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Case Report
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Newborn with Primary Sternal Osteomyelitis and Systemic Sepsis Caused by X-linked Hereditary Congenital Neutropenia: A Case Report and Literature Review

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Abstract

Introduction: We present a rare case of neonatal primary sternal osteomyelitis caused by a congenital be X-linked neutropenia.

Case Report: The baby was admitted for the first time at the age of 6 days with neonatal sepsis which recurred after few days along a subcutaneous pre-sternal abscess. After surgical drainage and debridement, the recovery was uneventful.

The baby received 4 G-CSF (Granulocyte Colony-Stimulating Factor) doses in addition to the IV antibiotics according to the microbiological investigations of the abscess material showing *Staphylococcus aureus* (MSSA). Histologically, a severe purulent florid osteomyelitis of the sternum. Follow up with MRI showed small residual infection of the original osteomyelitis with low bone edema, that was sufficiently treated with another IV antibiotic until full resolution of the inflammation.

Genetic analysis was carried out to reveal mutation in the WAS gene. According to protocol, the neonate was sent to the European Working Group of MDS and SAA in children (EWOG-MDS/SAA) for follow up.

Conclusion: X-linked hereditary congenital severe neutropenia should be suspected in neonatal sepsis with the corresponding inflammatory and laboratory parameters. Surgical intervention is adequate but has to follow complete medical diagnosis and protocols.

Keywords: Osteomyelitis; Sepsis; Neutropenia: MSSA

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Introduction

Primary Sternal Osteomyelitis is a very rare and interdisciplinary challenging disease in infants and children. So far, there are very few cases in the international literature. To the best of our knowledge, a newborn with sternal osteomyelitis, anterior mediastinal abscess, leukocytopenia and neutropenia has not yet been reported [1]. Osteomyelitis was treated by surgical debridement and prolonged therapy with antibiotics. The cause of the primary osteomyelitis was an idiopathic neutropenia that turned out to be X-linked hereditary.

We present a case of a newborn with increasing inflammatory parameters without fever and the development of a primary sternal osteomyelitis caused by a congenital neutropenia.

This manuscript was prepared following the CARE guidelines (https://www.care-statement.org).

Case Presentation

After an inconspicuous course of pregnancy, the spontaneous birth took place with 41+1 week of pregnancy under green amniotic fluid. The APGAR score was 9/9/10 after 1/5/10 minutes and pH of 7.24. The birth weight was 3,220 g (12th perc.), the height 52 cm (31st perc.) and head circumference

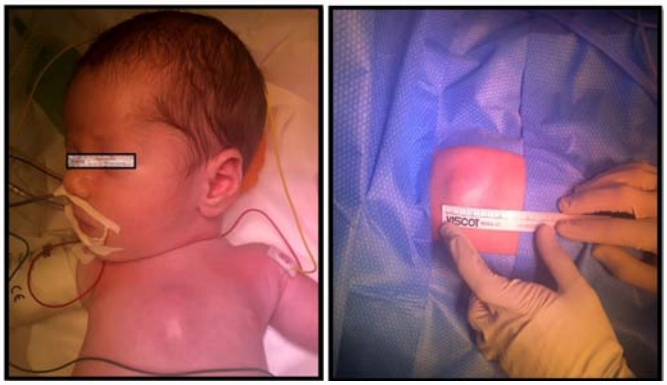

Figure 1 and 2: Frontal view of the fluctuating presternal abscess with 1 cm × 2 cm diameter.

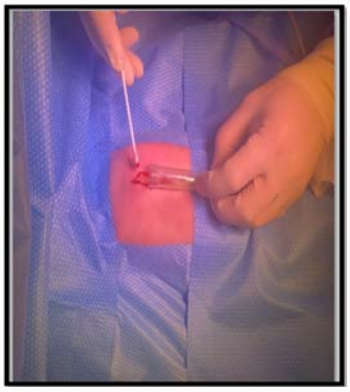

Figure 3: Intraoperative: The abscess was opened and creamy pus was everted and four milliliters of purulent material obtained.

35 cm (24th perc.). Postnatal adaptation was unremarkable.

The patient was admitted to our hospital for the first time at the age of 6 days with suspected neonatal sepsis. Laboratory studies showed leukocytopenia (2.53 G/l) and severe granulocytopenia (0.14 G/l). *Staphylococcus aureus* (MSSA) was detected in a blood culture and the antibiotic therapy with Ampicillin (200 mg/kg/day) and Gentamicin (4 mg/kg/day), started prior to admission was continued. In the following few days, the neonate's clinical condition improved and the granulocytes increased, allowing the patient to be discharged home after 6 days of treatment.

