

# Salmonella Osteomyelitis of the Rib Mimicking a Mammary Tumor: A Case Report

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Salmonella infection predominantly causes four clinical syndromes: enteric fever, gastroenteritis, bacteremia, and asymptomatic carrier state. Salmonella osteomyelitis is an extremely rare manifestation of salmonella infection except in children with hemoglobinopathies. Salmonella osteomyelitis has been reported to mostly affect the diaphysis of long bones and lumbar spine. Here, we describe a case of salmonella osteomyelitis of the right 6th rib in a 74-year-old woman who presented with breast pain, swelling, high fever and local heat. Her medical history showed myocardial infarction; namely, at the age of 71, the patient had undergone the drug-eluting stent placement in the left anterior descending artery. A computed tomography (CT) scan at the first visit to another hospital showed a mass in the chest that invaded the ribs. <sup>18</sup>F-fluorodeoxyglucose-positron emission tomography-computed tomography imaging showed a lesion suspected to be a mammary malignant tumor. A needle biopsy revealed mesenchymal cells and suspected mammary sarcoma. However, the osteomyelitis of the rib was diagnosed when pyogenic tissue was observed during an open biopsy. The bacterial culture examination identified Salmonella enterica. Surgical drainage and antibiotic treatment were performed. Importantly, there was no evidence for any underlying disease that could lead to an immunocompromised status of the patient. To our knowledge, this is the first report of salmonella osteomyelitis of the rib presenting in an older female that required differentiation from a mammary tumor. Clinicians should consider rib osteomyelitis when they find swelling and local heat in the female's breast tissue and detect no cancerous tissue.

**Keywords:** elderly woman; mammary tumor; osteomyelitis; rib; salmonella Tohoku J. Exp. Med., 2020 August, **251** (4), 273-277.

## Introduction

Acute osteomyelitis is usually hematogenously acquired, and the most common pathogen is *Staphylococcus aureus* (Yoshikawa and Cunha 2002). Chronic osteomyelitis, on the other hand, can be caused by *S. aureus* but is often caused by gram-negative bacteria (Yoshikawa and Cunha 2002). Other microorganisms include *Escherichia coli*, Streptococcus, Klebsiella and Proteus (Zhan et al. 2018). Osteomyelitis caused by Salmonella has been reported sporadically (Hashimoto et al. 2018; Stephanie and Schmalzle 2019; Zhan et al. 2018), but little is known about its pathogenesis. Salmonella can cause a variety of clinical forms, including sepsis, typhoid fever, gastroenteritis, localized organ disease, and asymptomatic chronic carrier state (Zhan et al. 2018). However, salmonella osteomyelitis is

rare, accounting for only 0.8% of all cases of salmonella infection, and is the causal microorganism in 0.45% of all cases of osteomyelitis (Sanchez et al. 1996). Salmonella osteomyelitis is predominantly common in patients with sickle cell disease or thalassemia and immunocompetent (Tóth et al. 2002; Stephanie and Schmalzle 2019). Salmonella osteomyelitis is an infection of the long bones, primarily the diaphysis of the femur and humerus; other bones that are involved include the lumbar spine, tibia, radius, and ulna (McAnearney and McCall 2015). Here we describe a case of salmonella osteomyelitis of the rib in an elderly woman.

## **Case Presentation**

The patient was a 74-year-old woman. The patient had noticed swelling and heat in her right breast for a few

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months and visited a nearby hospital complaining of pain and a mass on the medial side of the right breast five months ago. She also had repeated high fever that regressed spontaneously (37.5-39.0°C). At the age of 71, the patient suffered from myocardial infarction and underwent the drug-eluting stent placement in the left anterior descending artery (#6).

