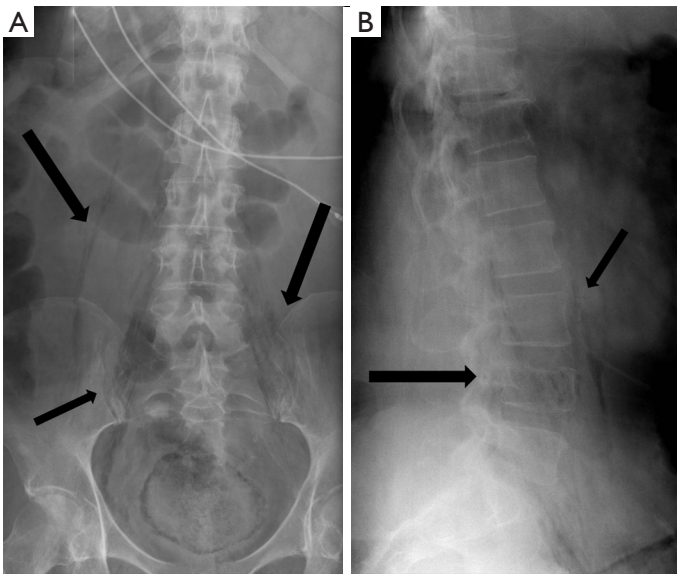

Figure 1 Radiographs of the lumbosacral spine. (A) Anteroposterior views of the lumbosacral spine. (B) Lateral views of the lumbosacral spine that demonstrate superior endplate depression at the L4 vertebrae. Black arrows highlight linear densities suspicious for retroperitoneal gas and gas forming infection.

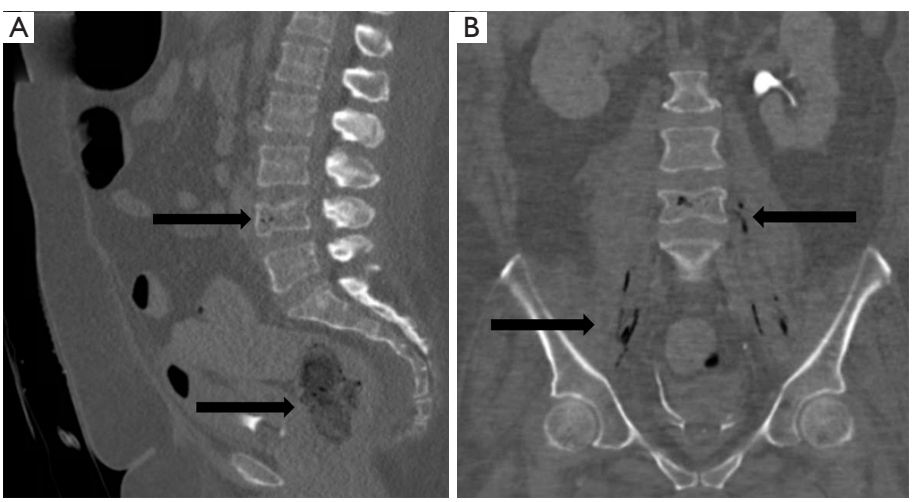

Figure 2 Computed tomography scans of the abdomen/pelvis with contrast shown on bone window. (A) Sagittal views of the abdomen/pelvis. (B) Coronal views of the abdomen/pelvis. Black arrows highlight confirmation of gas on CT imaging in the bilateral iliopsoas muscles, throughout the bladder wall, L4 vertebral body, and L3-L4/L4-L5 intervertebral discs. CT, computed tomography.

worsening mental status, and hypoxia a few days after admission. Repeat blood cultures and urine cultures were negative for growth. Imaging of the chest demonstrated consolidation concerning for pneumonia. The patient was intubated and admitted to the intensive care unit (ICU) on hospital day 12, where broad-spectrum antibiotics with IV vancomycin and cefepime were initiated. The patient at this point completed approximately two weeks of IV ceftriaxone therapy. Due to the concomitant nosocomial pneumonia (Gram stains positive for Gram-positive cocci and Gram-negative rods, no growth on sputum cultures), broader spectrum antibiotic coverage with vancomycin and cefepime was recommended by the infectious disease specialists to cover Gram positive organisms. As the *Klebsiella pneumoniae*

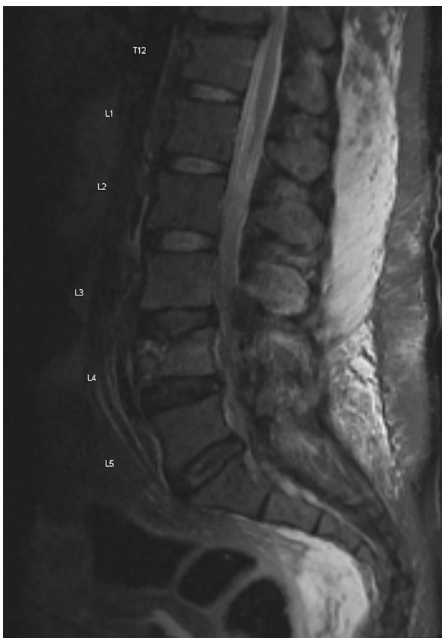

Figure 3 Magnetic resonance imaging sagittal cuts of the lumbar spine with/without contrast. Demonstrates hyperintense signal in the L4 lumbar vertebral body and the anterior/posterior spinal elements correlating with the affected areas noted on computed tomography.

cultures were pan-sensitive and only resistant to ampicillin/sulbactam, cefepime was deemed adequate coverage for the infection. She was extubated two days later and transferred to the floor. She was subsequently discharged after a total of four weeks of hemodialysis therapy and IV antibiotics with noted improvement. She remained afebrile and throughout her hospitalization, repeat blood cultures and urine cultures drawn every 5 days to 2 weeks apart were negative for growth.