Nine days later, the patient was transferred from a nearby hospital with sepsis and greatly increased infection parameters. The antibiotic therapy with ampicillin and gentamicin was restarted. The patient suffered again from neutropenia (0.11 G/l) and *Staphylococcus aureus* (MSSA) was again detected in the blood culture. On the 5th day of the inpatient stay, a fluctuating swelling occurred over the sternum clinically evident as a pre-sternal abscess with 1 cm × 2 cm in diameter (Figures 1-3).

The imaging diagnostics (MRI, X-ray and sonography; Figures 4-6) confirmed the evidence of a subcutaneous pre-sternal abscess (2.5 cm × 0.8 cm × 3.0 cm) with osteomyelitis to the Corpus Sterni and destruction of the anterior and posterior cortex and an intrathoracic and precardiac infiltration. The antibiotics were switched to cefuroxime (50 mg/kg/day) and the indication for operative abscess drainage and open wound treatment was determined as an emergency intervention under general anesthesia.

During surgery, the abscess was opened, and creamy pus was drained. After debridement of the wound and repeated rinsing with polyhexanide solution and NaCl 0.9% the wound was initially left open, and a wound tamponade was applied. The postoperative course was uncomplicated as feeding was well tolerated. The wound healing was unremarkable without any signs of inflammation.

Staphylococcus aureus (MSSA) was also detected in the microbiological investigations of the abscess material. Histologically, a severe purulent florid osteomyelitis of the sternum was confirmed without any pathological signs of malignancy.

In the control MRI of whole-body 7 days after the operation, a small residual infection (area 4 mm × 3 mm × 9 mm) of the original osteomyelitis with low bone edema was detected. Evidence of further inflammatory foci was excluded. The antibiotic therapy with cefazolin was continued for another 2 weeks until full resolution of the inflammation (Figure 7, 8).

Since a noticeable neutropenia was shown in both inpatient stays and a severe infection were present, the neonate received four G-CSF (Granulocyte Colony-Stimulating Factor) doses which resulted in subsequent but not sustained increase in neutrophil granulocytes.

Furthermore, diagnosis regarding neutropenia was intensified. The flow cytometry and histological examination revealed no evidence of a malignancy but rather of a hereditary form of idiopathic neutropenia was suspected at that point. No granulocytic autoantibodies or alloantibodies could be detected in the mother's blood.

For further clarification, additional blood and bone marrow samples were sent to other reference centers in Germany: Clonal aberrations and myelodysplastic syndrome were excluded.

At this point, "Severe Chronic Neutropenia" (SCN) and auto- or alloimmune neutropenia were excluded. During further genetic analyses the diagnosis of X-linked hereditary congenital severe neutropenia was suspected.

Genetic analysis was carried out at the University Hospital in Tübingen. A mutation in the WAS gene was found. According to the colleagues in Tübingen, variants in the WAS gene have been associated, among other things, with an X-chromosomally hereditary congenital severe neutropenia [2]. Based on the current state of knowledge for a similar case in literature, should be regarded as the probable cause of this disease [3]. The mother was identified as a heterozygous carrier.

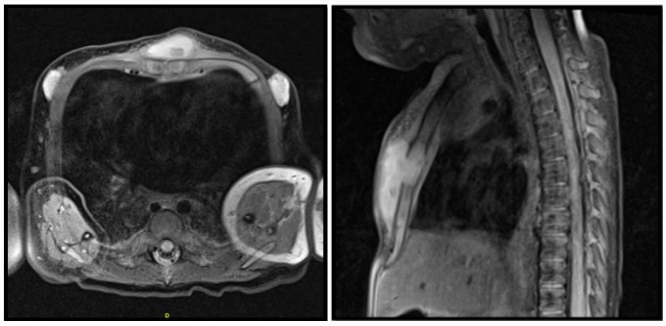

Figure 4 and 5: MRI Thorax: Detection of a circumscribed subcutaneous presternal abscess (2.5 cm × 0.8 cm × 3.0 cm), extension of inflammation/osteomyelitis to the corpus sterni with destruction of the anterior and posterior cortical and infiltration to intrathoracal precardiac.

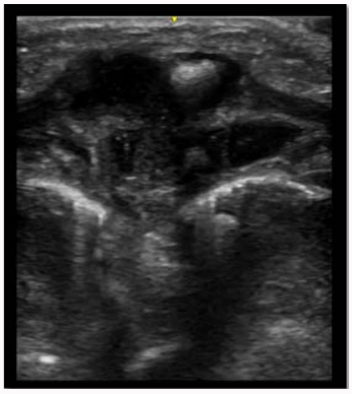

Figure 6: Preoperative Ultrasound: Soft tissue presternally represents a low-echo structure of 2 cm × 0.5 cm. Underneath, the cortical is of the sternum is interrupted. Communication according to retrosternal cannot be ruled out.

