Role of ultrasound and CT in the early diagnosis and surgical treatment of primary sternal osteomyelitis caused by *Salmonella:* Case reports

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Abstract. Primary sternal osteomyelitis (PSO) caused by *Salmonella* is a rare condition and most commonly associated with sickle cell disease. Only one such case has been previously reported in an infant (age, <1 year) worldwide. The present study reported on two infantile cases of PSO caused by *Salmonella* in the absence of any hematological diseases. A total of two male infants (age, ≤1 year) were referred to our hospital for fever and rapid breathing accompanied by a chest wall mass involving the lower end of the sternum. Imaging findings on CT and ultrasound, which included sternal segment dislocation, lytic destruction and periosteal elevation, confirmed the diagnosis of PSO. Blood and purulent material cultures confirmed that the causative pathogen was *Salmonella*. The infants were completely cured by sequential intravenous and oral antibiotics followed by surgical debridement. The infants remained symptom-free and local recurrence of PSO was not detected at follow-up. PSO caused by *Salmonella* in the absence of any hematological diseases is a rare condition. Unfamiliarity with this disease may lead to a delay in diagnosis and serious complications. The current case report presents two cases of PSO along with a brief overview of the characteristics and management modalities for this condition, and it provides a comprehensive reference for pediatricians regarding this rare disease, particularly in infants.

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Abbreviations: PSO, primary sternal osteomyelitis; US, ultrasound

Key words: primary sternal osteomyelitis, *Salmonella*, infancy, CT multiplanar reconstruction, ultrasound

Introduction

Osteomyelitis induced by a *Salmonella* strain is rarely reported in the literature (1). *Staphylococcus aureus* is the most common causative agent of osteomyelitis and osteomyelitis caused by *Mycobacterium tuberculosi*s is also found in endemic areas (2). Primary sternal osteomyelitis (PSO) caused by *Salmonella* is rare and has typically been associated with sickle cell disease, systemic lupus erythematosus, lymphoma and liver disease, occurring at the extremes of age (1,3). To date, only one case of *Salmonella osteomyelitis* infection of the sternum has been reported in an infant under 1 year of age (4); therefore, clinical experience in the timely diagnosis and management of such cases is lacking. Meanwhile, there is no consensus on the best treatment options for PSO in the pediatric population with respect to long-term outcomes (5). The present study reported on two cases of complicated PSO in infants caused by *Salmonella* in the absence of any hematological diseases. These two cases may be the youngest cases of sternal instability or abscess formation attributed to PSO and treated with surgical debridement reported to date. In addition, the study provided a preliminary discussion on the relationship between the pathogenesis of this rare infectious disease and the physiological and anatomical characteristics of infants. CT multiplanar reconstruction combined with ultrasound (US) is advantageous for the early diagnosis and surgical localization of PSO. Of note, the outcomes achieved with surgical debridement and prolonged antibiotic therapy (6) were satisfactory in the two infants.

Case reports

Case descriptions

Case A. A 12-month-old male infant suffered from fever (maximum temperature, 40.3˚C) and excessive irritability for 2 days. His symptoms did not improve after treatment with an alexipyretic at another clinic prior to admission to the First People's Hospital of Honghe Prefecture in Mengzi, China in August 2018. On physical examination, the patient had a body temperature of 40.0˚C, a heart rate of 150 beats/min, a respiratory rate of 46 breaths/min and a soft lump on the lower