She was subsequently discharged on IV vancomycin and cefepime administered by a home health nurse to complete. She did not require hemodialysis upon discharge. Labs upon discharge were WBC 10.2×10^9/L, CRP 16.6 mg/dL, ESR 138 mm/h, lactic acid 1.5 mmol/L, and creatinine of 0.7. She completed two weeks of outpatient IV vancomycin and cefepime with no issues for a total of 2 weeks of IV ceftriaxone therapy and four weeks of IV vancomycin/cefepime therapy. In accordance with recommendations by the Infectious Diseases Society of America (IDSA) guidelines, the patient was treated with at least six weeks of antibiotics targeted towards the sensitivity profile of the cultured organism—either via IV administration or oral with high bio-availability.

The patient however re-presented three weeks following discharge with altered mental status, fever (38.0 ℃), and tachycardia (110 bpm), which developed one week after the patient finished her IV antibiotics. Leukocyte count was again normal (7.3×10^9/L), CRP elevated at 8.4 mg/dL, ESR elevated at 141 mm/hr. Laboratory analysis confirmed renal failure with creatinine of 4.5 secondary to vancomycin toxicity. Again, initial repeat blood and urine cultures were negative and subsequent repeat blood/urine cultures drawn every week throughout her second hospitalization were negative for growth. Emergent hemodialysis therapy was started. IV metronidazole was also added to broaden coverage for gram-negative anaerobic organisms. After a week of IV cefepime, vancomycin, and metronidazole, the patient's vital signs and clinical picture improved.

However, two weeks after the second presentation, the patient's care was elevated to the ICU with intubation/sedation after suffering a left frontal parietal infarct and cardiac arrest requiring CPR. The patient approximately four weeks later contracted another nosocomial pneumonia caused by a multidrug resistant strain of *Acinetobacter baumannii*. The organism was resistant to all tested antibiotics at our institution including cefepime, ampicillin/sulbactam, ceftazidime, ceftriaxone, gentamicin, levofloxacin, meropenem, piperacillin/tazobactam, trimethoprim/sulfamethoxazole, and tobramycin. Tigecycline (100 mg loading dose, 50 mg IV q12 hour) was added during the patient's last week of admission. Antibiotics were continued for both the emphysematous infections and pneumonia. Repeat CT imaging of the pelvis/abdomen demonstrated improved soft tissue infection, decreased fluid collections, and elimination of gas components. Despite improvements in radiographic findings, the patient expired approximately three months after her initial presentation due to multiple organ system dysfunction (*Figure 4*).

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Methods

Searches of the SCOPUS and PubMed databases were performed on June 15, 2021 with the following search

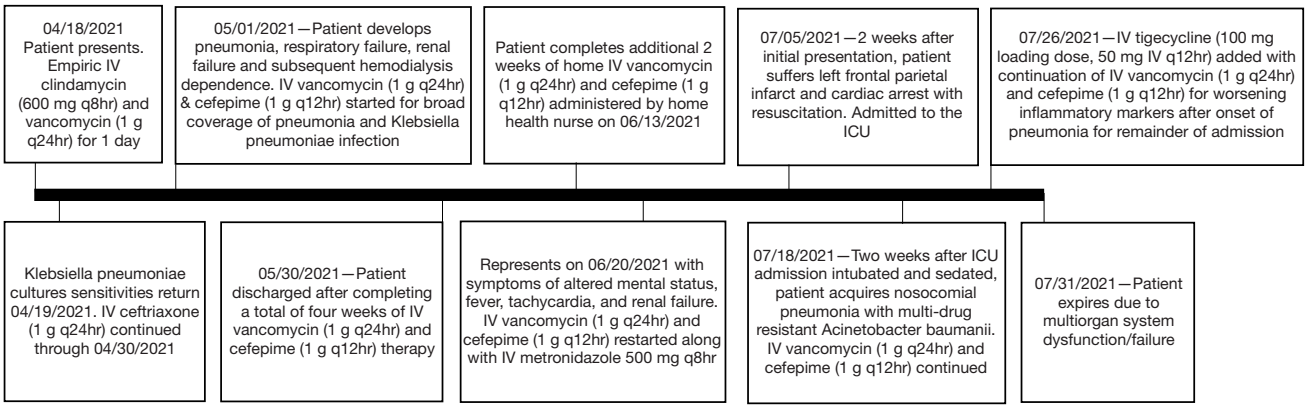

Figure 4 Timeline of antibiotic treatments and dosages with significant events denoted to help give a visual representation of the patient's hospital course; ICU, intensive care unit.

terms: "emphysematous osteomyelitis", "gas", and "spine". These search terms were then combined via Boolean operators. Databases were initially searched with search terms for [("emphysematous osteomyelitis" AND "gas") OR "spine"]. After the initial search yielded over 200,000 results, the search was then initiated with just "emphysematous osteomyelitis." The final search results were again narrowed by searching for ("emphysematous osteomyelitis" AND "spine"). Duplicate articles (found in both databases) were eliminated. Only articles published in the English language were included. Due to the low incidence of EO, no high-quality studies related to it were available and was limited to separate individual cases of spinal EO that have been previously reported in the literature. No exclusion criteria based on years was applied. The timeframe of publications included was the original description of EO up to the date of the search (June 15, 2021) (*Figure 5*) (*Table 1*).