Bone marrow examination was also sent to University Hospital Freiburg as part of the European Working Group of MDS and SAA in children (EWOG-MDS/SAA) according to protocol [4].

Currently, at the age of 2 months the patient is symptom-free and does not suffer from any increase of susceptibility in particular bacterial infections. The patient follows the protocol for clinical management of X-linked hereditary congenital severe neutropenia as described [4].

Discussion

Primary Sternal Osteomyelitis (PSO) is a rare condition. Sternal osteomyelitis is defined as primary when a cause of infection such as thoracic surgery, blunt chest trauma, closed cardiopulmonary resuscitation, or subclavian veins catheterization could not be identified [5].

Primary sternal osteomyelitis is a very rare condition in children and especially neonates. In case of recurrent infections in newborns, besides the common causes for neonatal sepsis, an x-linked hereditary congenital neutropenia should be suspected.

The sternal involvement is explained by the "fixation point theory": The slow blood flow through the porous sternal matrix facilitates the settlement of bacterial microthromboses [6]. The porous nature of the sternum, the extensive Volkmann channels and the Haversian system, together with a few reticuloendothelial cells and abundant bone marrow, make it susceptible to hematogenous spread [1].

The most common infectious organism in primary and secondary sternal osteomyelitis are *Staphylococcus aureus* and *Pseudomonas aeruginosa*, the most common infecting organism in intravenous drug addicts. *Mycobacterium tuberculosis* in endemic areas, *Aspergillus fumigatus* in immunocompromised patients, and Candida albicans have also been reported to cause sternal osteomyelitis [7]. Other pathogens have been described in isolated cases, including *Salmonella typhi* in patients with sickle cell disease [1].

Primary sternal osteomyelitis should be considered in children with fever, anterior sternal pain, redness and swelling in the chest area [6]. Other conditions as deferential diagnose such as cellulitis, soft tissue abscess, and tumors, should also be considered, especially aseptic bone infarction in patients with sickle cell anemia [8].

As with other sites of involvement in acute hematogenous osteomyelitis, primary infection of the sternum appears to have a male predominance with a male: female ratio of 2.3:1 [9] and representing only 0.3% of all cases of osteomyelitis in the literature [10].

Osteomyelitis is confirmed by the presence of pus aspirated from bone or the presence of bacteria in blood or bone aspirate culture coupled with suggestive symptoms and signs of bone infection (severe pain and swelling around the infected area, warmth and redness in the infected area). Other symptoms include fever and/or chills; general fatigue; inability to gain weight. Infants may be irritable and lethargic, refuse to eat, or vomit or by radiologic findings consistent with osteomyelitis [8].

Scintigraphy with three-phase ^{99m}Tc-Methylene Diphosphonate (MDP) and magnetic resonance imaging have a sensitivity of 90% and specificity of about 80% for detection PSO. In our patient the MRI provided not only a specific diagnosis, but also excellent preoperative delineation of the extent of soft tissue and bony involvement [9]. Serial ultrasound imaging has also been shown to be useful for monitoring response to treatment and postoperatively [11].

MR imaging is preferred in all these instances for preoperative evaluation of children with osteomyelitis. It has greater spatial resolution than skeletal scintigraphy and can show purulent collections in the soft tissues. Most importantly, contrast-enhanced MR imaging can show intramedullary and subperiosteal abscesses and thus indicate which patients need drainage [12].

Reported treatment options range from prolonged antibiotics for uncomplicated osteomyelitis to surgical debridement in recalcitrant cases. Treatment of sternal osteomyelitis should be promptly started to avoid chest wall deformity and mediastinal extension. Tissue biopsy is mandatory to exclude primary bone pathology and to obtain a microbiological isolate that will direct appropriate antimicrobial

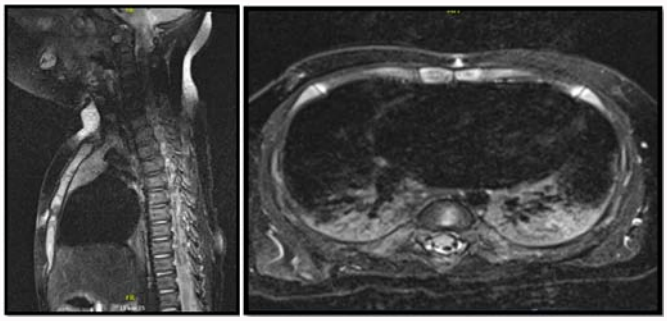

Figure 7 and 8: Postoperative MRI: Findings declining with small residual T2-hyperintense (approx. 4 mm × 3 mm × 9 mm) focus and constantly low bone edema in the middle third of the sternum.

therapy [1].

