

Successful Diagnosis and Treatment of Acute Osteomyelitis in Children: A Retrospective Analysis: Are Severity Scores Help?

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Received: 28 Sep 2021

Accepted: 13 Oct 2021

Published: 19 Oct 2021

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Citation:

Brunner J, Successful Diagnosis and Treatment of Acute Osteomyelitis in Children: A Retrospective Analysis: Are Severity Scores Help?. *J Clin Med Img.* 2021; V5(17): 1-3

1. Introduction

Acute Osteomyelitis (AOM) during childhood presents with a variety of clinical symptoms and laboratory findings. The incidence of AOM has been reported retrospectively by former studies and showed a decreasing as well as an increasing incidence depending on the evaluated geographical area [1]. AOM is usually caused by bacterial infection following haematogenous distribution spread or by direct inoculation from trauma or surgery [1-3]. An acute haematogenous osteomyelitis is defined via onset of symptoms less than 14 days before [Riise, 2008] [1]. The most common causative bacteria worldwide is *Staphylococcus aureus*, followed by *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Kingella kingae* and *Pseudomonas aeruginosa* [2, 4, 3]. Before the area of antibiotics AOM caused high morbidity and mortality rates [3,5]. In the last decade an emerge of AOM caused by Multi-drug Resistant *Staphylococcus Aureus* (MRSA) was detected during the last years in many countries [2,4,3,6]. MRSA as causative agent of AOM in children is associated with an increase in severity of illness caused by an increase of complication rates (deep venous thrombosis, septic pulmonary embolism, deep abscesses) [4, 7,8,9]. In many cases of acute osteomyelitis the blood culture remains negative [2, 4, 3, 6, 10]. The diagnosis of AOM is based on characteristic clinical symptoms, laboratory findings and radiographic findings. C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR) and White Blood Cell counts (WBC) are used to objective clinical findings and were described as a severity of illness scoring system [6,10,4]. Despite all attempts to ascertain a scoring system for AOM, currently no consistent severity scoring system exists.

The current study was aimed to analyze retrospectively changes in pathogens patterns and antibiotic resistance patterns in our geographical area, and to evaluate the role of objective clinical signs, laboratory findings and medical imaging according to recently published severity of illness scoring systems described for AOM. A further aim was to prove the efficacy of the current evidence-based clinical diagnosis and treatment guidelines which were used in the study .

2. Material and Methods

Retrospectively all cases of AOM from January 2001 to December 2011 were evaluated. Data on CRP, WBC ESR, blood culture results, antibiotic therapy, length of hospital stay and radiographic findings were obtained retrospectively from the electronic charts. Patients were included in our study when they showed clinical signs of an AOM and an AOM defining pathology was detected by medical imaging (MRI, ultrasound, X-ray). Exclusion criteria were: certain medical conditions (oncological underlying disease (Ewing sarcoma, h amangioma), postinfectious arthritis), lacking pathologies in the medical imaging, patients who were diagnosed at our hospital but were treated elsewhere and, patients with chronic osteomyelitis. All children were admitted to a multidisciplinary ward and no admission to an ICU was needed. For statistical analysis SPSS®-Statistic (von IBM Inc®, USA, Version 20, 2011) was used. Differences of dichochrome varibales (e.g. TCR diversity distribution) were compared using Chi Square test. To correlate specific CRP, WBC, ESR, chronological age, blood culture results and length of hospital stay spearman rank correlation coefficient was used. P-values less than 0.05 were considered as statistically significant.

The study was conducted in accordance to Good Clinical Practice guidelines, the Declaration of Helsinki 2008

3. Results

3.1. Study Population

Sixty-five children were admitted to our clinic with AOM during the study period. Twenty two cases were excluded. Thirty patients (19 boys, 11 girls) were included into our study. The average age was 6.50 years (\pm 5.16 years, median 6 years, range 1 day – 16 years). In ten cases a positive blood culture was obtained. The most common pathogen was *Staphylococcus aureus* (6 cases), followed by coagulase negative staphylococci (2 cases), 1 case of *Moraxella catarrhalis* and 1 case of *Enterococcus* sp..

In eighteen cases the blood culture remained negative. In two cases no blood culture was sent. No MRSA was detected.

All patients were haemodynamically stable at hospital admission. The mean initial CRP was 9.50 mg/dl (\pm 11.32, median 3.80 mg/dl, range <0.09 – 33.00 mg/dl). According to initial CRP no significant difference was detected between blood culture positive versus blood culture negative cases. In eighteen cases of AOM an ESR was measured. The mean value after one hour was 45.68 mm/h (\pm 43.55, median 31.00 mm/h, range 3.00 – 138.00 mm/h). Accord-

ing to initial ESR no significant difference was detected between blood culture positive versus blood culture negative cases. The mean initial WBC count was 9.73 mg/dl (\pm 5.19, median 8.90 mg/dl, range 4.00 – 24.00 mg/dl). According to initial WBC counts no significant difference was detected between blood culture positive versus blood culture negative cases (Table 1).