Demographics and comorbidities

Out of the 29 cases reported of EO of the spine in the literature (*Table 2*), including the one presented in this review, the incidence in women (51.7%) and men (48.3%) are nearly equal. As such, specific gender does not appear to be associated with the development of EO of the spine (2-5,9-26).

The average age of the patients in all 29 cases reported was 59.9 years, with a median age of 61 years. An overwhelming majority of these cases (96.6%) were reported in adult patients—only one case was reported in a female adolescent (3). Although there is a wide range of reported ages of EO of the spine, it is clear that this rare infectious phenomenon is more commonly found in the middle-aged to elderly population. However, whether or not age is an associated risk factor for spinal EO remains difficult to ascertain.

Compared to the patient's age, the particular comorbidities a patient may have likely contributes to the development of EO of the spine. While only four of the reported cases had no comorbidities (or no mention was made), the remaining 25 cases had significant ones including diabetes mellitus (44.8%) (2,4,9,11,14,15,19,20,22-24,26), malignancy (10.3%) (10,12,18,25) alcoholism (10.3%) (5,16) or steroid therapy (6.9%) (5,21). These findings are unsurprising as diabetes mellitus has a multifactorial role in increasing susceptibility to infection through various means such as cytokine production impairment and dysfunction of macrophages/neutrophils (27). The effects of malignancy, alcoholism, and steroid therapy on the increased risks of infection are also well documented (28-30). In the present report, our patient similarly had a history of poorly controlled diabetes with a glucose admission of 204 mg/dL.

Patient symptoms/presentation and early diagnostic evaluation

Low back pain was the most common presenting complaint in spinal EO (65.5%)—the location of the pain universally localized to the involved level on advanced imaging (9,12,26) (*Table 2*). In other cases, referred pain was present in the surrounding areas including the abdomen/flank (20.7%) (12,13,15) and lower extremities (17.2%) (3,12,17,19,23) (*Table 2*). Other symptoms such as a neurological deficit, defined as a motor weakness on physical exam, have also been reported. Other unrelated symptoms such as

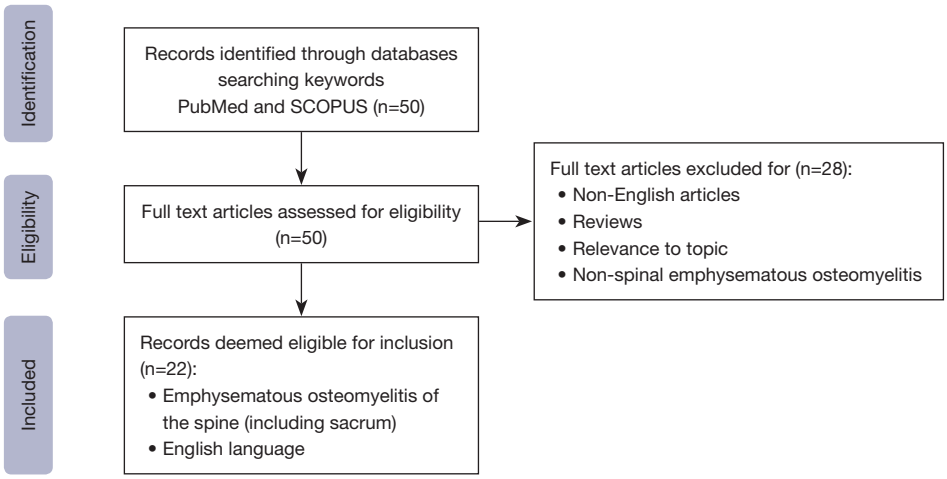

Figure 5 Flowchart demonstrating overview of article selection process.

Table 1 Search strategy summary

Items	Specification
Date of search	June 15, 2021
Databases and other sources searched	PubMed, SCOPUS. Review articles that were excluded were reviewed for reports as well
Search terms used (including MeSH and free text search terms and filters)	Search terms: "emphysematous osteomyelitis", "gas", and "spine" Example search strategy of PubMed database: Databases were initially searched with search terms for (("emphysematous osteomyelitis" AND "gas") OR "spine"). After the initial search yielded over 200,000 results, the search was then initiated with just "emphysematous osteomyelitis." The final search results were again narrowed by searching for ("emphysematous osteomyelitis" AND "spine")
Timeframe	From origin to June 15, 2021
Inclusion and exclusion criteria	Inclusion criteria: (I) English articles (II) Emphysematous osteomyelitis of the spine (including sacrum) Exclusion criteria: (I) Duplicate articles (II) Review articles (III) Relevance to topic (IV) Non-spinal emphysematous osteomyelitis
Selection process (who conducted the selection, whether it was conducted independently, how consensus was obtained, etc.)	Authors DL and KR conducted the searches independently and sources identified were then reviewed by authors DL, KR, and NM for consensus on inclusion or exclusion based on the criteria above
Any additional considerations, if applicable	None

altered mental status, chronic weakness due to previous cerebrovascular accidents (CVA), etc. were excluded. After applying these criteria, 27.6% of patients with a diagnosis of spinal EO presented with a neurological deficit. In contrast, 41.4% of patients, including the case reported in this review, did not have neurological deficits (*Table 2*).

