CASE REPORTS

LONG TERM EVALUATION OF RADIOGRAPHICALLY UNDETECTED ACUTE OSTEOMYELITIS RESULTING CHRONIC OSTEOMYELITIS WITH MRSA

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ABSTRACT

Osteomyelitis is an infection and inflammation of the bone that may spread into all parts of the bone. Methicillin-resistant Staphylococcus aureus or MRSA complicates the management of diseases, 28% of hospitals in Indonesia are suspected to be MRSA endemic. Osteomyelitis combined with MRSA have obscured prognosis knowing its assessment and management are still being developed. Presenting a case of Chronic Osteomyelitis and MRSA of an 11-year old girl that had been monitored for 5 years after the reported onset in July 2015. The patient complained of severe pain in the left hip region causing her to stop using her left limb in July 2015. Signs of acute osteomyelitis couldn't be confirmed by sequential assessments of X-Ray and USG examination. Cefazolin and Gentamicin injections were administered for 23 days. The family requested the patient to be discharged, claiming they were unable to see significant clinical improvement. Intravenous of antibiotic regimens were changed into oral regimens, consisting; Co-Amoxiclav and Gentamicin. The patient was never present for routine check-up, her family conceded that they went to traditional alternative medication and stated the patient's clinical outcomes were showing signs of improvement; in which the patient was able to walk normally. 6 months after, the patient's mother observed abnormal gait, however the patient didn't mention nor complain of anything. Furthermore, an X-ray assessment was performed, with the result of the entire left femoral head being reportedly destroyed. In January 2016 the patient was referred to Dr.Soetomo Hospital, then diagnosed with chronic osteomyelitis and pathological fracture of 1/3 proximal left femur with a suspicion of avascular necrosis. The patient was given prophylactic antibiotics. Closed biopsy couldn't be performed, hence open biopsy was suggested. The patient had routine check-ups to monitor the disease progression, alongside radiologic assessment and laboratory assessments prior to the surgery. Episodes of localised swelling and tenderness in the hip area were present. Scenes of seropurulent discharges were additionally reported. In june 2017 patients had surgical debridement and sequestrectomy in addition to an open biopsy, where MRSA was diagnosed. No antibiotics had been given after the surgery and had routine wash with Chlorhexidine Gluconate 4%. Currently, the patient still undergoes routine check-ups at the outpatient facility, as radiologic and laboratory examination are routinely observed. As of now, the patient has no issue in its daily living activities. However, there is still limited range of movement at the infected site, with 90 degree of hip flexion and constrained internal rotation. A lower limb length discrepancy is present due to local growth aggravation at the left hip. The patient wears a lift modified shoe on her left leg. In any case, there has not been any complaints of pain, swollen or seropurulent releases throughout the last 18 months

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INTRODUCTION

Osteomyelitis is a bone infection that grows from trabecular areas of the bone. This infection could also invade the bone marrow, bone cortex, periosteum and surrounding tissues[1].

Approximately 75% of osteomyelitis is caused by gram-positive *Staphylococcus* that arise from blood vessels or from adjascent soft tissues. In facts, although the most common bacteria causes osteomyelitis are *S. aureus* and *S.epidermidis*, bone biopsy remains the Gold Standard for starting treatment. Biopsy may determine the most sensitive antibiotics, besides to detect MRSA (*Methicillin Resistant Staphylococcus aureus*) or MRSE (*Methicillin Resistant Staphylococcus epidermidis*) as early as possible to eliminate further complication[2].

Some areas have shown higher incidence of antibiotic resistance for osteomyelitis, especially in Asia. Lack of antibiotics regulations have resulted in an increased number of antibiotics abuse, leading to greater transmission and antibiotics resistance. As a result, some Asian countries have one of the highest prevalence of MRSA incidence, it is common for hospitals in Asia to be MRSA endemic. In early 2010s, the estimation of hospitals with MRSA endemic were 28% in Indonesia and Hong Kong and >t-;' 70% in South Korea[3].

In 2016 a research from Dr. Soetomo Academic General Hospital Surabaya -- teaching hospital in Indonesia, showed 8% of all surgery patients suffered from MRSA (including the inpatients). From the results, there is a continuous increase of numbers of MRSA patients within Hospitals in Indonesia[4].

Children with acute osteomyelitis in developing countries often came too late to be treated, due to lack of awareness and proper medical facilities. Not only chronic osteomyelitis that had worsened with multiple antibiotics resistance reported, but also it is also hard to differentiate between osteomyelitis and malignancies. This issue causes chronic osteomyelitis in developing countries to be the main factor of musculoskeletal disabilities and morbidities [5,6].

CASE REPORT

We present a case of chronic osteomyelitis and MRSA of an 11-year-old girl, this patient had been monitored for the last 5 years after the reported onset since July 2015. The patient monitored routinely, routine physical examination and radiologic examination on her left hip region to assesed patient's improvement.