Patients were treated regarded our evidence-based treatment guidelines. The mean length of intravenous antibiotic therapy were 16.85 days (\pm 7.21, median 14.00 days, range 7.00 – 31.00 days). Patients were treated with oral antibiotics for a mean of 36.40 days (\pm 38.73, median 21.00 days, range 4.00 – 179.00 days). The longest duration of hospital stay was 95 days in a preterm infant due to other underlying conditions (bronchopulmonary dysplasia). The mean length of hospital stay in AOM with a positive blood cultures were 27.42 days (\pm 24.05, median 21.00 days, range 5.00 – 95.00 days). The mean length of hospital stay in AOM with a negative blood culture were 13.84 days (\pm 11.63, median 14.00 days, range 1.00 – 62.00 days). The mean length of hospital stay according to positive versus negative blood cultures ($p=0.016$) showed. significantly difference. No correlation was found according to CRP values, WBC and leukocyte counts.

Table 1: Characteristics of AOM in patients with positive blood culture (n=10) versus negative blood culture (n=18)

	Positive blood culture	Negative blood culture	p-value
Gender (Male/Female)	17/14	9/3	
Age (years) Mean values on admission	6.26 \pm 4.75; 6.00 (0.00-14.00)	8.08 \pm 5.66; 9.50 (0.00-16.00)	0.336
C- reactive protein (mg/dl)	8.36 \pm 10.36; 3.93 (<0.60-30.00)	7.30 \pm 10.53; 2.54 (<0.60-27.00)	0.786
Erythrocyte sedimentation rate (mm/h)	45.40 \pm 40.42; 41.00 (3.00-138.00)	46.00 \pm 36.63; 30.00 (20.00-108.00)	0.976
White blood cell count (/ μ l)	9.48 \pm 5.10; 8.90 (4.00-21.00)	9.46 \pm 5.66; 7.95 (5.00-24.00)	0.855
Duration of treatment Intravenous (days)	15.96 \pm 8.22; 14.00 (1.00-32.00)	25.58 \pm 13.31; 23.50 (5.00-51.00)	0.016
Oral (days)	58.55 \pm 57.62; 30 (21.00-179.00)	25.77 \pm 18.16; 21.00 (4.00-91.00)	0.93

Notation: values are given as mean \pm standard deviation; median (range); p-value <0.05 are considered as statistically significant

4. Discussion

There is clinical evidence that severity of AOM in children leads to different ways of treatment (surgical treatment, conservative antibiotic only treatment) [4, 6, 10, 8, 11]. In our study no patient suffered from a severe osteomyelitis due to the fact that no patient needed surgical treatment or restoration. Former studies detected a great variability of severity of AOM in children [4, 6, 10, 8, 12]. Variations may be caused by different geographic areas and connected local epidemiology of bacteria and antibiotic resistance patterns. *Staphylococcus aureus* is worldwide detected as one of the leading pathogens causing AOM during childhood [2, 4, 3, 13]. Former studies of a finish group suggest that lower degree of severity of AOM is detected in countries with a lack of MRSA within the geographic area [6,10,12,4]. This supports our data, which show that antibiotic treatment without surgery is effective in patients suffering from moderate AOM. Former studies showed that MRSA is more likely to cause complications like

subperiosteal abscesses or pathological fractures [10].

It was reported before, that AOM with a negative blood culture result were treated shorter regarding to a slightly milder disease [10]. However no accepted severity schedule as well as no representative treatment recommendation exists for blood culture negative AOM cases. It is still unclear if patients with a blood culture negative AOM may need shorter antibiotic treatment when compared to blood culture positive patients. A recent study recommended 16 days of oral antibiotic therapy following adequate response to 3-4 days of intravenous antibiotics in children with uncomplicated osteomyelitis [2]. One limitation of these study is that no criteria for an adequate response are given.

Another consideration in choosing the right treatment is to focus on laboratory findings and clinical parameters which could be determined within the first few days after hospitalization. We showed that although no significant difference was detected according to CRP values of blood culture positive versus blood culture negative

patients slightly higher initial CRP values were detected in blood culture positive patients. One limitation of our study is the small number of patients enrolled. However, it must be considered that children initially presenting with mildly elevated CRP might gain higher CRP values 24-48 hours later [4]. In contrast to other findings we detected more blood culture negative AOMs than former studies [6,10,12,4]. Copley et al predict that children with blood culture negative AOMs suffer from more severe AOM. It is discussed if blood culture negative AOM cases should however be considered to be MRSA positive and if treatment schedules should therefore be adopted [10, 4, 14]. One limitation of our study might be that our first-line therapy includes cephalosporines and fosfomycin as intravenous agents. Another limitation of our study is that no patient showed any radiological signs of a severe osteomyelitis and therefore no patient underwent primary surgical procedures.

No significant difference was detected according to the length of hospital stay when blood culture negative and blood culture positive cases were compared. A former study dealing with a severity of illness scoring system, showed that children with a low severity score are discharged earlier regardless of CRP values leading to a decrease in length of hospital stay [4].

5. Conclusion

In conclusion CRP, BSR and WBC are early available parameters for severity of AOM. We showed that blood culture negative AOM and blood culture positive AOM in our geographic area present with the same distribution of pathogens and antibiotic resistance patterns with no major differences in needed first-line treatment schedules and prognosis.

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