In the appropriate clinical setting, early diagnostic work-up is essential given the devastating outcomes of spinal EO. While articles that did not provide initial vitals were excluded, of those that did, a majority of patients with EO of the spine presented with fever (62.1%). Similarly, WBC, CRP and ESR were almost universally elevated upon patient presentation (*Table 2*). 87.5% of patients (n=14) presented in sepsis on admission with two or more SIRS criteria (*Table 2*). Further management should involve lactate, CRP and ESR levels to determine the degree of systemic hypoperfusion and inflammation, respectively (3,11,12,14,16). An infectious work-up should begin immediately with blood and urine cultures.

Microbiology and histopathology

Of the 29 documented cases of EO of the spine, including our reported case, 26 were via a hematogenous spread (89.6%), two were via a contiguous intra-abdominal abscess (6.9%), one was via direct inoculation from a steroid injection (3.4%), and the other from an unknown source (3.4%) (2-5,9-26). The majority of cases were monomicrobial

Table 2 Emphysematous osteomyelitis of the spine

Author	Age	Sex	Comorbidities	Pain/ location	Neurological symptoms	WBC $\times 10^9$/L	CRP (mg/dL)	ESR (mm/hr)	Fever? Celsius	SIRS criteria 1-4
Lee	55	F	DM, obesity, HTN, peripheral vascular disease	Low back pain	No neurological deficits	Normal (6.7)	Elevated (42.2)	Elevated (137.0)	No (37.3)	No; 0/4
Ono (2)	75	F	DM	Low back pain	Yes; lower extremity weakness	Elevated (21.5)	Elevated (21.2)	Not reported	No (35.8)	Yes; 2/4
Luey (3)	15	F	None	Right hip pain	Yes; BLE weakness, urinary incontinence	Normal (3.9)	Not reported	Not reported	Yes (NVA)	Yes; 2/4
Tatakis (4)	57	F	Obesity, smoker, hypothyroidism, DM	Not reported	Yes; lower extremity weakness	Elevated (NVA)	Elevated (43.2)	Not reported	No (NVA)	No; 1/4
Bielecki (5)	51	M	Asthma, oral steroid therapy	Low back pain	Yes; lower extremity weakness	Not reported	Not reported	Not reported	Not reported	Unable to determine
Bielecki (5)	64	F	Hemolytic anemia, oral steroid therapy	Low back pain	No neurological deficits	Elevated (NVA)	Not reported	Not reported	Yes (NVA)	Unable to determine
Bielecki (5)	58	M	Alcoholism	Not reported	Yes; leg paresis	Not reported	Not reported	Not reported	Yes (NVA)	Unable to determine
Le Moal (9)	78	F	None	Low back pain	No neurological deficits	Not reported	Not reported	Not reported	Yes (40.0)	Unable to determine
Le Moal (9)	62	M	HTN	Low back pain	No neurological deficits	Not reported	Not reported	Not reported	No (38.0)	Unable to determine
Le Moal (9)	61	M	DM, arteritis	Low back pain	No neurological deficits	Not reported	Not reported	Not reported	Yes (40.0)	Unable to determine
Philippe (10)	60	M	Smoker, alcoholism, liver cirrhosis, metastatic lung small cell carcinoma	Low back pain	No neurological deficits	Elevated (22.3)	Not reported	Not reported	No (NVA)	Unable to determine
Al-Wakeel (11)	70	M	DM	Low back pain	Yes; paraplegia	Elevated (25.0)	Not reported	Not reported	Yes (39.3)	Yes; 2/4

Table 2 *(continued)*

Table 2 *(continued)*

Author	Age	Sex	Comorbidities	Pain/ location	Neurological symptoms	WBC $\times 10^9$/L	CRP (mg/dL)	ESR (mm/hr)	Fever? Celsius	SIRS criteria 1-4
Merine (12)	35	M	Crohn disease	Low back pain	No neurological deficits	Elevated (29.5)	Not reported	Not reported	Yes (38.5)	Yes; 2/4
Merine (12)	57	F	Cervical squamous cell carcinoma	Right hip and RLQ pain	Not reported	Elevated (15.0)	Not reported	Not reported	Yes (NVA)	Yes; 2/4
McDonnell (13)	60	M	Not reported	Abdominal pain	Yes; bilateral hip flexor weakness	Not reported	Elevated (3.5)	Not reported	Yes (NVA)	Unable to determine
Aiyappan (14)	53	F	DM	Low back and pelvic pain	No neurological deficits	Elevated (NVA)	Not reported	Not reported	Yes (38.2)	Yes; 2/4
Aiyappan (14)	45	M	DM	Low back pain	Not reported	Not reported	Not reported	Not reported	Yes (NVA)	Unable to determine
Larsen (15)	72	M	DM, a. fib, hepatic hematoma	Abdominal pain	Not reported	Not reported	Elevated (NVA)	Not reported	Not reported	Unable to determine
Chen (16)	46	M	Alcoholism, liver cirrhosis	Low back pain	No neurological deficits	Elevated (NVA)	Not reported	Not reported	Not reported	Yes; septic shock
Velickovic (17)	62	M	Not reported	Low back pain & left leg pain	No neurological deficits	Elevated (16.0)	Elevated (132.7)	Not reported	Yes (38.4)	Yes; 2/4
Park (18)	74	F	Multiple myeloma	Abdominal pain	Not reported	Not reported	Not reported	Not reported	Yes (NVA)	Unable to determine
Sung (19)	72	F	HTN, DM	Mid/low back pain, buttocks	No neurological deficits	Elevated (11.7)	Elevated (9.88)	Elevated (52)	No (37.6)	No; 1/4
Mujer (20)	56	M	HTN, DM, gout, nephrolithiasis	Flank pain	Not reported	Elevated (21.4)	Not reported	Elevated (70)	Yes (39.0)	Yes; 2/4
Mahesh (21)	65	F	HTN, RA, scoliosis	Low back pain	Yes; BLE weakness, bowel/bladder incontinence	Elevated (14.0)	Not reported	Elevated (NVA)	Yes (NVA)	Yes; 2/4
Kim (22)	79	F	HTN, DM	Not reported	Not reported	Elevated (25.2)	Elevated (2.3)	Not reported	No (36.0)	Yes; 3/4
Garg (23)	65	F	HTN, DM, pacemaker	Low back pain, BLE pain	Not reported	Elevated (NVA)	Not reported	Not reported	Yes (NVA)	Yes; 2/4
Smorgick (24)	68	M	DM, a. fib	Low back pain and dysuria	No neurological deficits	Elevated (23.4)	Elevated (28.9)	Not reported	Yes (38.1)	Yes; 2/4
Famularo (25)	72	F	Metastatic bronchial carcinoma	None, altered mental status	Not reported	Elevated (NVA)	Not reported	Not reported	Yes (NVA)	Yes; 2/4
Ko (26)	53	F	DM	Low back pain	Not reported	Not reported	Not reported	Not reported	Not reported	Unable to determine