The patient complained of severe pain and continuous pain in the left hip region causing her to stop using her left limb in July 2015. It is reported the patient did not want her left hip region to be touched because it would escalate the pain resulting limited range of movement. The pain decreased when she didn't move her left hip. She had felt this complaint for approximately 1 week. Slight fever also reported. The patient was finally brought to the hospital, physical examination and radiological examination were performed. Signs of acute osteomyelitis couldn't be confirmed from X-Ray and USG examinations (figure 1a and 1b). Patient then referred as an inpatient. Cefazolin and Gentamicin injections were administered for 23 days and her left hip joint movement was limited. After her first week in the hospital, repeated radiologic and USG examinations performed, however signs of acute osteomyelitis couldn't be confirmed from the sequential assessments (figure 1c and 1d). MRI examination was not an option considering the patient's background.

(a)

(b)

(c)

(d)

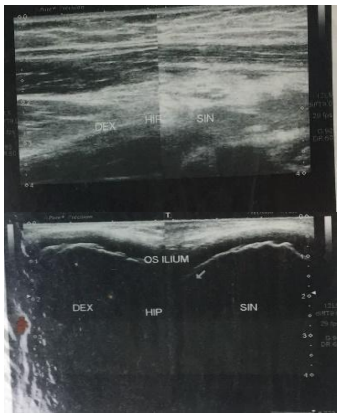

Figure 1. (a and b) First radiological examination, signs of acute osteomyelitis couldn't be confirmed; (c and d) sequential assessments with radiological and USG examination, signs of acute osteomyelitis couldn't be confirmed yet.

The family requested the patient to be discharged, claiming they were unable to see significant clinical improvement. Intravenous antibiotic regimens were changed into oral regimens, consisting; Co-Amoxiclav and Gentamicin. The patient was never present for routine check-up, her family conceded that they went to traditional alternative medication and stated the patient's clinical outcomes were showing signs of improvement; in which the patient was able to walk normally.

Six months later, the patient's mother observed abnormal gait, however the patient didn't mention nor complaint of anything. The patient also reported having difficulties in her P.E. class, limited range of movement in her left hip, especially when squatting. Patient did not complaint about pain, swelling and fever. An X-ray assessment was performed, with the result of the entire left femoral head being reportedly destroyed. In January 2016 the patient was referred to Dr.Soetomo General Hospital, where the patient was then diagnosed with chronic osteomyelitis and pathological fracture of 1/3 proximal left femur with a suspicion of avascular necrosis. (figure 2)

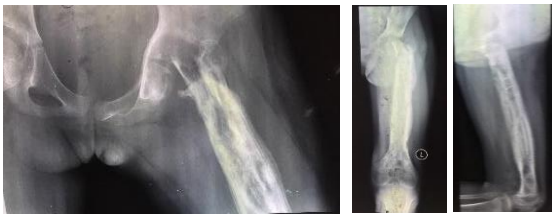

Figure 2 Left femoral head destruction present, accompanied by the sequester and involucrum on the left femur with solid periosteal reaction. Femoral head deformity present. From these images, concluded that the patient had osteomyelitis and a pathological fracture of 1/3 proximal left femur with a suspicion of avascular necrosis on the left femoral head.

The patient was given prophylactics antibiotics. Closed biopsy couldn't be performed, hence open biopsy was suggested. The patient had routine check-ups to monitor the disease progression, alongside radiologic assessment and laboratory assessments prior to the surgery. Episodes of localised swelling and tenderness in the hip area were present. Scenes of seropurulent discharges were additionally reported. Closed biopsy couldn't be performed hence open biopsy was suggested.

In june 2017 patients had surgical debridement and sequestrectomy in addition to an open biopsy, where MRSA was diagnosed. No antibiotics had been given after the surgery and had routine wash with Chlorhexidine Gluconate 4%. Currently, the patient still undergoes monthly check-ups at the outpatient facility for the next 1,5 years, radiologic and laboratory examinations were routinely observed.

RESULTS

As per 19th January 2020, the patient no longer had any issues in its daily living activities. In any case, there had been no complaint of pain, swelling or seropurulent discharges throughout the last 18 months.

There is still limited range of movement at the infected site, with 90 degree hip flexion

and constrained internal rotation, however, according to them these complaints do not really affect her daily activities

A lower limb leg-length discrepancy is present due to local growth aggravation at the left hip. The patient wears a lift modified shoe (orthotic) on her left leg. The patient had already replaced her orthotic once. (figure3)

(a)

(b)

(c)

Figure 3 (a) Limited range of movement is present on her left hip, with 90 degree of hip flexion at best (b) A leg-length discrepancy is present (c) The patient wears a lift modified shoe on her left leg (orthotic).

From the latest radiological examination (Figure 4) Bone trabeculation outside of the lesion, joint gap and the joint surface appeared well. Lucency on distal third of the left femur could be interpreted as a representation of an active lesion.