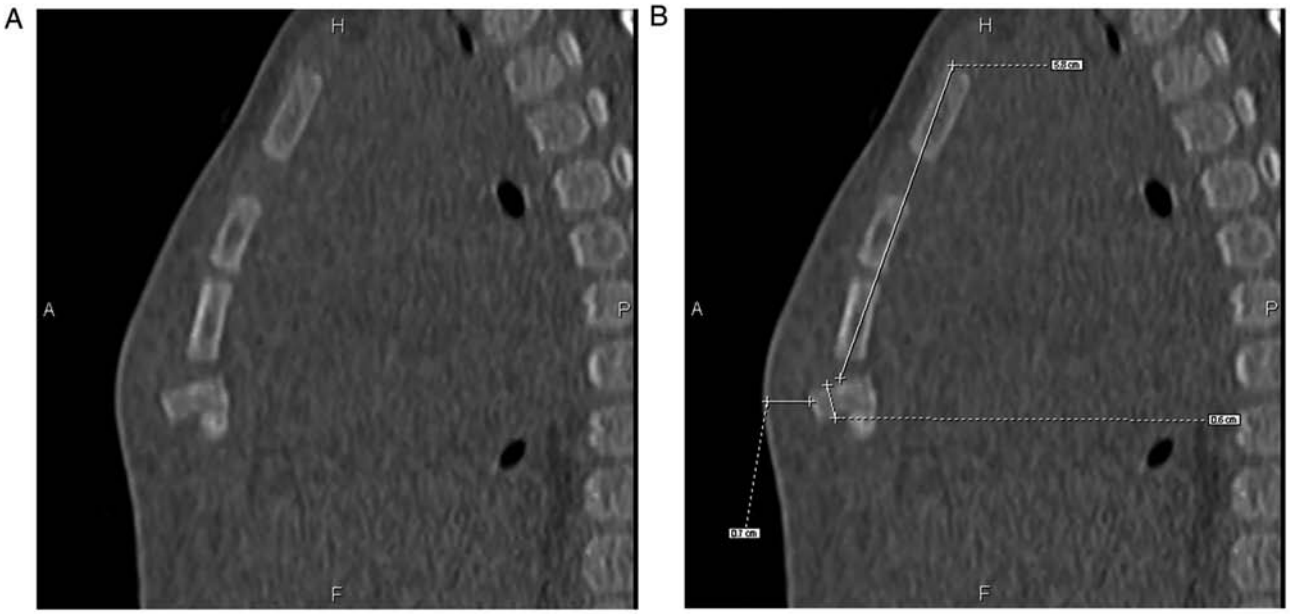

Figure 1. Preoperative CT findings in case A. (A) Multiplanar reconstruction image indicating that the 4th sternebra was rotated 90˚ forward, its margin was rough and the density of the bone cortex was decreased. Soft-tissue swelling of the anterior chest wall was seen. (B) CT measurements: The distance between the suprasternal fossa and the site of dislocation was ~5.8 cm; the thickness of the sternal lesion was ~0.6 cm and the depth of the skin incision to the sternal lesion was ~0.7 cm. A, anterior; H, head; P, posterior.

end of the sternum measuring 2.5 cm in diameter. The unclearly defined swelling was tender and warm with reddening of the local skin. The infant had leukocytosis ($8.69x10^9$/l) with neutrophilia (48.2%, $4.2x10^9$/l) and an elevated level of C-reactive protein (67.8 mg/l). X-ray examination did not indicate any obvious sternal abnormalities. On CT imaging, the 4th sternebra exhibited angular forward dislocation and a decrease in the density of the bone cortex with overlying peripherally enhancing soft tissue was observed (Fig. 1). US suggested that the position of the lower sternum was abnormal and peripheral echo enhancement was observed due to periosteal elevation (Fig. 2). Blood culture was positive for *Salmonella enteritidis* sensitive to cefoperazone-sulbactam sodium and the infant immediately received an intravenous regimen of cefoperazone sodium and sulbactam sodium (40 mg/kg b.i.d).