F, female; M, male; HTN, hypertension; DM, diabetes mellitus; RLQ, right lower quadrant; RA, rheumatoid arthritis; a. fib, atrial fibrillation; BLE, bilateral lower extremities; WBC, white blood cell count; NVA, no value available; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; SIRS, Systemic Inflammatory Response Syndrome.

(89.7%), in which 26.9% were anaerobes (four were *Fusobacterium*, two were *Peptostreptococcus*, one was *Clostridium*) and 65.4% were a member of the *Enterobacteriaceae* family (eleven were *E. coli*, eight were *Klebsiella*) (2-5,9-26) (*Table 3*). Treatment of sepsis when indicated should be initiated via broad-spectrum antibiotics, intravenous fluids and vasopressors. Furthermore, it must be emphasized that in the setting of hemodynamic instability, aggressive management of sepsis should not be delayed for further laboratory analysis.

Histopathology of EO obtained via biopsy can demonstrate global areas of necrosis similar to pyogenic OM (19). However, on a more microscopic level, unorganized empty spaces that are inconsistent with normal osseous structures can be seen in between osteons (15). Interestingly, there may be no evidence of destruction surrounding these microscopic empty areas, indicating intraosseous air was responsible for the disorganized architecture in these areas rather than necrosis (15).

Table 3 Emphysematous osteomyelitis of the spine continued

Author	Microbiology	Mode of infection	Location & imaging findings	Medical treatment	Surgical treatment	Outcomes
Lee	Klebsiella	Hematogenous	CT – IO gas in L4; L3-4 disc space; gas in epidural space/ paraspinal muscles	IV vancomycin, cefepime (*Figure 4*: therapy details)	None	Died 3 months after initial presentation
Ono (2)	*Klebsiella*	Hematogenous	CT—IO gas in L1 & L2; gas in epidural space/ paraspinal muscles	IV meropenem (wks N/A)	None (fulminant sepsis, unstable)	Died 10 days after admission
Luey (3)	*F. necrophorum*	Hematogenous	CT—large epidural abscess at T12-S1; IO gas at S1 and ilium	IV Metronidazole/ Clindamycin (4 wks; PO Phenoxymethylpenicillin (4 wks)	Decompression, I&D	Discharged 15 wks later; residual BLE weakness requiring crutches and self-catheterization
Tatakis (4)	*Klebsiella*	Hematogenous	CT—IO gas in L3 & L4, gas in epidural space; emphysematous pyelonephritis	IV ceftriaxone/ meropenem (wks N/A)	None (fulminant sepsis, unstable)	Died 2 days after admission
Bielecki (5)	Peptostreptococcus	Hematogenous	CT—abscess w/ narrowing of L4-L5 disc, IO gas/destruction at L4 & L5 endplates	IV Penicillin & IV Clindamycin (>6 wks)	Anterior lumbar decompression, fusion, I&D	Discharged after recovery, no f/u reported
Bielecki (5)	*E. coli*	Hematogenous	CT—IO gas L1 body; bone scan also showed increased uptake at L3 and L4	IV Cefazolin (wks N/A)	None	Discharged after recovery, no f/u reported
Bielecki (5)	*S. viridans, S. mitis, S. milleri, Bacteroides*	Hematogenous	CT—IO gas at T6 body and paraspinal abscess	IV Penicillin (wks N/A)	None	Died 56 days after admission
Le Moal (9)	*F. necrophorum*	Hematogenous	CT—narrowing and IO gas at L5-S1 disc space, IO gas at endplates of L5, S1 MRI—confirmed OM	IV (4 wks) & PO (8 wks) Clindamycin	None	No symptoms at 2-year f/u
Le Moal (9)	*F. necrophorum*	Hematogenous	MRI—increased signal indicating OM at L4, L5	IV (4 wks) & PO (8 wks) Clindamycin	None	No symptoms at 2-year f/u
Le Moal (9)	*F. nucleatum*	Hematogenous	MRI—increased signal indicating OM; IO gas at T6, T7, T8, and T6-T7/T7-T8 discs	IV (4 wks) & PO (8 wks) Clindamycin	None	No symptoms at 2- & 3-year f/u