Computed tomography (CT) scan showed a mass in her right breast invasive to the 6th rib (Fig. 1A). Because the doctor suspected the mass was a hematoma, a cytological aspiration examination of the breast mass was performed. Neither hematoma nor tumor cells were identified, but mesenchymal cells were aspirated. After two months, she visited the hospital again because the mass increased rapidly. CT scan was performed again, and the image showed an increased mammary mass and rib destruction (Fig. 1B). She was referred to our department because the previous doctor suspected a mammary sarcoma. Laboratory blood examination showed elevation of inflammatory markers: C-reactive protein (CRP) = 1.126 mg/dl, white blood cells (WBC) =  $4,680/\mu$ l (neutrophils, 66.5%; lymphocytes, 25.6%; monocytes, 6.6%; eosinophils, 1.1%; basophils, 0.2%), and erythrocyte sedimentation rate (ESR) = 95 mm/ h. A needle biopsy of the breast mass was performed. The result revealed only inflammatory cells with no tumor cells. An <sup>18</sup>F-fluorodeoxyglucose-positron emission tomography-CT examination was performed and an accumulation was observed in her right breast near the right 6th rib (SUVmax = 11.91) (Fig. 1C) and the axilla lymph nodes (SUVmax = 3.33) (Fig. 1D). According to the results, we suspected the mass was breast cancer invasive to the 6th rib. At the department of breast surgery, an ultrasound-guided needle biopsy was performed again, and the result showed inflammatory granulation tissue with no tumor tissues. An enhanced MRI was performed and the result showed the lesion in which the surrounding tissue was darkly stained and the center of the lesion was stained relatively poorly, which was suspected of being an abscess in the chest wall involving the 6th rib bone (Fig. 1E). According to the MRI findings, we suspected osteomyelitis and inflammation spread to surrounding the soft tissue.

We performed resection of the affected soft tissues and curettage of the affected rib. We observed granulation tissue and pus through the rib. The resected specimen was reddish yellow (Fig. 2A) and was submitted for pathology examination. Culture of resected tissues revealed *Salmonella enterica*. Histology examination of the granulation tissue revealed infiltrated lymphocytes, plasma cells, macrophages, and partially purulent inflammation of mainly neutrophils (Fig. 2B). We diagnosed salmonella osteomyelitis of the rib. After surgical treatment, we started intravenous drip infusion of levofloxacin 500 mg/day for 7 days and oral medical treatment of antibiotics, levofloxacin 500 mg/day for 2 weeks according to the sensitivity of the salmonella. The chest pain, fever, and chest swelling all disappeared and laboratory blood tests improved (CRP = 0.21

mg/dl, WBC = 3,790/ $\mu l$ , and ESR = 42 mm/h).

This case report is in compliance with the Declaration of Helsinki. The patient provided written informed consent for the publication of this information.

### **Discussion**

Salmonella osteomyelitis of the rib is extremely rare, with only five reported cases (Table 1) (Vartian 1997; Andrianopoulos et al. 1998; Wilson et al. 2005; Zheng et al. 2009; Scarci et al. 2010). This is the first case of salmonella osteomyelitis of the rib in an elderly woman.

In general, salmonella infection causes four clinical symptoms: fever, gastroenteritis, bacteremia with or without metastatic infection, and the symptomatic carrier state (McAnearney and McCall 2015). Previous reports show that salmonella infects the soft tissue of the breast and causes abscesses (Baran et al. 2016; Deshpande et al. 2019). In the present case, the osteomyelitis of the rib was thought to have spilled over into the surrounding soft tissues of the chest. Especially in women, a swelling of the chest needs to be differentiated from a breast tumor.

Salmonella osteomyelitis is often seen in patients with sickle cell disease, other hemoglobinopathies, or compromised immunities such as diabetes mellitus, chronic lymphocytic leukemia, collagen disease, malignancy, and chronic alcoholism (Zheng et al. 2009). Salmonella osteomyelitis also can occur in healthy women with no apparent history, as previously described (Hashimoto et al. 2018).

Osteomyelitis is one of the most common diseases in the elderly because they are potentially immunocompromised (Yoshikawa and Cunha 2002, Huang et al. 2016). The average age of the 18 patients reported was 63.5 years, and 81.8% of patients had underlying immunocompetent status such as being under steroid therapy, malignancy, and immunodeficiency syndrome (Schneider et al. 2009). The current case was the oldest and the only female report compared to previous reports (Table 1). There was no underlying disease in the current case, but the patient might have been potentially immunocompromised due to old age.

In general, hematogenous dissemination has been advocated as a mechanism for the development of osteomyelitis. (Lew and Waldvogel 2004; Kim et al. 2009). Moreover, the ribs also receive blood flow from a branch of the internal thoracic artery (Knudsen et al. 1993). Anatomically, the main trunk of the internal thoracic artery terminates mostly near the 6th ribs and then bifurcate in the intercostal space (Puri et al. 2007). In previous reports of salmonella osteomyelitis, the 6th rib was involved, as also noted in this case (Table 1). It is possible that stagnation of blood flow at the end of the main trunk of the internal thoracic artery causes Salmonella to build a nest.

