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Utility of magnetic resonance imaging in the follow-up of children affected by acute osteomyelitis.

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Abstract

Acute osteomyelitis is characterized, especially in children, by high morbidity due to extension of the infectious process or its chronicization. No guidelines exist for the post-discharge follow-up of children affected by acute osteomyelitis, especially regarding the utility of magnetic resonance imaging (MRI). To investigate if MRI is useful in the follow-up of AO pediatric patients.

We reviewed medical records and MRI studies of children admitted to our Pediatric Department for acute osteomyelitis from 2008 to 2015. All children who had a follow-up MRI performed at least 10 days after diagnosis were included in the study. We analyzed if MRI follow-up prompted a change in patients' treatment.

A total of 28 MRI studies were performed in 27 children (13 males and 14 females). Infection involved the appendicular skeleton in 64.3% of patients. Five (18%) of these studies prompted a change in patients' treatment. The only statistically significant indication for change in the therapeutic approach was MRI performed for persistence or worsening of the disease (p=0.0058). Change in bone signal at MRI, and time interval (more or less than 28 days) between MRI at diagnosis and at follow-up were not significantly associated with change in the patients' treatment (p=0.40; p=0.40, respectively).

Routine MRI follow-up is not useful in children affected by acute osteomyelitis who adequately respond to antibiotic treatment. It can be useful, in adjunct to clinical evaluation, in non-responders patients. Clinical monitoring remains the mainstay in the follow-up of these patients.

Keywords: Acute osteomyelitis, Magnetic resonance imaging, Children, Follow-up.

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Introduction

Acute Osteomyelitis (AO) is an inflammation of the bone generally due to bacterial infection, which affects the bone by the haematogenous route, by secondary inoculation or consequently to the spread of a contiguous infectious process [1]. Incidence of AO in the pediatric population is estimated to be 13-20 cases/100.000 children/year in the *high income* countries and 43-200 cases/100.000 children/year in the *low income* countries [2]. Incidence of AO in the overall population has increased in the last decades [3]. AO generally resolves with proper antibiotic treatment; nevertheless, it may be associated with the development of complications or evolution to chronic osteomyelitis, with permanent sequelae and disabilities. Diagnosis of AO is based on clinical findings, laboratory investigations, isolation of the causative agent, and imaging studies. Among these, Magnetic Resonance Imaging (MRI) is actually the diagnostic *gold standard*, since it precisely defines localization and severity of the bone infectious process, the eventual involvement of contiguous juncture, growing cartilage or soft tissues [4]. MRI has high sensibility and specificity in the diagnosis of AO in children, and is particularly useful in the pediatric population as it allows to reduce children's exposure to ionizing radiation [2,5]. On the other hand, MRI is expensive, scanning time is long and there is the need for sedation in infants and toddlers, who cannot maintain a fixed position for such a long time. Whereas the crucial role of MRI in the diagnosis

of AO is well recognized, the indications for its use in the patient's monitoring during the post-discharge follow-up are instead not similarly clear. Some studies performed in the adult population failed to demonstrate the utility of MRI in the follow-up of patients affected by AO as it did not correlate with clinical findings [6-10]; on the contrary, in some cases, the use of MRI resulted in the performance of unnecessary therapeutic procedures. Clinical and laboratory parameters may be useful in selecting patients who may benefit most from the MRI studies during follow-up [11]. To date, there is only one retrospective study performed in children affected by AO evaluating utility of MRI in the follow-up of their disease. Only 11 MRI studies out of the total 104 performed prompted a change in patients' treatment; suggesting its only limited role in the routine surveillance of children affected by AO [12]. We performed a study investigating the usefulness of MRI in the follow-up of AO pediatric patients.

