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Case Report

Culture-negative primary sternal osteomyelitis in a patient with uncontrolled type 2 diabetes mellitus^{☆,☆☆}

David H. Chan, MD^{a,b,*}, Michael T. Lee, MD^{a,b}, Amy Q. Zhang, MD^{a,b}, Erinn H. Ton, MD^{a,b}, Shyh-Jeun Wang, MD^{a,b}

^a Southern Hills Hospital and Medical Center, 9300 W Sunset Rd, Las Vegas, NV, 89145, USA

^b HCA Healthcare, Nashville, TN, USA

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ABSTRACT

Primary sternal osteomyelitis (PSO) is a rare condition defined as an infection of the sternal bone marrow with no contiguous source of infection. The overlap in symptoms of PSO with other cutaneous and malignant pathologies often leads to misdiagnosis and delay of appropriate care. In this case report, we outline the presentation of PSO in a 30 year-old male patient who was newly diagnosed with type 2 diabetes mellitus. The patient was successfully treated with antibiotic therapy alone, without need for surgical intervention. Interestingly, the patient's workup returned with negative microbial cultures. To our knowledge, this patient represents the first reported case of a spontaneously presenting, culture-negative PSO.

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Introduction

Primary sternal osteomyelitis (PSO) is an exceedingly uncommon diagnosis, historically accounting for only 0.3% of all reported osteomyelitis cases [1]. Patients will often present with nonspecific symptoms such as chest pain and fever, with some patients also presenting with painful swelling of the anterior chest wall and an associated rash [2]. Given the rarity

of PSO, diagnosis and treatment of this disease is often delayed, resulting in increased morbidity and mortality. In this report, we describe a case of PSO in a 30 year-old male who was newly diagnosed with uncontrolled type 2 diabetes mellitus (DM). He had no history of other immunocompromising conditions or prior chest injury. Of note, the patient's microbial cultures returned negative, making this an extremely unusual case of culture-negative PSO.

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* Corresponding author.

E-mail address: David.chan@hcahealthcare.com (D.H. Chan).

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Case presentation

A 30 year-old male patient without any known prior medical history presented to the emergency department with a 2 week history of anterior chest wall swelling and erythema. Approximately 1 month prior to presentation, the patient was diagnosed with community-acquired pneumonia and hospitalized for 3 days, after which he was discharged home on oral antibiotics for 2 weeks. After discharge from this hospitalization, however, he noted a mild area of non-tender erythema developing on his anterior chest wall. The lesion gradually increased in size over the following weeks. About 4 days prior to presentation, he began having intermittent, sharp pain in his left lower anterior chest wall that worsened with deep inspiration and cough. However, the lesion on his anterior chest wall remained painless. The patient also stated that he noted night sweats the day prior to presentation. Otherwise, in the emergency department he denied any fevers, chills, headaches, dizziness, shortness of breath, abdominal pain, nausea, vomiting, diarrhea, or back pain. He denied any prior surgery or known trauma to the area. He also denied any intravenous (IV) drug use, history of immunocompromising conditions, known sick contacts, or recent travel. While the patient presented after the start of the Covid-19 pandemic, he denied any history of Covid-19 infection. The patient did report being vaccinated with 2 doses of the mRNA-1273 (Moderna) Covid-19 vaccine. At the time of presentation, he had not received a third dose of the vaccine. His family history and social history were otherwise unremarkable.

Initial vital signs showed temperature of 97.8°F, heart rate of 103 beats per minute, respiratory rate of 16 breaths per minute, and blood pressure of 154/88 mm Hg. On physical exam, he was alert, in no acute distress, and obese with a body mass index of 41.6 kg/m². His cardiovascular exam showed normal heart sounds with tachycardia. His pulmonary and gastrointestinal examinations were normal. He was noted to have a circular area of swelling and erythema on his anterior chest wall measuring approximately 4 cm in diameter without tenderness or palpable fluctuance.

Laboratory evaluation of the patient demonstrated an elevated white blood cell count of 14.8 10⁹/L with 78.9% neutrophils. The patient's basic metabolic panel was notable for sodium of 131 mmol/L, chloride 85 mmol/L, and glucose of 403 mg/dL. Hemoglobin A1C was elevated at 12.4%. Erythrocyte sedimentation rate was elevated at 90 mm/h, and C-reactive protein was elevated at 14.40 mg/dL. Blood cultures were obtained. The patient tested negative for human immunodeficiency virus (HIV). His Covid-19 nasopharyngeal swab reverse transcriptase-polymerase chain reaction test was negative.