Table 3 *(continued)*

Table 3 *(continued)*

Author	Microbiology	Mode of infection	Location & imaging findings	Medical treatment	Surgical treatment	Outcomes
Philippe (10)	*P. indolicus*	Hematogenous	CT—bilateral abscesses along iliopsoas muscles, IO gas in T5, T6, LI, L4, L5, spinal canal, pelvic bones	IV Penicillin (wks N/A)	None	Died 34 days after admission
Al-Wakeel (11)	*E. coli*	Hematogenous	CT—IO gas in T12-L5 vertebral bodies, epidural abscess at these levels	IV Ceftriaxone/ metronidazole (wks N/A)	L3–L4 laminectomy; I&D epidural space & septic L4-5 disc	Died 16 days after admission
Merine (12)	*E. coli, B. fragilis*	Contiguous	CT—presacral abscess involving anterior sacrum; IO gas in anterior sacrum	No information provided	I&D	No information provided
Merine (12)	*E. coli, T. glabrata Peptostreptococcus, Veillonella, S. epi, C. tropicalis*	Contiguous	CT—IO gas in sacrum and iliac bone w/ presacral & posterior soft tissue gas	No information provided	I&D of spine; I&D of abdomen with laparotomy	No information provided
McDonnell (13)	*Klebsiella*	Hematogenous	CT—IO gas L5 body, gas in epidural space T9-S1, paraspinal/ psoas muscles MRI—increased signal at L5, extensive gas noted in surrounding tissues	IV (6 wks) & PO (2 wks) ciprofloxacin & cefazolin	None	Discharged after recovery, no f/u reported
Aiyappan (14)	*Klebsiella*	Hematogenous	CT—IO gas at L2 & L3 bodies; gas in soft tissues including psoas muscles	IV Ceftriaxone (4 wks) & PO levofloxacin (2 wks)	None	Discharged after recovery, no f/u reported
Aiyappan (14)	Not reported	Hematogenous	CT—gas/abscesses in soft tissue of L4 and L5, epidural gas noted MRI—increased signal at psoas, L4, L5 bodies suggestive of gaseous OM scan	No information provided	None	Death after sudden cardiac arrest
Larsen (15)	*E. coli*	Hematogenous	CT—IO gas in lumbar vertebrae/pelvic bones (unspecified)	IV Ceftriaxone, meropenem, clindamycin (wks N/A)	None (fulminant sepsis, unstable)	Death after unspecified amount of time
Chen (16)	*Klebsiella*	Hematogenous	CT—IO gas in lumbar vertebrae/pelvic bones (unspecified); gas in epidural space, psoas muscles, right buttock	Antibiotics (no name or time provided)	I&D	Died 2 days after admission
Velickovic (17)	*E. coli*	Hematogenous	CT—IO gas in sacral ala, paraspinal muscle edema; abscess around piriformis muscle w/OM in ilium 12 days later	IV (3 wks) & PO (9 wks) Amoxicillin/Clavulanate	None (patient refused)	2 months f/u – gait disturbance w/leg muscle wasting & pain

Table 3 *(continued)*

Table 3 *(continued)*

Author	Microbiology	Mode of infection	Location & imaging findings	Medical treatment	Surgical treatment	Outcomes
Park (18)	*E. coli*	Hematogenous	CT—IO gas at T6 vertebrae and sternum	IV meropenem (wks N/A)	None	Discharged after recovery, no f/u reported
Sung (19)	*E. coli*	Contiguous (steroid injection)	CT—IO gas in T12 & L1 bodies MRI—heterogeneous signal in T12 & L1, consistent with gas formation	IV vancomycin/ cefepime (1.5 wks) + IV cefotaxime (5 wks)	I&D; T12-L1 Laminectomy; T10-L3 post. inst.	Discharged after recovery, no f/u reported
Mujer (20)	*E. coli*	Hematogenous	CT—IO gas in L5 & S1, gas in L5-S1 disc; left emphysematous pyelonephritis	IV Meropenem/ linezolid (1 wks) + IV aztreonam (wks N/A)	None	Discharged after recovery, no f/u reported
Mahesh (21)	*E. coli*	Hematogenous	CT—IO gas in L5, gas in epidural space/psoas muscles MRI—multilevel stenosis w/signal change at L5 body and epidural abscess	IV Sulbactam/ cefoperazone, meropenem, clindamycin (1 wks) + PO antibiotics (name & wks N/A)	I&D; L1-ilium post. inst.; L2-L5 laminectomy	6 months f/u - improved pain & bladder control; residual ankle weakness
Kim (22)	*Klebsiella*	Hematogenous	CT—IO gas in L5 & sacrum; L3-S1 epidural/muscle abscesses w/gas; septic brain/pulmonary emboli, liver abscesses	IV ceftriaxone, metronidazole, clindamycin (wks N/A)	None (fulminant sepsis, unstable)	Died <1 day after admission
Garg (23)	*Klebsiella*	Hematogenous	CT—IO gas in L5 & S1; gas in paraspinal muscle/epidural space from L3-S1	IV antibiotics (name & wks N/A)	I&D, decompression (no specifics provided)	Discharged after recovery, no f/u reported
Smorgick (24)	MSSA	Hematogenous	CT—IO gas in L4 & L5; gas in epidural space/ paraspinal muscles w/psoas and inguinal extension	IV vancomycin, cefazolin, clindamycin (wks N/A)	I&D of muscles; L1-L5 laminectomy; L4-L5 discectomy	Died 5 days after admission
Famularo (25)	*C. perfringens*	Hematogenous	CT—IO gas in L3-S1 vertebrae; gas in epidural space/pelvis/ inferior vena cava	Not reported	None (fulminant sepsis, unstable)	Died <1 day after admission
Ko (26)	*E. coli*	Hematogenous	CT—IO gas in L5 and sacrum; gas in epidural space from L4-S1 MRI—epidural abscess from L4-S1 with multi-focal signal	IV antibiotics (name & wks N/A)	I&D, decompressive laminectomy (no specifics provided)	Discharged after recovery, no f/u reported