Case B. A 10-month-old male infant had received anti-infection therapy at another clinic due to fever for 1 week. On admission to the First People's Hospital of Honghe Prefecture (Mengzi, China) in December 2018, the patient had a body temperature of 38.1˚C, a heart rate of 144 beats/min and a respiratory rate of 38 breaths/min. A 2-cm firm but tender mass was detected on the right side of the lower sternum. Laboratory analysis revealed that the complete blood cell count was remarkable for leukocytosis ($19.2x10^9$/l) with 52.5% neutrophils and thrombocytosis ($384x10^9$/l), and C-reactive protein levels were elevated to >81.6 mg/l. CT scans indicated an obviously angled 5th sternebra, lytic destruction of the 4-5th sternebrae and adjacent soft-tissue swelling (Fig. 3). US indicated that the periosteum of the lower sternum was thickened and a 1.6x0.6 cm subcutaneous heterogeneous hypoechoic mass was present (Fig. 4), suggestive of osteomyelitis of the sternum with abscess formation in the adjacent tissue. Although the blood and stool cultures were negative, the infant was treated empirically with intravenous cefoperazone-sulbactam sodium, as described above.

Interventions and outcomes. At ~1 week after antibiotic therapy, decreases in the inflammatory indexes and clinical improvement were observed, and the two patients underwent surgical debridement at this time point. Both cases were assessed by CT multiplanar reconstruction; based on the assessment, a minimally-invasive vertical incision was made close to the site of dislocation on the basis of the distance from the suprasternal fossa to the site of dislocation, and the incision length was also based on the thickness and depth of the sternal lesion (Figs. 1 and 3). The surgical procedures were similar in the two cases. After perforation of the subcutaneous tissue, purulent flow was noted. The portion of the sternum was destroyed due to dissolution. Once the pus was drained from the wound, bony sequestra were detected in the pleural cavity in both cases. Only one oval-shaped bony sequestrum, with an approximate size of 1x1 cm, was detected and removed in case A (Fig. S1). Two sequestra were removed during the debridement process in case B, and both sequestra were irregular in shape and ~0.5x0.5 cm in size.

The upper and lower ends of the sternum were resected until healthy osseous tissue was reached. After sequestrectomy was performed, the wound was flushed with saline and hydrogen peroxide solution. Bilateral muscles around the pus cavity were detached from the adjacent 4-5th costal cartilages with preservation of the primary blood supply. After extension of ~2 cm to both sides, partial flaps of bilateral pectoralis major muscles were neatly created to cover the defect and the wound was closed primarily with a drain.

Intraoperative purulent material cultures were positive for *Salmonella* in both cases and the preoperative antimicrobial