A chest radiograph with posterior-anterior and lateral views was obtained; however, there were no identifiable cardiopulmonary, bony, or soft tissue changes seen.

Ultrasound of the anterior chest wall lesion showed an ill-defined 6.2 × 2.5 × 2.5 cm subcutaneous fluid collection anterior to the ribs that appeared to curve posteriorly (Fig. 1). Within the lesion, echogenic debris was seen appearing to flow into the chest during respiration. However, no increased color flow signal was seen within the fluid collection.

A computed tomography (CT) chest with IV contrast was obtained and showed a phlegmonous area in the anterior subcutaneous tissues overlying the sternum measuring 3.4 × 7.0 × 13.2 cm (Fig. 2). There was a bony defect of the sternum measuring 19 × 10 mm noted below this phlegmonous area, extending into the medullary space. Furthermore, posterior to this area there was an area of retrosternal thickening noted measuring 1.0 × 5.0 cm, likely reactive inflammatory changes. These findings were consistent with osteomyelitis of the sternum. No mature abscess or drainable fluid collection was identified, and no extension into the chest cavity was noted.

In the emergency department, the patient was started on empiric IV antibiotics including vancomycin, clindamycin, and metronidazole. Based on his significantly elevated hemoglobin A1C, the patient was diagnosed with uncontrolled type 2 DM and started on basal-bolus insulin. He was also started on lisinopril and amlodipine for hypertension.

The infectious disease service was consulted for recommendations regarding antibiotic management. The patient was switched from vancomycin to daptomycin due to his obesity. Clindamycin and metronidazole were discontinued, and he was started on cefepime for empiric Gram-negative bacterial coverage.

Cardiothoracic surgery was consulted for possible surgical intervention for the subcutaneous fluid collection. However, they elected not to pursue surgery since there was no drainable fluid collection identified on CT, and they recommended continuing IV antibiotics with close clinical monitoring.

Interestingly, the patient's blood cultures obtained in the emergency department, prior to administration of antibiotics, were negative several days after admission. They remained negative for the duration of the patient's hospitalization.

CT-guided fine needle aspiration biopsy of the area of focal lytic destruction in the sternum was obtained on the fifth day of admission. Histologic and cytologic evaluation of the biopsy showed no malignant cells. Cultures obtained from this biopsy were negative for any microbial growth; however, the biopsy was obtained several days after initiation of IV antibiotics. Acid fast bacillus cultures and fungal cultures of the biopsy were also negative.

The patient's clinical condition improved on IV antibiotics alone. His white blood cell count normalized, and the skin lesion on his anterior chest reduced in size. Repeat CT chest with IV contrast was obtained 10 days after admission showing mildly improved soft tissue inflammation and phlegmon in the anterior chest wall superficial to the sternum (Fig. 3). The bony lytic defect in the mid-sternum was redemonstrated from the prior CT exam, with no drainable fluid collection or abscess.

Given his profound clinical improvement, he was discharged after 12 days of hospitalization with a peripherally inserted central catheter line to complete a 4-week course of IV daptomycin, followed by oral linezolid for an additional 2 weeks to complete a 6-week course of antibiotics. He also was transitioned from IV cefepime to oral levofloxacin after discharge as part of this 6-week antibiotic course. He was continued on lisinopril, amlodipine, and insulin on discharge, and he was started on metformin for control of his type 2 DM. He fol-