Previous reports suggested that CT imaging is useful as a diagnostic tool for detecting osteolysis of affected ribs and the spread of inflammation to the surrounding soft tissue (Andrianopoulos et al. 1998; Wilson et al. 2005). In addition, culture tests of turbid pyogenic aspirate, blood,

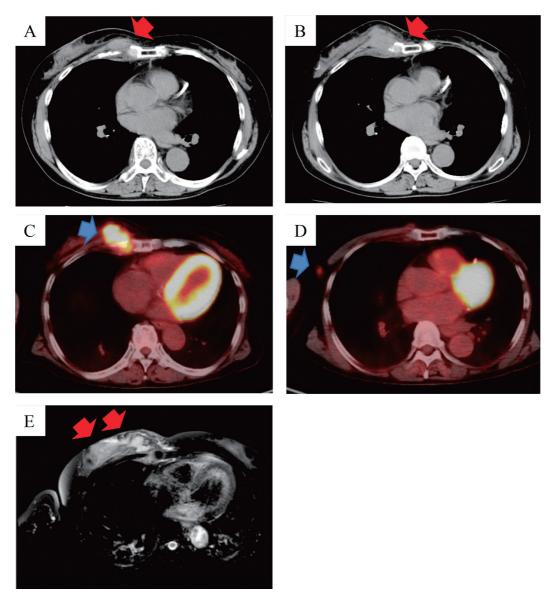


Fig. 1. CT, PET-CT, and MRI findings.

A) Computed tomography (CT) image of the chest at the first visit to the hospital. The right breast shows a mass and suspected rib infiltration (Red arrow). B) CT image of the chest 2 months after the initial diagnosis. The image of a suspected mass of the right breast that increased in size (Red arrow). C) <sup>18</sup>F-fluorodeoxyglucose-positron emission tomography-CT imaging shows accumulation in the right breast tissue (Blue arrow) and ribs, and in D) the right axillary lymph node (Blue arrow). E) Enhanced MRI image shows an occupational lesion on the chest wall involving the right 6th rib (Red arrows). The margins of the lesion are darkly stained, and the center of the lesion is stained relatively poorly. The contrasted extent is wide, suggesting the spread of inflammation.

and tissues are useful for definitive diagnosis (Andrianopoulos et al. 1998; Wilson et al. 2005; Zheng et al. 2009). In some reports, additional histopathological examination of excised tissues was performed for diagnosis (Wilson et al. 2005; Scarci et al. 2010).

MRI images of osteomyelitis often show a penumbra sign, which is useful for the diagnosis (Grey et al. 1998). A penumbra sign is defined as a transitional zone with relatively high signal intensity located between the abscess and sclerotic bone marrow on unenhanced T1-weighted images (Grey et al. 1998). Relative to muscle, the penumbra sign

is isointense on T1-weighted images, enhances on contrast administration, and shows hypointensity on T2-weighted images (Grey et al. 1998; Dartnell et al. 2012).

In this case, a suspicious abscess was detected on an enhanced MRI scan, and a definitive diagnosis was made by a pyogenic soft-tissue culture test, which showed a spread of inflammation.

Although no randomized or case-controlled studies for the treatment of salmonella osteomyelitis have been reported, and there is no consensus for antimicrobial guidelines and indications of surgery for treatment of infection

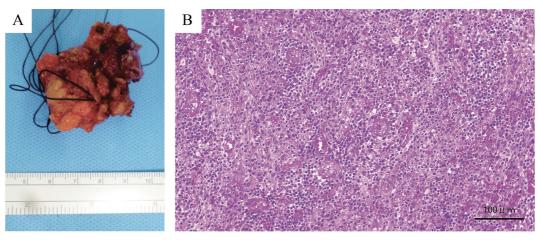


Fig. 2. Excised specimen and pathological finding.

A) Excised soft-tissue specimens are mainly red-yellow and somewhat hard. B) Infiltration of lymphocytes, plasmocytes, and macrophages is present. There is a granulomatous area with enlarged capillaries. Magnification: 200  $\times$ . The scale bar = 100  $\mu$ m.