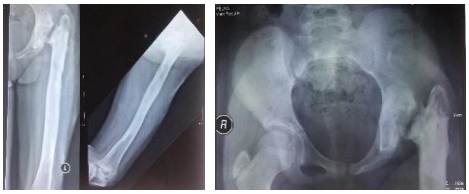

Figure 4 Latest radiological examination

DISCUSSION

There are two hypotheses that are able to explain the pathophysiological findings on children with osteomyelitis, that are Inside Outside Theory and Outside Inside Theory. The focus on Inside Outside theory is the inability of children's immunity to suppress the process of inflammation, and the intramedullary pressure causing sinuses and capillaries suppression which would cause bone infarction. Outside Inside Theory focuses more on the pathogen invasion abilities to enter periosteum causing periosteal abscess, eventually damaging the bone structure[7].

The pathophysiology, radiological description and its classifications are complex due to its connection with multiple factors; such as patient's age, duration, route of infection, immunity and patient's vascular condition on the infected site[6].

Differences in mode of infection, intraosseous vascular anatomy and subperiosteal abscess formation in children caused different clinical manifestations compared to adults. In paediatrics patients, long bones such as tibia and femur are the most common site of infection, whereas on adult patients, axial structures are the most common site. Femur (36%), tibia (33%), humerus (10%) and pelvis (2,8%) are the most common site of infection[,8,9].

Routes of infections are also varied. In children, hematogenous routes are more common[9]. Hematogenous osteomyelitis in long bones frequently attacks the metaphysis, slowing down the blood flow on metaphysis (which is closed with the epiphysis) and directing the microbes deposition that eventually leading to focal infection. Focal infection triggers an inflammatory response that increases the medullary pressure. This pressure can compress cortex and periosteal blood vessels, resulting bone necrosis. Microbial factors also play an important role of the disease progression, Adhesins on *S. aureus* able to identify the molecular matrix that its main function is to connect the polysaccharide structures and have connections to fibronectin, fibrinogen, collagen and heparin which are the structures that maintained the bone matrix. *S. aureus* that is ingested by the osteoclast still could survive and might become more resistant to antibiotics[10]. Osteomyelitis that is essentially a bone marrow inflammation could develop to

osteonecrosis, bone destruction and septic arthritis, ending as a permanent disability[8].

Radiographic presentation of osteomyelitis depends on the clinical presentation and age of the patient[9]. Simple X-Ray imaging has low sensitivity and low specificity to detect acute osteomyelitis. 80% of patients that come at least 2 weeks after the onset will have normal radiographic presentation due to its incapability to detect the spreading infection in the bone tissue. Few osteomyelitis aspects that could be shown by simple x-ray are periosteal reactions, because of the increasing periosteal thickness; tissue swelling visible at least 2 week after the onset and the border between that differs thickness of the bone appears clearly with intraosseous abscess. But these features are not specific on osteomyelitis and could also be seen in stress fracture, bone tumour and tissue's infection. Therefore the radiological examination is possible to postpone for 10 to 14 days from the onset to confirm the diagnosis 8[,9,10].

Ultrasound examination is also limited because of its inability to examine the bone, bone marrow and competence of operator. This examination is decently accurate, fast and adequately effective to compare both extremities, but with its limitations, this examination is rarely used as a first line additional examination. In acute osteomyelitis this examination used mainly to observe the progressing infections in subperiosteal area because of the loosening on the tissue attachments at periosteum. Color Doppler is also able to identify tissue swelling with its ability to locate hyper vascularities around the bone. Ultrasound is also helpful to guide needle aspiration if tissue swelling is observed 7[,9,10]

Although with its limitations, simple x-ray is still the first line examination to confirm acute osteomyelitis and to exclude other diagnoses such as fractures. Simple X-Ray can also be used to observe disease's progression. Simple X-Ray is still recommended as a first step and Ultrasound Examination could performed if needed[,9,10]

The disease causing microbes also contributes to the clinical presentation and the severity of the osteomyelitis. *S. aureus* caused 80% of osteomyelitis, where *methicillin sensitive Staphylococcus aureus* (MSSA) and *methicillin resistant Staphylococcus aureus* (MRSA) are also the two most common pathogens. Some forms of more aggressive osteomyelitis reported caused by MRSA/MSSA, it is known that these two pathogens contain genotype-300, pvl and fnbB that affect fibronectin where this polysaccharide associated with the binding force and severity of infection. Two previous studies in America showed increasing numbers of osteomyelitis incidents and more severe cases are associated with higher prevalence of MRSA and most of them are community acquired. Higher incidence of MRSA infection associated with extra-osseous events, increasing number surgical intervention and duration of hospitalization. At the same time, the more severe the infection contributes to longer duration of hospitalization. Where osteomyelitis is not treated adequately, chronic osteomyelitis could develop into osteonecrosis, intraosseous disruption and disruption of periosteal vascularization 7[,8,10].

CONCLUSION

Acute osteomyelitis is a clinical diagnosis. Simple X-Rays need to be routinely performed in inpatients, with an addition of Ultrasound Examination. Thorough and intensive education plays important role for the patient and patient's family to achieve comprehensive understanding of the disease. For some cases in which the diagnosis is not yet confirmed, complete and accurate treatments are supposed to prevent bone necrosis, later contributing to the formation of irreversible leg-length discrepancy and limited range of movement with the result that permanent limited daily functions.

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