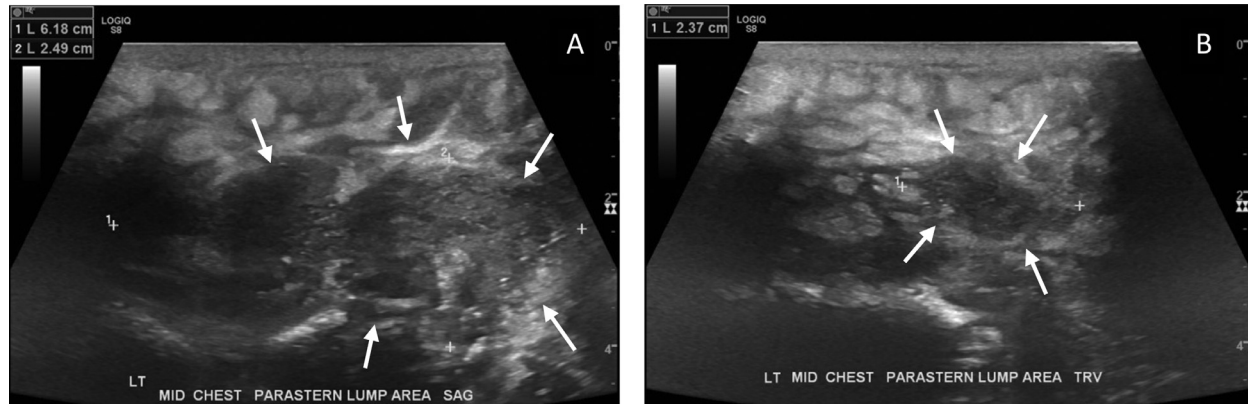


Fig. 1 – Ultrasound images of the anterior chest wall lesion obtained in the emergency department appear to show a subcutaneous fluid collection measuring approximately 6.2 x 2.5 x 2.5 cm (arrows). Sagittal (A) and transverse (B) views of the lesion.

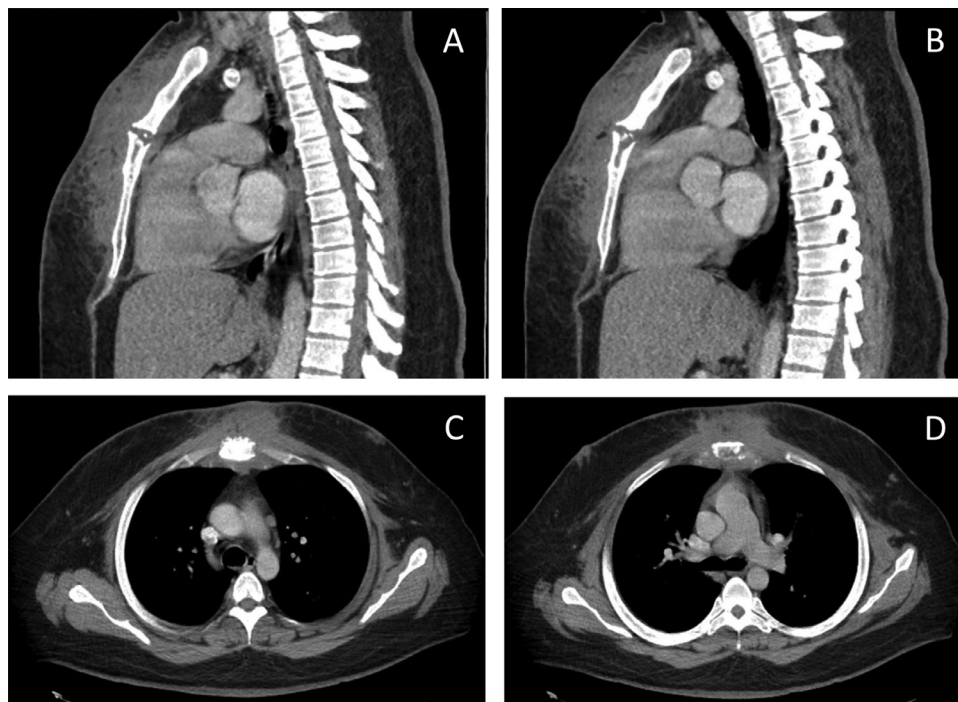


Fig. 2 – Sagittal (A, B) and coronal (C, D) views of the CT chest with IV contrast obtained on admission demonstrate a bony lytic defect in the sternum. There is a phlegmonous area in the subcutaneous tissue anterior to the sternum. Retrosternal thickening is also exhibited. No drainable abscess or fluid collection is seen.

lowed up in the infectious disease and cardiothoracic surgery clinics after discharge, and his condition resolved upon completion of the antibiotic regimen.

Discussion

Osteomyelitis is defined as destructive inflammation of bone due to infection, typically bacterial or fungal in nature [3]. Sternal osteomyelitis is a condition most commonly associated with sternal trauma or cardiac surgery, in which it is

termed secondary sternal osteomyelitis [4]. PSO, on the other hand, is more rare and has no identifiable primary focus of infection [4]. It is hypothesized that PSO arises via hematogenous seeding of the sternum during episodes of bacteremia [5]. There are approximately 100 cases of PSO identified in American literature [6], and our literature review showed 6 more cases reported since 2019. Most cases of PSO are associated with IV drug use and immunocompromising conditions such as HIV [7]. The nonspecific presentation and the paucity of reported cases makes accurate diagnosis and appropriate management of PSO challenging. The mortality rate for PSO is 27% without antibiotic treatment [6], compared to a mor-