Table 1. Main features of salmonella osteomyelitis of the rib.

Author and Year	Age (years) and Sex	Past history	Site	Preceding systemic symptoms and duration	Presentation	Diagnosis tool	Operation	Salmonella Type	e Antibiotics
Vartian 1997	59, M	IA and DM	6 <sup>th</sup> and 7 <sup>th</sup> ribs	Decreasing urinary stream and dribbling for few months	Anterior chest wall pain with heating pad and high fever	None	Extensive debridement and removal of ribs	Not identified	Ceftriaxone 1 g, every 12 hours, IV infusion
Andrianopoulos et al. 1997	33, M	None	2 <sup>nd</sup> rib	High temperature for 1 month	Discharging sinus and soft- tissue swelling in the anterior chest wall	CT	Resection of affected rib	Group D	Appropriate antibiotics
Wilson et al. 2005	28, M	None	5 <sup>th</sup> and 6 <sup>th</sup> ribs	High fever, headache, malaise, and vomiting for 7 days	Pain, swelling and redness of the lower costal margin	CT	None	S. enterica serotype typhi	Ceftriaxone 2g, IV infusion
Zheng et al. 2009	42, M	DM	Multiple ribs	High fever for 10 days	Pain of thoracolumbar spine and chest	XRAY and MRI	CT-guided drainage	Group B	IV Levofloxacin <sup>a</sup> and oral SMZco <sup>b</sup>
Scarci et al. 2010	58, M	None	6 <sup>th</sup> rib	Two sinuses for 2 months	Pain and swelling of the chest	None	Debridement and rib resection	S. typhi- murium	Ciprofloxacin
The current case	74, F	MI	6 <sup>th</sup> rib	High fever for a few months	Pain and swelling of the chest and high fever	MRId	Debridement	S. enterica	IV Levofloxacin <sup>c</sup>

IA, inflammatory arthritis; DM, diabetes mellitus; CT, computed tomography; MRI, magnetic resonance imaging; IV, intravenous; MI, myocardial infarction; SMZco, compound sulfamethoxazole; XRAY, plain radiography.

(Scarci et al. 2010), drainage or resection of the affected rib portion and use of antibiotics have been previously described (Andrianopoulos et al. 1998; Wilson et al. 2005). In the current case, we performed curettage of the affected rib and soft tissue with antibiotic (levofloxacin) treatment after the surgery. The maximal curettage of lesions and antimicrobial treatment based on the susceptibility results of the bacterial culture are important.

In conclusion, we experienced a case of rib osteomyelitis in which the inflammation spread into the surrounding soft tissues and it was misdiagnosed as a breast tumor. Only a combination of CT, MRI, and pathology tests revealed the true cause of the patient's symptoms. Thus, clinicians should consider rib osteomyelitis when they see swelling and heat in a woman's breast tissue and detect no cancerous tissue.

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 $<sup>^</sup>a$ dosage 0.5 g × every day;  $^b$ dosage two tablets twice a day;  $^c$ dosage 0.5 g × every day;  $^d$ enhanced using contrast.

## **Author Contributions**

K.H., S.N., D.M., and K.O. managed the case and redaction and correction of the manuscript. M.A. assisted with redaction, correction, and reconstruction of the manuscript.

### **Conflict of Interest**

The authors declare no conflict of interest.