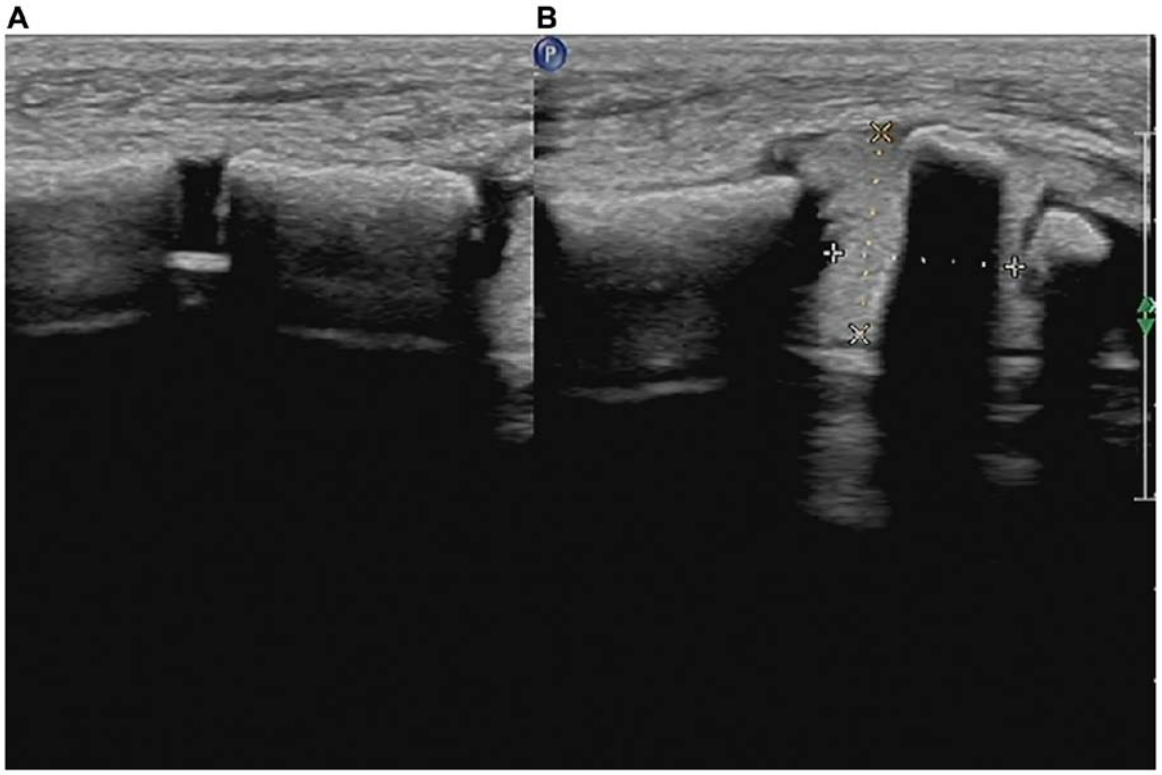

Figure 2. Sternal Doppler US findings in case A. (A) Normal ultrasound image of the superior sternal segment. (B) The position of the lower sternal section was abnormal and the peripheral periosteum displayed with echo enhancement, and the crosshairs indicated the length and width of the sternal lesion.

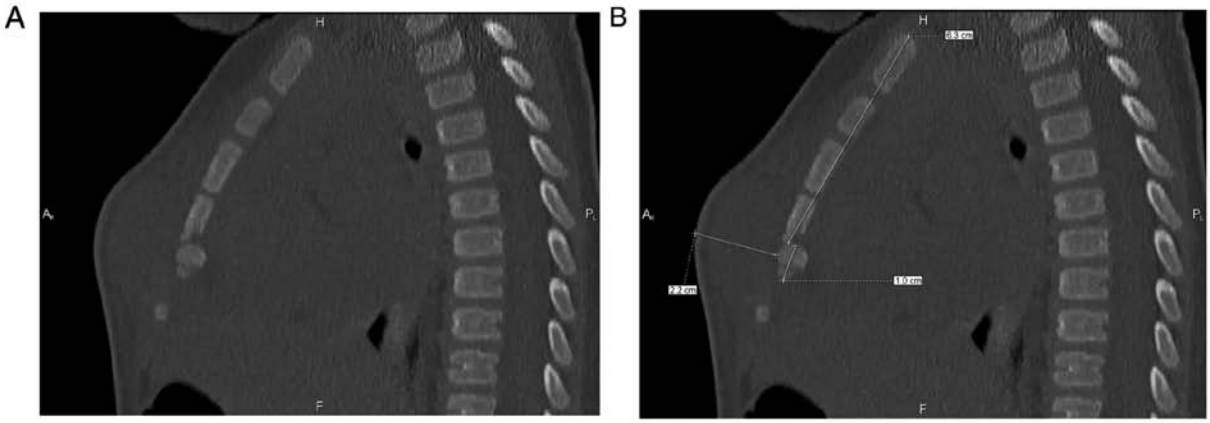

Figure 3. Preoperative CT findings in case B. (A) Multiplanar reconstruction image reveals lytic destruction of the 4-5th sternebra and the boundary of the skin and pulp was not clear. Soft-tissue swelling of the anterior chest wall was particularly evident and it was bulging forward, suggestive of osteomyelitis of the sternum. (B) CT measurements: The distance between the suprasternal fossa and the site of dislocation was ~6.3 cm; the thickness of the sternal lesion was ~1.0 cm; and the depth of the skin incision to the sternal lesion was ~2.2 cm. A, anterior; H, head; P, posterior.

therapy was continued according to the results of the drug sensitivity test (minimum inhibitory concentration=16 μg/ml). Simultaneous culture tests for *Mycobacterium* in both cases provided no evidence of co-infection with other bacteria, including *Mycobacterium tuberculosis*. The same preoperative antimicrobial prescription was administered for 14 days. Once the leukocyte count, C-reactive protein level and neutrophil granulocyte count returned to normal ranges (Table I), the infants were discharged, and oral trimethoprim/sulfamethoxazole was continued for 2 months (1,5). The patients remained symptom-free and local recurrence of PSO was not detected at the one-year follow-up. Follow-up CT scan was performed regularly from 3-6 months, which indicated a local sternal defect without any bony sequestrum or abscess formation in both cases. At the time of publications, no signs of spontaneous closure of the sternal defect had been identified.