Materials and Methods

We conducted a retrospective study including children and adolescents admitted to the Pediatric Department of Vittore Buzzi Children's Hospital in Milan with a diagnosis of AO between January 2008 and January 2015. After a review of clinical records, we identified 39 patients. The only inclusion criterion was the performance of at least one MRI study during the follow-up of the disease, at least 10 days after the diagnosis. Age ≥ 18 years, time interval ≥ 1 year between MRI at diagnosis and at first follow-up, suspected or confirmed tubercular osteomyelitis, subacute or chronic osteomyelitis, were the exclusion criteria. Based on these criteria, we enrolled in this study a total of 27 patients. We obtained written informed consent by parents or legal guardians of the all the subjects included in the study. We analyzed clinical, laboratory and imaging findings for all included patients at the time of the diagnosis and at follow-up points. We reviewed the follow-up orthopedic evaluations and classified the indications for repeating MRI as follows: by routine or by clinical indication for persistence or worsening of the disease. We collected all C-reactive protein (CRP) values (mg/dl) performed at the diagnosis and concomitantly with the MRI follow-ups. MRI studies were reviewed by an expert radiologist who classified them according to the following four parameters: presence and type of pathologic bone signal, presence of abscess, involvement of soft tissues, involvement of the adjacent juncture for appendicular AO or of the intervertebral disc in case of spinal AO. We determined that the patient underwent a treatment change after the repeat MRI if antibiotic treatment was modified and/or duration of therapy was prolonged above the expected time, and/or if surgical procedures (abscess drainage, biopsy) were performed. We also considered the association between treatment change after repeat MRI and indication for repeating MRI, time interval between MRI studies at diagnosis and follow-up, and values of CRP. We performed a descriptive statistical analysis and results are expressed as mean ± standard deviation (± SD). Variables correlations were investigated using the two-tailored Fischer's exact test, with level of significance <0.05. Statistical analysis was performed with IBM SPSS Statistics 20 and Stata release 13 software. The study was approved by local Ethical Committee.

Results

The population included in the study was made up of 27 children, 13 males (48.1%) and 14 females (51.9%). Mean age (± SD) at diagnosis was 4.4 years (± 4.2), ranging from 0 to 13 years. A MRI study was performed in all 27 children at diagnosis, one patient was affected by multifocal AO (tibia and cuboid bone) and so the total number of MRI studies was 28. AO was localized in the axial skeleton in 10/28 (35.7%) cases and in the appendicular skeleton in 18/28 (64.3%) cases. Infection sites and characteristics are summarized in Table 1. At diagnosis, blood examinations were performed in all children, mean white blood cell count was 12037/μL (±4574), mean CRP dosage was 6.5 mg/dL (± 7.7) (normal value<0.8 mg/dl), mean ESR was 44.8 mm/h (± 18.5). Blood culture resulted positive in 5/27 (18.5%) cases, culture of the synovial fluid resulted positive in 4/7 (57.1%) cases. Globally, cultural specimens retrieved a positive result in 24% of cases. Microorganisms isolated from cultural examinations are reported in Table 2. All children were treated with antibiotic therapy for a mean total duration of 33 (± 7) days; the most frequently prescribed antibiotic was ampicillin-sulbactam (78%), followed by vancomycin (22%). 1 MRI study was performed at follow-up in 10 patients, 2 MRI studies in 14 patients, 3 MRI studies in 4 patients, resulting in a total of 50 MRI studies performed during the post-discharge follow-up. Giving the differences in the number of follow-up MRIs among patients, for the statistical analysis, we

Table 1. *Sites and characteristics of bone infections*

Site of infection	N=28 (%)	Abscess	Soft tissues	Intervertebral disc
Appendicular skeleton	18 (64.3)	5 (27.8)	17 (94.4)	10 (61.1)
Foot	12 (42.9)	2 (16.7)	11 (91.7)	6 (50)
Tibia	5 (17.9)	2 (40)	5 (100)	4 (80)
Femur	1 (3.6)	1 (100)	1 (100)	0 (0)
Axial skeleton	10 (35.7)	3 (30)	10 (100)	5 (50)
Spine	9 (32.1)	2 (22.2)	9 (100)	5 (55.6)
Pelvis	1 (3.6)	1 (100)	1 (100)	0 (0)

Table 2. *Microorganism isolated by cultural studies*

Culture specimen	N=27	%
Blood	27	100
Positive	5	18.5
- *Methicillin-sensitive staphylococcus aureus (MSSA)*	2	
- *Methicillin-resistant staphylococcus aureus (MRSA)*	2	
- *Streptococcus pyogenes*	1	
Negative	22	81.5
Synovial fluid	7	25.9
Positive	4	57.1
- *Methicillin-sensitive staphylococcus aureus (MSSA)*	4	
Negative	3	42.9