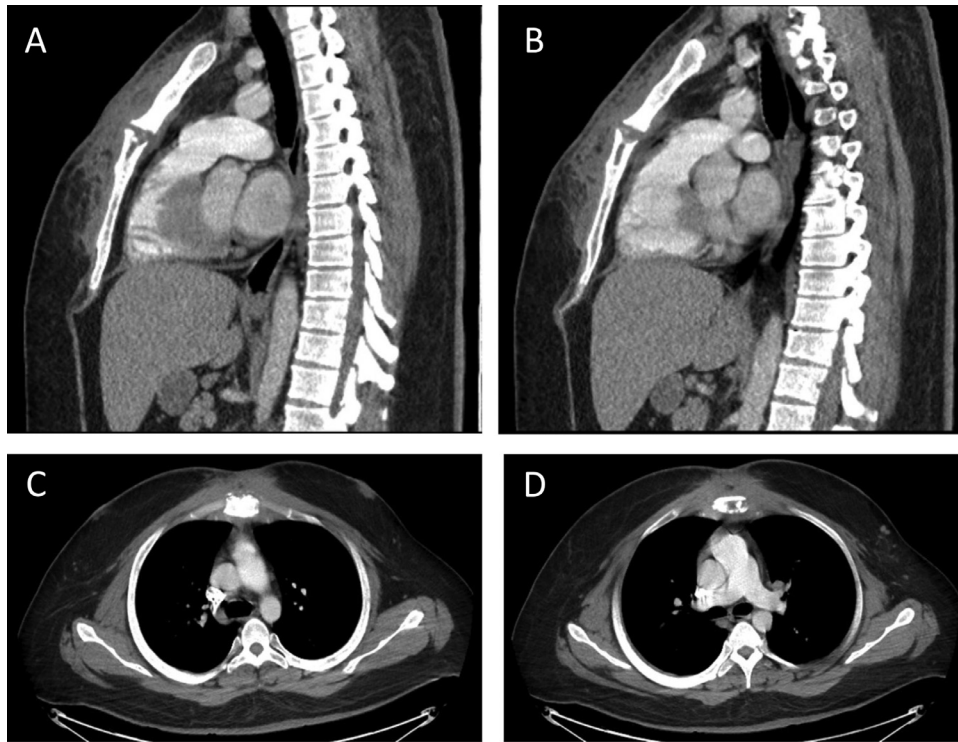


Fig. 3 – Sagittal (A, B) and coronal (C, D) views of the CT chest with IV contrast obtained after 10 days of IV antibiotics. There is interval improvement of the phlegmonous area anterior to the sternum, along with a decrease in soft tissue inflammation.

tality rate of 0% with appropriate treatment, making development of a clinical gestalt for this disease necessary in everyday practice.

In our case report, we outlined the presentation of PSO in a 30 year-old male patient with uncontrolled type 2 DM (A1C of 12.4%) and no other predisposing risk factors. He had no history of HIV or prior IV drug use. He also denied any recent history of trauma to his sternum. Uncontrolled type 2 DM was most likely the major contributing factor in the patient developing PSO, as DM confers a 10.5 times increased risk for PSO [8].

The diagnosis of PSO is based on a combination of different factors, including clinical suspicion, laboratory and microbiologic findings, and radiologic imaging [5]. The differential diagnosis for superficial chest and sternal pain is extensive, including costochondritis, cellulitis, soft tissue abscess, benign soft tissue tumors, and soft tissue or bony sarcoma [9]. The initial diagnostic workup of PSO should begin with a detailed history, with questions focused on the duration of systemic symptoms and any predisposing factors such as type 2 DM, history of IV drug use, or history of HIV. Patients will typically exhibit symptoms such as fever, malaise, and localized pain and erythema of the chest wall [10]. Physical exam should assess for any possible nidus of infection or any subcutaneous fluid collections [10]. Interestingly, our patient presented with anterior chest swelling and erythema, but denied any significant pain to the area upon palpation. Laboratory findings such as leukocytosis and elevated erythrocyte sedi-

mentation rate and C-reactive protein are helpful in the diagnosis of osteomyelitis but lack specificity [11].