Final diagnoses. CT multiplanar reconstruction and US provided evidence of PSO and microbial cultivation revealed that *Salmonella* was the causative agent. Based on these results, a diagnosis of PSO caused by *Salmonella* was established in each case.

Table I. Relevant laboratory data at baseline and at significant time-points for the two cases.

Variable	Normal range	Case A			Case B		
		Admission	Pre-operation	Discharge	Admission	Pre-operation	Discharge
Leukocyte count (10^9/l)	1.0-3.0	8.69	4.7	4.2	19.2	8.3	3.5
C-reactive protein level (mg/l)	0-5.0	67.8	10.6	2.3	81.6	10.8	4.8
Neutrophil granulocyte count (10^9/l)	1.8-7.8	4.2	3.8	3.5	10.1	2.5	3.3

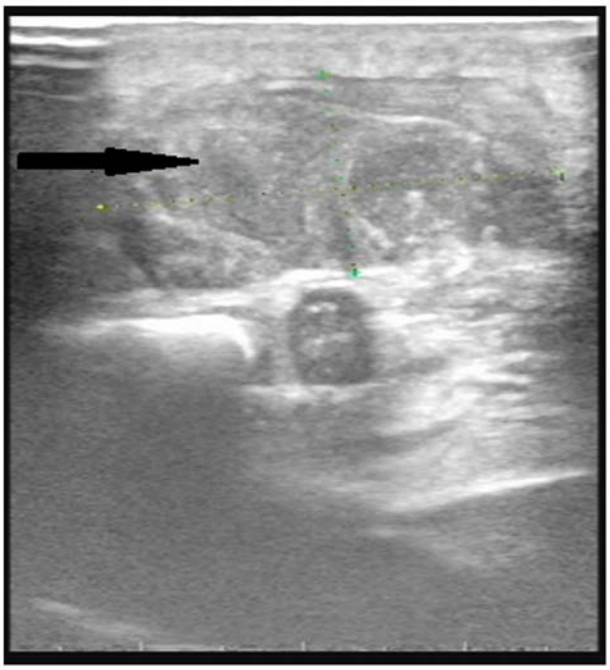

Figure 4. Sternal Doppler US findings in case B. The periosteum of the lower sternum was thickened. The black arrow indicates a 1.6x0.6 cm subcutaneous heterogeneous hypoechoic mass, suggestive of abscess formation.

Discussion

Kingella kingae, Streptococcus pneumonia and *coagulase-negative Staphylococci* have been frequently reported to be pathogenic bacteria isolated from pediatric patients with PSO (4). However, two consecutive cases of PSO caused by *Salmonella* were encountered within 6 months and the ages of these two patients were 10 and 12 months. At this stage of life, infants start receiving supplementary food daily in addition to breastfeeding. With respect to the 10-month-old infant, his parents recalled that the baby had been fed a small amount of shellfish only 1 month prior to the occurrence of fever. The other 1-year-old infant, who lived in a remote mountainous area, may have consumed unsterilized water as a result of poor sanitation and living conditions. Infants and young children are susceptible to *Salmonella* infection through the ingestion of contaminated food or water (7). However, not all infants with *Salmonella* infection develop a clinical manifestation of PSO. It may be associated with non-identification of the etiology of the infection and nonreceipt of effective anti-infective therapy in the early stages of infection, as parents of the infants in the present case report recalled that there was an absence of common symptoms of *Salmonella* infection, including gastrointestinal complaints and diarrhea (8). However, whether this condition occurs as a result of a particular *Salmonella* strain requires further study and observation. Of note, extensive Volkmann canals and a Haversian system are present in the infant sternum (3). As a result, as pathogens are transmitted through the gastrointestinal tract into the blood and bacteremia occurs in an infant, the porous nature of the sternum and abundant bone marrow in the sternum may make it susceptible to hematogenous spread of *Salmonella enteritidis,* particularly in subjects with a weak immune system (4).