MSSA, methicillin-susceptible staphylococcus aureus; CT, computed tomography; IO, intraosseous; MRI, magnetic resonance imaging; OM, osteomyelitis; IV, intravenous; wks, weeks; I&D, irrigation and debridement; post. inst., posterior instrumentation; BLE, bilateral lower extremity; f/u, follow-up; N/A, not available.

CT/MRI findings & the role of image-guided biopsy

The diagnosis of EO of the spine is confirmed via a CT scan that may identify small amounts of intraosseous gas within the vertebrae, which may not be readily visible on plain radiographs (2-4,24). Additionally, unlike spondylodiscitis and spinal epidural abscesses where MRI is preferred, CT scans are able to provide the diagnosis of EO in an efficient manner to avoid delaying surgical management when indicated (2-4,24). However, unlike the appendicular skeleton, the presence of intraosseous gas involving the spine may be secondary to a wide range of diagnoses, including degenerative diseases, osteonecrosis and neoplasms (5,6,19,26). Utilizing CT imaging to localize EO on the spine, an overwhelming majority of cases reported (86.22%; n=25) had involvement predominantly of the lumbosacral spine, both with and without extension into the pelvic bones and thoracic levels. Only 10.3% (n=3) involved purely the thoracic spine (5,9,18). In the current case presentation, our patient's involvement included the L4 vertebral body, L3-L4 & L4-L5 disc spaces, and surrounding tissues.

Small *et al.* highlighted radiologic features of EO that distinguishes it from other non-infectious causes (31). He noted that in 96% of reported cases of EO, CT scans demonstrated a "pumice stone" pattern of intramedullary gas, defined as at least three irregularly irregular millimetric (2–5 mm) foci of gas (31). This contrasts with the benign, degenerative pneumatocysts or subchondral cysts which have a paucity of distinct locules, are relatively large/similar in size and have thin sclerotic margins (31). This is due to the preservation of the evenly spaced bony trabeculae as compared to the aggressive gas-forming infection leading to rapid destruction of the trabeculae and formation of numerous foci of different sizes and shapes (31). Additionally, suspicion for emphysematous osteomyelitis should be heightened with the presence of fluid collections or abscess formations which may be detected in the adjacent tissue (19,31). While CT scans are utilized for confirmation of the diagnosis, a multidisciplinary approach to care is essential for efficient work-up in the appropriate clinical setting and formulation of a subsequent treatment plan.

Similar to MRI scans, PET-CT scans may demonstrate areas of increased focal uptake that indicate an active inflammatory process is ongoing. However, PET-CT scans are not routinely utilized in the diagnosis of EO. Instead, CT imaging coupled with MRI remain the gold standard for diagnosing EO as CT imaging will best demonstrate cortical destruction/intraosseous gas and MRI will demonstrate areas of inflammation and soft tissue involvement.

Infectious disease guidelines indicate image-guided biopsy is recommended only when a microbiologic diagnosis is not known from blood, urine, or other serologic tests. In fact, other reports in the literature indicate image guided biopsy demonstrates a low probability of identifying specific microbes (32). Generally, the Infectious Disease Society of America (IDSA) recommends image guided biopsy and/or open biopsy when a causative organism cannot be identified or if antibiotic therapy is ineffective (33). However, in cases where an organism cannot be identified in the setting of worsening symptoms of infection, image guided aspiration/open biopsy can potentially provide information for targeting antimicrobial therapy.

Treatment: medical therapy

In treating EO of the spine, efficient recognition and rapid initiation of antibiotic therapy is imperative. Although targeted therapy is ideal, in many of the reported cases, empiric antibiotic therapy was initiated. All documented cases, excluding reports with no information on antibiotic regimen, initiated IV antibiotic therapy. Frequently reported antimicrobials included IV clindamycin (3,9), cephalosporins (4,11,14), and penicillins (5,10,17). The authors' recommendation is the administration of IV vancomycin, cefepime and metronidazole to ensure broad coverage for gram-positive, gram-negative and anaerobic organisms, respectively, prior to tailoring based on organism sensitivity/speciation (*Table 3*). Out of those cases with antibiotic treatments provided, a significantly lower proportion (n=8, 33.3%) have oral antibiotic components following intravenous therapy.

Treatment: surgical intervention

The indications for surgical intervention in EO of the spine are similar to those of pyogenic vertebral OM. Surgery is typically pursued for (I) diagnostic purposes when a microorganism cannot be identified, (II) stability in the setting of progressive deformity, and (III) source control with a suboptimal response to appropriate medical therapy. Progressive symptoms of cord compression or cauda equina syndrome are urgent/emergent indications for both spine EO and pyogenic vertebral OM/spondylodiscitis. However,

Table 4 Emphysematous osteomyelitis: a summary of 29 reported cases

Patient factors	Results
Average age	59.9 years
Female: male distribution	51.7% to 48.3%
Significant comorbidities	Diabetes mellitus, malignancy, immunocompromise
Presenting symptoms	Low back pain (65.5%), neurological deficit (27.6%)
SIRS* criteria	87.5% classify as septic with ≥2 SIRS criteria on presentation
Method of spread	Hematogenous spread (86.2%)
Most common organism	*Enterobacteriaceae* family (65.4%)
Mortality rate	Up to 44.4%
Full recovery, no sequalae	Up to 44.4%
Neuro deficit at 6 months	Up to 11.1%

*, Systemic Inflammatory Response Syndrome.

the risks and benefits of surgical intervention and patient specific factors, such as prognosis and optimization for surgery, should always be weighed.