There are numerous imaging modalities that can aid in the diagnosis of PSO. Plain chest radiographs may show swelling of the soft tissues and destructive bone lesions; however, plain radiographs have low sensitivity and specificity for osteomyelitis, with bone destruction typically not apparent on plain radiographs until after 10-21 days of infection [10]. Ultrasound, while also of limited use in the diagnosis of osteomyelitis, may be helpful in identifying soft tissue fluid collections or subperiosteal involvement [12]. Ultrasound was performed on our patient to initially characterize the phlegmonous region anterior to the sternum, prior to CT imaging. Nuclear imaging studies may be performed if multifocal osseous involvement is suspected and will show areas of increased radionuclide uptake [13]. CT and magnetic resonance imaging (MRI) allow for greater characterization of the area of osteomyelitis, demonstrating bony destruction, periosteal reaction, articular damage, and soft tissue damage [10]. MRI is the preferred method of imaging, with its high sensitivity and specificity and ability to provide excellent anatomic detail without exposure to ionizing radiation [13]. However, CT allows for superb delineation of osseous changes, and may be superior to MRI for the detection of sequestrum, foreign bodies, or intraosseous gas [13]. Moreover, CT is widely available, is typically less expensive than MRI, and can guide aspiration and biopsy [5]. CT imaging was chosen in our case due to its relative ease and availability at the time of patient presentation.

Microbial cultures are essential in the workup of PSO. Blood cultures are simple to obtain during the initial evaluation of the patient, although they may inconsistently demonstrate growth in osteomyelitis [14]. The preferred method of diagnosis for osteomyelitis is through bacterial cultures obtained from bone biopsy [11]. The most common bacterial cause of PSO is *Staphylococcus aureus*, with *Pseudomonas aeruginosa* common in IV drug users [9]. There have also been pediatric cases of idiopathic PSO caused by organisms other than *S. aureus*, including *Streptococcus pneumoniae*, *Candida albicans*, and *Enterococcus sp.* [4,15]. Interestingly, the patient described in our report had negative blood and bone biopsy cultures. Although our patient stated his symptoms started after a brief episode of community-acquired pneumonia, this was likely coincidental, given the full resolution of his pulmonary symptoms after treatment for pneumonia and lack of significant pulmonary findings on his imaging studies. Moreover, the negative bone biopsy culture may be explained by the fact that the biopsy was performed several days after initiating IV antibiotics. The microbiologic yield of bone biopsies from non-vertebral osteomyelitis can be quite limited, as low as 28% [3]. However, the patient's blood cultures, which were obtained prior to the administration of any antibiotics, perplexingly remained negative for the duration of the patient's hospitalization.

Culture-negative osteomyelitis has been previously documented, mostly in pediatric populations [14]. However, to our knowledge, our patient is the first known case of culture-negative PSO in the literature. Of note, one study found that patients with culture-negative osteomyelitis are less likely to have history of prior trauma, have less prominent overlying skin changes, and have longer duration of pain and other symptoms [14]. This same study also found that cases of culture-negative osteomyelitis can be empirically managed as presumed staphylococcal disease, with low rates of long-term complications.

The mainstay of treatment for PSO is IV antimicrobial therapy. Empiric antibiotics should cover Gram-positive and Gram-negative organisms, and it is important to consider coverage for methicillin-resistant *S. aureus* [16]. Surgical debridement should also be considered in PSO and may be required in patients who present with subperiosteal collection or abscess, necrotic bone, or simultaneous joint infection [5]. Positive blood or wound cultures enable the identification of a causative organism, possibly allowing for de-escalation of the antibiotic regimen. Patients should generally continue on antibiotic therapy for at least 6 weeks [5]. Our patient was empirically treated for Gram-positive and Gram-negative organisms with daptomycin and cefepime, respectively. He was able to de-escalate these IV antibiotics to oral linezolid and oral levofloxacin after discharge, for a total of 6 weeks of antibiotic therapy. Although the patient described in our report had negative culture results, the patient's clinical condition improved dramatically with use of IV antibiotics, without need for surgical intervention. Furthermore, malignancy was ruled out by negative histologic and cytologic examination of samples obtained by CT-guided fine needle aspiration biopsy.

Although PSO is a rare diagnosis, physicians should consider PSO as a diagnostic possibility when evaluating patients with anterior chest pain, given the importance of early recognition and management to reduce morbidity and mortality.

The diagnosis of PSO is multifactorial, involving a thorough history and physical exam, laboratory testing, and imaging findings. Clinicians should have a high index of suspicion for this condition in patients with the appropriate clinical picture and a history of IV drug use or immunocompromising conditions such as HIV or type 2 DM. Patients suspected of having PSO should be started on IV antibiotics with Gram-positive and Gram-negative coverage as soon as possible, and surgical debridement should be considered if the infection is extensive [5,16]. Microbial cultures and CT or MRI imaging of the chest should also be obtained. However, as demonstrated by the patient in our case, the absence of positive microbial cultures does not exclude the diagnosis of PSO if characteristic history, physical exam, laboratory, and imaging findings are present.

Patient consent

Written informed consent was obtained from the patient for the publication of this case report.

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