considered only the 28 MRIs performed at the first follow-up. After the first follow-up MRI, a treatment change, in terms of antibiotic change and/or prolongation of expected therapy, was performed in 5/28 patients (18%). Bone signal has worsened or has remained unchanged in 12/28 (43%) patients; in 3 of these patients a treatment change was subsequently performed. In the remaining 16 MRI studies, bone signal has improved or completely resolved; nevertheless, in 3 of these patients a treatment change was subsequently performed. The association between worsening of bone signal at follow-up MRI and antibiotic change and/or treatment prolongation was not statistically significant (p=0.40). In only 1 patient, the treatment change consisted of a surgical procedure; for this reason, we did not perform a statistical analysis. In 20/28 (71.4%) patients, the first follow-up MRI was routinely performed, among these, bone signal has improved or resolved in 12 cases, whereas it has worsened or remained unchanged in 8 cases. Among these patients, antibiotic was changed and/or therapy was prolonged in only 1 case. In 8/28 (28.6%) patients, first follow-up MRI was performed by clinical indication, and in half of these patients the treatment was changed. The association between the indication for repeating MRI during follow-up and treatment change and/or prolongation was statistically significant (p=0.0058). Fischer's exact test demonstrated the significant association between these two variables (p=0.015). Time interval between MRI study at diagnosis and first follow-up was 40.7 (± 33.7) days; a treatment change was performed in 3/12 patients in whom first follow-up MRI was performed in the first 28 days from the diagnosis, whereas a treatment change was performed in 2/16 patients in whom first follow-up MRI was performed more than 28 days from the diagnosis. The association between the two variables was not statistically significant (p=0.40) (Table 3). Mean CRP value at the first MRI follow-up was 0.7 mg/dL (± 2.0). CRP values were reducing in 24/28 (86%) patients, and increasing in the remaining 4/28 (14%). Among these 4 patients, bone signal has worsened in only 1 patient who underwent a treatment change; we did not perform a statistical analysis based on this single observation only.

Discussion

MRI plays a primary role in diagnosis of AO in children, particularly in the very first stage of the disease, when classic radiologic diagnosis with X-ray cannot always detect the first signs of bone involvement by the infectious process. In this study, utility of MRI in the diagnosis of AO was confirmed by identification of the involvement of soft tissues (96%), adjacent junctures and/or vertebral disc (54%) and by the recognition of bone abscesses (29%). Moreover, MRI offers the undeniable advantage of reducing children's exposure to ionizing radiation respect to X-ray, computed tomography (CT) and scintigraphy. On the other hand, MRI is expensive, representing an important cost for the healthcare system, and requires long procedural time with the necessity for sedation in the infants and younger children. Since the incidence of pediatric AO is increasing, the number of affected patients needing a follow-up of the disease is expected to increase, too [13,14]. To date, no accepted guidelines are available for the post-discharge follow-up of children affected by AO; normally, series of orthopedic evaluations, blood examinations and radiologic studies are differently performed in these children. Utility of MRI in the follow-up of AO has been called into question by some authors, who demonstrated that MRI bone signal may persist to be pathological even when the disease is clinically improving or completed resolved, and is not useful for guiding the therapeutic approach during the follow-up [6,8,10]. In our study, the association between the worsening or the persistence of pathologic MRI bone signal and treatment change, in terms of modification and/or prolongation of antibiotic therapy was not significant, confirming the greater importance of the clinical

Table 3. *Associations among variables*

	First follow-up MRI N=28 (%)	Treatment change* N=5 (%)	Odds Ratio (OR)	*P*
Bone signal				
Improved/resolved	16 (57)	2/16 (12.5)	2.33	0.4013
Worsened/unchanged	12 (43)	3/12 (25)		
Indications for follow-up MRI				
Routine	20 (71)	1/20 (5)	19.00	0.0058**
Clinical indication	8 (29)	4/8 (50)		
Time interval between MRI at diagnosis and first follow-up				
≤ 28 days	12 (43)	3/12 (25)	0.43	0.4013
>28 days	16 (57)	2/16 (12.5)		