#### References

- Andrianopoulos, E.G., Lautides, G., Papachristos, I. & Papaefthimiou, O. (1998) Salmonella osteomyelitis of the rib. *Scand. Cardiovasc. J.*, 32, 181-182.
- Baran, I., Aksu, N. & Aksoy, A. (2016) Breast abscess due to Salmonella Typhimurium in a patient with rheumatoid arthritis: a case report. BMC Infect. Dis., 16, 348.
- Dartnell, J., Ramachandran, M. & Katchburian, M. (2012) Haematogenous acute and subacute paediatric osteomyelitis: a systematic review of the literature. J. Bone Joint Surg. Br., 94, 584-595.
- Deshpande, A., Dash, L., Pandya, J.S. & Zende, M. (2019) Salmonella paratyphi A infection presenting as breast abscess. *BMJ Case Rep.*, 12.
- Grey, A.C., Davies, A.M., Mangham, D.C., Grimer, R.J. & Ritchie, D.A. (1998) The 'penumbra sign' on T1-weighted MR imaging in subacute osteomyelitis: frequency, cause and significance. *Clin. Radiol.*, 53, 587-592.
- Hashimoto, K., Nishimura, S., Iemura, S. & Akagi, M. (2018) Salmonella osteomyelitis of the distal tibia in a healthy woman. Acta Med. Okayama, 72, 601-604.
- Huang, C.C., Tsai, K.T., Weng, S.F., Lin, H.J., Huang, H.S., Wang, J.J., Guo, H.R. & Hsu, C.C. (2016) Chronic osteomyelitis increases long-term mortality risk in the elderly: a nationwide population-based cohort study. *BMC Geriatr.*, 16, 72.
- Kim, Y.J., Jeon, H.J., Kim, C.H., Park, J.Y., Jung, T.H., Lee, E.B., Park, T.I., Jeon, K.N., Jung C,Y., & Cha, S.I. (2009) Chest wall tuberculosis: clinical features and treatment outcomes. *Tuberc. Respir. Dis.*, 67, 318-324.
- Knudsen, F.W., Andersen, M., Niebuhr, U., Nielsen, P.L. & Krag, C. (1993) The role of the internal thoracic artery in the sternal

- blood supply. Scand. J. Thorac. Cardiovasc. Surg., 27, 3-8.
- Lew, D.P. & Waldvogel, F.A. (2004) Osteomyelitis. *Lancet*, **364**, 369-379.
- McAnearney, S. & McCall, D. (2015) Salmonella osteomyelitis. *Ulster Med. J.*, **84**, 171-172.
- Puri, N., Gupta, P.K., Mahant, T., & Puri, D. (2007) Bilateral internal thoracic artery harvesting; anatomical variations to be considered. *Indian J. Thorac. Cardiovasc. Surg.*, 23, 192-196.
- Sanchez, A.A., Mazurek, M.T. & Clapper, M.F. (1996) Salmonella osteomyelitis presenting as fibrous dysplasia. A case report. *Clin. Orthop. Relat. Res.*, 185-189.
- Scarci, M., Attia, R., Routledge, T. & Harrison-Phipps, K. (2010) Look what's eroding through the chest wall? Salmonella osteomyelitis of the ribs in an immunocompetent adult not associated with sickle cell disease. *Ann. R. Coll. Surg. Engl.*, 92, W59-61.
- Schneider, L., Ehlinger, M., Stanchina, C., Giacomelli, M.C., Gicquel, P., Karger, C. & Clavert, J.M. (2009) Salmonella enterica subsp. arizonae bone and joints sepsis. A case report and literature review. *Orthop. Traumatol. Surg. Res.*, 95, 237-242.
- Stephanie, S. & Schmalzle, S.A. (2019) Salmonella enterica serovar Typhi osteomyelitis in a young adult with sickle cell and thalassemia traits: a possible association. *IDCases*, **15**, e00478
- Tóth, F., Szabó, G., Abed, R. & Lovász, G. (2002) Multifocal simultaneous Salmonella typhi osteomyelitis in an immunocompetent adult. Scand. J. Infect. Dis., 34, 770-772.
- Vartian, C.V. (1997) Salmonella urosepsis complicated by metastatic osteomyelitis of the chest wall. J. Travel Med., 4, 150-151.
- Wilson, G., Prabhu, N., Easow, J.M. & Mukhopadhyay, C. (2005) Ciprofloxacin-resistant Salmonella enterica serotype typhi in a patient with osteomyelitis of the rib. *Med. J. Malaysia*, 60, 667-669.
- Yoshikawa, T.T. & Cunha, B.A. (2002) Osteomyelitis in elderly patients. Clin. Infect. Dis., 35, 287-293.
- Zhan, C., Du, J. & Chen, L. (2018) Salmonella osteomyelitis in a previously healthy neonate: a case report and review of the literature. *Ital. J. Pediatr.*, **44**, 28.
- Zheng, X., Wang, J., Wu, C. & Mehbod, A.A. (2009) Salmonella osteomyelitis of multiple ribs and thoracic vertebra with large psoas muscle abscesses. *Spine J.*, **9**, e1-4.