The literature review comprised all reported cases of PSO, as it is a rare condition. Its presentation may be nonspecific and the diagnostic value of plain radiography is not reliable (4). MRI, positron emission tomography and single-photon emission CT are reliable modalities for establishing the diagnosis of osteomyelitis, but further research on their diagnostic accuracy in children is required (9,10). In the present cases, these imaging methods were not used due to the disadvantages of harmful ionizing radiation, lack of cooperation by infants, long nursing time and other considerable uncertainties in infants (age, ≤1 year). Although US is only able to reveal outer changes in the bone cortex, cortical destruction and periosteal elevation are visible within a few days after the onset of clinical symptoms of osteomyelitis and osteomyelitis is more obvious on US in the immature bones of children (11,12). CT scanning is also able to clearly visualize the pathological changes of osteomyelitis, such as cortical destruction, heterogeneous bone density and bony sequestration (12). CT with multiplanar reconstruction is suitable for the sternum and is able to display the anatomy in great detail (12). Therefore, US and CT with multiplanar reconstruction were used as the diagnostic means and for the precise surgical localization of the sequestrum or angular displacement in the present cases. Soft-tissue swelling on the anterior chest wall was extensive in these infants and accurate determination of the location of the site of infection was performed to reduce the amount of unnecessary surgical injury.

Although PSO has been managed with antibiotics only in most cases in the pediatric population, the long-term outcomes of this treatment regimen remain undetermined (3,5). Numerous scholars hold the opinion that an aggressive approach should be adopted to decrease the morbidity of indolent osteomyelitis and mediastinitis in complicated PSO (3,5). As a subcutaneous abscess over the anterior chest wall and sternal instability were detected in the present cases, it was

decided to proceed with the aggressive approach. Considering the uninvolved anterior mediastinum and the adjacent costal cartilage, the surgical debridement procedures preserved the posterior periosteum (5) and the wounds were closed by using the medial margin of the pectoralis muscle flaps. Based on the identification and sensitivity of purulent material cultures, *Salmonella* was the causative agent in the two infants. A therapeutic regimen involving sequential intravenous and oral antibiotics was adopted (13); parenteral cefoperazone sulbactam sodium was administered for 2 weeks, followed by oral trimethoprim/sulfamethoxazole for 2 months. At the follow-up, the patients' wounds had healed without any recurrence and CT imaging of the sternum indicated no instability.

Due to the rarity of this disease, most pediatricians have not had the opportunity to attend to and treat such cases (14). Unfamiliarity with PSO may contribute to a delay in diagnosis (4), and the consequences of such a delay may be hazardous due to the seriousness of potential complications, such as fistula formation, indolent osteomyelitis and mediastinitis, as well as erosion of large vessels (5,15). The present study reported on two cases of PSO along with a brief overview of the characteristics and management modalities of this disease, which may serve as a guide for pediatricians regarding this rare disease caused by *Salmonella*, particularly in infants.

In infants who present with fever, elevated inflammatory indices and a chest wall mass, PSO should be highly suspected. If the patient has a history of an unhygienic diet, the possibility of *Salmonella* infection should not be overlooked. CT multiplanar reconstruction combined with US has the practicability and maneuverability to establish an early diagnosis and to achieve surgical localization of PSO in infants. Surgical debridement and prolonged therapy with antibiotics (6) is key to achieving satisfactory outcomes for cases of complicated PSO.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

MQ and YL conceived the study, participated in its design and coordination, and drafted the manuscript. JW, XC, and XP performed the clinical diagnosis and treatment of the patients. SW, ZW, JL, and HO were responsible for the collection and analysis of the experimental data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the ethics committee of The First People's Hospital of Honghe Prefecture (Mengzi, China). All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Patient consent for publication

Informed written consent was obtained from the infants' guardians for publication of their data and images.