*Antibiotic change and/or treatment prolongation

**Statistically significant

factors and of the laboratory data in the post-discharge monitoring of response to treatment. Only one of the MRI study performed as routine follow-up respect to 4 of the 8 MRIs performed for a clinically persistent or worsening disease resulted in a change in the therapeutic approach, demonstrating the existence of a significant association between the indication for which MRI study is repeated and the probability to change the treatment approach. This evidence suggests that routine MRI is not useful in the patients' follow-up, on the contrary, its utility is limited to those patients who clinically present a complicated disease. The indication for repeating MRI studies should be formulated based on clinical findings rather than simply as routine follow-up. Our result is in accordance with that presented in the only other published study by Courtney and colleagues on utility of MRI in the follow-up of AO in children [12]. In this study, authors found a significant association between indication for repeating MRI and treatment change. The association between time interval between MRI at diagnosis and first follow-up and treatment change was not significant, suggesting that it is not possible either to predict the patients who may require MRI follow-up or to establish which time interval between MRI at diagnosis and follow-up may be the best. Clinical data are more useful for guiding timing of follow-up, too. Differently from our study, Courtney and colleagues found a significant association between time interval between MRI at diagnosis and at follow-up and treatment change, and suggested that MRI studies performed within 14 days from diagnosis, especially in children with persistently elevated CRP dosage, were more probably associated to a change in therapy than studies performed thereafter [12]. We did not find a similar association; the fewer number of MRIs considered in our study respect to Courtney's (28 cases vs 60 cases) may explain the lack of association. Other similar studies, performed in the adult population and especially focusing on spinal AO showed similar results, suggesting that routine follow-up of AO with MRI did not significantly correlate with clinical response to treatment [7-11]; on the contrary, they suggested that an uncontrolled use of MRI studies may be confounding in some cases and may complicate the clinical decision-making process. Our study has some limitations, the first being its retrospective nature. Secondly, the limited number of cases may explain some imprecision and low confidence in the statistical data analysis. Another limitation may be represented by a possible patients' selection bias, since we included in our study only the patients who underwent a follow-up MRI, and these patients may have been characterized by a more severe course of the disease. For these reasons, we cannot draw any definitive conclusion about utility of MRI in the follow-up of children affected by AO. Studies conducted on a greater population and prospective in nature are still needed to confirm the impact of follow-up MRI on AO treatment course and long-term disease outcome. Nevertheless, our study is the second performed on a pediatric population and our data suggest that routine MRI study is probably not useful in the follow-up of those patients who show a good clinical response to treatment. It may be more useful in non-responders patients who continue to present clinical signs and symptoms of a still active disease. Selecting patients who may benefit most from a MRI follow-up study may be advantageous for avoiding unnecessary sedation in children and for containing healthcare-related costs.

Conclusion

Routine MRI study in the follow-up AO pediatric patients is not useful. Clinical follow-up remains the mainstay of post-discharge medical management of children affected by AO.

References

1. Lew DP, Waldvogel FA. Osteomyelitis. Lancet 2004; 364:369-379.
2. Dartnell J, Ramachandran M, Katchburian M. Hematogenous acute and subacute pediatric osteomyelitis: A systematic review of the literature. J Bone Joint Surg Br 2012; 94: 584-595.

3. Kremers HM, Nwojo ME, Ransom JE, et al. Trends in the epidemiology of osteomyelitis: A population-based study, 1969 to 2009. J Bone Joint Surg Am 2015; 97: 837-845.
4. Pugmire BS, Shailam R, Gee MS. Role of MRI in the diagnosis and treatment of osteomyelitis in pediatric patients. World J Radiol 2014; 6: 530-537.
5. Linet MS, Kim KP, Rajaraman P. Children's exposure to diagnostic medical radiation and cancer risk: epidemiologic and dosimetric considerations. Pediatric Radiology 2009; 39: 4.
6. Gillams AR, Chaddha B, Carter AP. MR appearances of the temporal evolution and resolution of infectious spondylitis. AJR Am J Roentgenol 1996; 166: 903-907.
7. Carragee EJ. The clinical use of magnetic resonance imaging in pyogenic vertebral osteomyelitis. Spine 1997; 22: 780-785.
8. Zarrouk V, Feydy A, Sallès F, et al. Imaging does not predict the clinical outcome of bacterial vertebral osteomyelitis. Rheumatology 2007; 46: 292-295.
9. Kowalski TJ, Layton KF, Berbari EF, et al. Follow-up MR imaging in patients with pyogenic spine infections: Lack of correlation with clinical features. Am J Neuroradiol 2007; 28: 693-699.
10. Baxi S, Malani PN, Gomez-Hassan D, et al. Association between follow-up magnetic resonance imaging and clinical status among patients with spinal infections. Infect Dis Clin Pract 2012; 20: 326-329.
11. Kowalski TJ, Berbari EF, Huddleston PM, et al. Do follow-up imaging examinations provide useful prognostic information in patients with spine infection? Clin Infect Dis 2006; 43: 172-179.
12. Courtney PM, Flynn JM, Jaramillo D, et al. Clinical indications for repeat MRI in children with acute hematogenous osteomyelitis. J Pediatr Orthop 2010; 30: 883-887.
13. Malcius D, Trumpulyte G, Barauskas V, et al. Two decades of acute hematogenous osteomyelitis in children: Are there any changes? Pediatr Surg Int 2005; 21: 356-359.
14. Gafur OA, Copley LA, Hollmig ST, et al. The impact of the current epidemiology of pediatric musculoskeletal infection on evaluation and treatment guidelines. J Pediatr Orthop 2008; 28: 777-785.

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