In spine EO, 37.9% of patients (n=11) underwent some type of surgical intervention including surgical debridement, decompression, or decompression with instrumentation for fusion (3,5,11,12,16,19,21,23,24,26). In many of the reported cases, surgical intervention was not pursued due to patient hemodynamic instability (2,4,15,22,25). In cases where multi-level laminectomies were performed, posterior instrumentation was placed in 2 out of the 3 cases (19,21,24). In contrast, single-level laminectomy procedures (11) and anterior procedures (5) required no posterior instrumentation. The authors recommend instrumentation when laminectomies are required at multiple levels as previous literature has demonstrated worse outcomes of spine infection in the setting of instability. For instance, in a database study of 2,662 patients who underwent surgery for spinal infection, Dietz *et al.* report better outcomes in several parameters when fusion and decompression are performed compared to decompression alone (34). The fused cohort had shorter lengths of stay (4 *vs.* 6 days), lower rates of new infection (3.99% *vs.* 11.25%) and revision surgery (8.16% *vs.* 12.7%), and overall, less complications at index hospitalization (23.96% *vs.* 34.95%) compared to the non-fused cohort (34). However, there is a very limited amount of literature regarding the most effective treatment of EO of the spine.

Outcomes

Outcomes following EO of the spine are also varied (*Table 4*). Although a significant majority of patients recovered without any sequalae out of the cases with reported outcomes (n=12; 44.4%), an equal number of cases resulted in mortality (n=12, 44.4%) anywhere between <24 hours and up to 3 months after presentation (*Table 3*). 11.1% (n=3) of cases had persistent neurological deficit up to 6 months later (*Table 3*). The wide variation of patient outcomes in cases of spinal EO highlight a need for stronger evidence-based guidelines for both medical therapy and surgical interventions.

Pyogenic vertebral osteomyelitis & emphysematous osteomyelitis

Similarities can be seen between both spine EO and pyogenic osteomyelitis/spondylodiscitis. The patient populations are similar as patients typically have multiple medical comorbidities—diabetes mellitus and immunocompromised states are among the most common (7) (*Table 2*). Treatment for both is also similar with antibiotic therapy being the primary treatment with surgical intervention required for diagnostic, stability, or source control purposes (7). However, spine EO has several characteristics that distinguish it from typical pyogenic vertebral osteomyelitis/spondylodiscitis. Spine EO is more likely to be associated with Gram-negative organisms that produce gas through fermentation (*Table 3*). In contrast, pyogenic osteomyelitis/spondylodiscitis can be equally associated with a wide variety of organisms (7). Spine EO, perhaps due to its association with Gram-negative organisms, is also more likely to have a more severe/septic clinical course as patients can rapidly deteriorate or succumb to complications. As a result, the mortality rate of spine EO approaches 45% (*Table 3*)—exceeding the mortality rate of pyogenic OM/spondylodiscitis reported to be 2–11% (7). This further highlights the need for hypervigilance by clinicians when a diagnosis of spine EO is suspected on CT imaging as the infection can be more aggressive than typical infections. The authors recommend a low threshold of suspicion for potential complications, including thromboembolic events and secondary infections, in this patient population.

Limitations and strengths

There were several factors that could have contributed to

the overall negative outcome in the present report. Overall, the patient had an elevated 10-year mortality risk with a Charlson Comorbidity Index score of 4 at baseline due to her multiple comorbidities. In addition, despite initial improvement, the infection was inadequately cleared at the end of the first antibiotic treatment period and the patient thus required readmission with recurrent symptoms. The patient also sustained a parietal lobe infarct, resuscitation after a prolonged period of cardiac arrest/CPR, and renal failure during the hospitalization. These severe complications undoubtedly contributed to the patient's overall negative outcome. Finally, perhaps the largest limitation of the present report and review is the paucity of literature relevant to spine EO. At the present time, there is no high-quality level of evidence regarding the treatment and natural history of this rare infection. The lack of literature on spine EO, however, highlights the strength of the present report. Further data, especially objective data such as vital signs and laboratory values, is imperative for this rare infection as the low incidence of the disease makes it difficult to formulate strong evidence-based treatment guidelines.

Conclusions

EO of the spine is an exceedingly rare phenomenon and prompt recognition is essential given its devastative complications. Emergent initiation of broad-spectrum IV antibiotics is typically indicated as patients are often septic on presentation. While surgical intervention is beneficial for both source control and organism identification, the operative indications and treatment guidelines remain unclear. Further high-quality studies are warranted to establish risk factors for early diagnosis and a standardized treatment protocol to reduce the morbidity/mortality associated with this rare condition.

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Footnote

Reporting Checklist: We present the following article in accordance with the CARE and Narrative Review reporting checklists. Available at https://jss.amegroups.com/article/view/10.21037/jss-22-6/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jss.amegroups.com/article/view/10.21037/jss-22-6/coif). JPG consults for device feedback and suggestions, academic conferences/travel/continuing medical education from NuVasive, Depuy Synthes; research support for materials from Nuvasive. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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