The presented patient was successfully treated with antibiotics, surgical debridement and open wound treatment. Postoperatively, antibiotic treatment was continued for six weeks until a complete healing has taken place. Classical approaches recommend the antibiotic to be maintained at least 2 weeks intravenously and up to 4 weeks orally [6].

Current clinical management for X-linked Hereditary Congenital Neutropenia includes subcutaneous G-CSF injections every 5 days. Every 2 weeks, the patient is presented to the pediatric clinic for repeated blood counts and once a year to the hematological-oncological outpatient clinic.

The European Working Group of MDS and SAA in children (EWOG-MDS/SAA) is an international registry to gather clinical data and archiving biomaterials that established diagnostic standards for national reference laboratories as well as developing therapy guidelines and basic research [4].

According to protocol, a bone marrow puncture is performed once a year with co-assessment by the EWOG-MDS study as well as a cytogenetic analysis and a somatic mutation analysis, since those patients suffering from severe chronic neutropenia and requiring regular stimulation by G-CSF [13].

According to specialist information, affected patients are susceptible to an increased risk of developing malignant degeneration of the bone marrow (e.g., leukemia or myelodysplastic syndrome).

Conclusion

X-linked hereditary congenital severe neutropenia should be suspected in neonatal sepsis with the corresponding inflammatory and laboratory parameters. Surgical intervention is adequate but has to follow complete medical diagnosis and protocols.

References

1. Upadhyaya M, Keil A, Thonell S, Orford J, Burgner D. "Primary sternal osteomyelitis: A case series and review of the literature." J Pediatr Surg. 2005;40(10):1623-7.
2. National Center for Advancing Translation Sciences and Genetic and Rare Diseases Information Center, "Severe congenital neutropenia X-linked." [Online] 2023.
3. Patil RB, Shanmukhaiah C, Jijina F, Bamborde S, Wasekar N, Toshniwal M, et al. "Wiskott-Aldrich syndrome presenting with JMML-like blood picture and normal sized platelets." Case Rep Hematol. 2016;2016:1-3.
4. European Working Group of Myelodysplastic Syndrome (MDS) and Severe Aplastic Anemia (SAA) in children and adolescents, "Prospective non–randomized multi-center study for epidemiology and characterization of Myelodysplastic Syndromes (MDS) and Juvenile Myelomonocytic Leukemia (JMML) in childhood," [Online] 2006.
5. Kara A, Tezer H, Devrim I, Caglar M, Cengiz, AB Gür D, et al. "Primary sternal osteomyelitis in a healthy child due to community-acquired methicillin-resistant Staphylococcus aureus and literature review." Scand J Infect Dis. 2007;39(5):469-72.
6. Conejo-Fernández AJ, Martín FJG, de SV Merino CM. "Primary sternal osteomyelitis and septicemia in a neonate." Pediatr Infect Dis J. 2013;32(6):704-5.
7. Pettas NS, Apostolopoulos AP, Flieger I, Leonidou O. "Primary sternal osteomyelitis in a 40 days old infant: A case report and review of the literature." Cases J. 2009;2(6):7504.
8. Narchi H. "Primary sternal osteomyelitis in children with sickle cell disease." Pediatr Infect Dis J. 1999;18(10):940-2.
9. Edina M, Chung T, Baker CJ. "Magnetic resonance imaging in a child with primary sternal osteomyelitis." Pediatr Infect Dis J. 2001;20(5):547-50.
10. Jang YN, Sohn HS, Cho SY, Choi SM. "Primary sternal osteomyelitis caused by *Staphylococcus aureus* in an immunocompetent adult." Infect Chemother. 2017;49(3):223-6.
11. Sayed S, Prabhu S, Thomas M, McBride CA, Alphonso N. "Primary sternal osteomyelitis with extensive mediastinal abscess in a neonate." Ann Thorac Surg. 2015;100(4):e85-e87.
12. Jaramillo D, Treves ST, Kasser JR, Harper M, Sundel R, Laor T. "Osteomyelitis and septic arthritis in children: Appropriate use of imaging to guide treatment," Am J Roentgenol. 1995;165(2 399-403.
13. Christensen RD. "Recombinant G-CSF treatment of severe chronic neutropenia in neonates and infants." In: neonatology: A practical approach to neonatal diseases. Buonocore G, Bracci R, Weindling M, editors. Cham: Springer International Publishing, 2018. p. 1561-73.