Competing interests

The authors declare that they have no competing interests.

References

1. Araiza-Garaygordobil D, Soto-Nieto GI, Aguilar-Rojas LA and Catrip J: Primary sternal osteomyelitis caused by *Salmonella enteritidis*. Enferm Infecc Microbiol Clin 35: 60-62, 2017.
2. Pettas NS, Apostolopoulos AP, Flieger I and Leonidou O: Primary sternal osteomyelitis in a 40 days old infant: A case report and review of the literature. Cases J 2: 7504, 2009.
3. Sayed S, Prabhu S, Thomas M, McBride CA and Alphonso N: Primary sternal osteomyelitis with extensive mediastinal abscess in a neonate. Ann Thorac Surg 100: e85-e87, 2015.
4. Schweitzer A, Della Beffa C, Akmatov MK, Narchi H, Abaev YK, Sherry DD and Pessler F: Primary osteomyelitis of the sternum in the pediatric age group: Report of a new case and comprehensive analysis of seventy-four cases. Pediatr Infect Dis J 34: e92-e101, 2015.
5. Bryant R III, Morales DL and Phalak K: Multimodality therapy for primary sternal osteomyelitis. Pediatr Infect Dis J 28: 73-74, 2009.
6. Muesse JL, Blackmon SH, Ellsworth WA IV and Kim MP: Treatment of sternoclavicular joint osteomyelitis with debridement and delayed resection with muscle flap coverage improves outcomes. Surg Res Pract 2014: 747315, 2014.
7. Thomson RM, Henderson HJ and Smith-Palmer A: An outbreak of *Salmonella* Saintpaul in a Scottish childcare facility: The influence of parental under-reporting. BMC Infect Dis 19: 847, 2019.
8. Ngogo FA, Joachim A, Abade AM, Rumisha SF, Mizinduko MM and Majigo MV: Factors associated with *Salmonella* infection in patients with gastrointestinal complaints seeking health care at Regional Hospital in Southern Highland of Tanzania. BMC Infect Dis 20: 135, 2020.
9. Crone AM, Wanner MR, Cooper ML, Fox TG, Jennings SG and Karmazyn B: Osteomyelitis of the ribs in children: A rare and potentially challenging diagnosis. Pediatr Radiol 50: 68-74, 2020.
10. Llewellyn A, Jones-Diette J, Kraft J, Holton C, Harden M and Simmonds M: Imaging tests for the detection of osteomyelitis: A systematic review. Health Technol Assess 23: 1-128, 2019.
11. Lu CH, Hsiao YF, Hsu HC, Ko YL, Lin TS, Chen LF, Hsieh SC and Li KJ: Can ultrasound differentiate acute erosive arthritis associated with osteomyelitis, rheumatoid arthritis, or gouty arthritis? Int J Rheum Dis 22: 1972-1977, 2019.
12. Sammak B, Abd El Bagi M, Al Shahed M, Hamilton D, Al Nabulsi J, Youssef B and Al Thagafi M: Osteomyelitis: A review of currently used imaging techniques. Eur Radiol 9: 894-900, 1999.
13. Ecury-Goosssen GM, Huysman MA, Verhallen-Dantuma JC and Man P: Sequential intravenous-oral antibiotic therapy for neonatal osteomyelitis. Pediatr Infect Dis J 28: 72-73, 2009.
14. Joshi P, Bavdekar SB and Save SU: A swelling over sternum in a child: Reminder of an uncommon diagnosis. Case Rep Pediatr 2016: 3765786, 2016.
15. Singal R, Singh P, Mittal A, Gupta S, Singla S and Kenwar DB: Primary sternal tuberculous ulcer with dissemination to the bone marrow: A clinical rarity. Ann Saudi Med 31: 542-545, 2011.