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Severe Transient Synovitis Differential Dianosis from Septic Arthritis

Hideaki Watanabe[1], Ichiro Kikkawa[1], Kayo Hagiwara[1], Ryo Sugawara[1], Hirokazu Inoue[2], Katsushi Takeshita[2]

[1]Department of Pediatric Orthopedic Surgery, Jichi Medical Children's Center Tochigi, Tochigi, Japan

[2]Department of Orthopedic Surgery, Jichi Medical University, Tochigi, Japan

Abstract：We report useful factors for the differential diagnosis between severe transient synovitis（TS）and septic arthritis（SA）in 14 children, seen between 2006 and 2013. We investigated various factors in 7 children with TS, and compared these with findings in 7 children with SA. Factors included age, sex, body temperature, involved joint, duration of onset, white blood cell（WBC）count, platelet count, C-reactive protein, MRI findings on contrast enhancement of surrounding synovial membrane, muscle, and osteomyelitis of the affected joint. Significant differences between TS and SA were found in age, WBC count, platelet count, and MRI findings of signal intensity in muscle around the affected joint. These factors may be useful in differential diagnosis between TS and SA in children.

Introduction

Children with transient synovitis（TS）and septic arthritis（SA）visit clinics with the same symptoms, namely, joint swelling and pain. TS is a disease with an as yet unknown cause, but it resolves spontaneously and is associated with favorable prognosis[7]. However, SA causes growth arrest or bone necrosis in the absence of early treatment, such as lavage and drainage, and this may result in poor outcome[3]. Therefore, it is important to differentiate these diseases early, and various guidelines have been proposed[1)3)6)9)12)]. These guidelines target all forms of TS, from mild cases in patients capable of standing and walking with minor restriction in the range of motion, to severe cases in patients incapable of standing or walking with marked restriction in the range of motion. However, differentiation between severe TS and SA is difficult in clinical practice, and there have been few studies on their prediction. This study evaluated the practical predictors for differentiation between severe TS and SA at initial examination.

Materials and Methods

The present study was a cross-sectional single-center study. Patients with juvenile idiopathic arthritis or arthritis associated with other diseases such as leukemia were excluded. Ninety-

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Corresponding author：Hideaki Watanabe
Department of Pediatric Orthopedic Surgery, Jichi Medical Children's Center, 3311-1 Yakushiji, Shimotuke-shi, 329-0498, Japan
TEL: +81-285-58-7374
e-mail：watahide1968@jichi.ac.jp

seven patients who complained of joint swelling and pain and showed joint fluid retention on ultrasonography were visited between October 2006 and August 2013. Patients with mild and moderate arthritis, capable of standing and walking with minor restriction in the range of motion were excluded. We enrolled 14 children (8 male and 6 female, with a mean age of 46.3 months) with severe arthritis, marked restriction of joint motion preventing active or passive joint movement, and difficulty in standing and walking at initial examination. As a result of culturing or pathological examination of joint fluid, those who were diagnosed with definite or suspected SA according to Kocher's classification[3)4)], when the patient had a positive finding on culture of joint fluid or a white blood-cell (WBC) count in the joint fluid of ≥50,000 cells/μl with positive findings on blood culture, and underwent arthrotomy and lavage formed the SA group. Children who were diagnosed with TS according to Kocher's classification[3)4)], when the patient had a WBC count in the joint fluid <50,000 cells/μl with negative findings on culture, resolution of symptoms without antimicrobial therapy, and no further development of disease and recovered by only rest without administering antibiotics formed the TS group. The age, sex, body temperature, involved joint, duration of onset, WBC count, platelet count, C-reactive protein (CRP), contrast enhancement of the synovial membrane and surrounding muscles of the affected joint, and presence or absence of osteomyelitis around the affected joint on contrast-enhanced magnetic resonance imaging (MRI)[5)12)] at initial examination were compared. Contrast-enhanced MRIs were read by a radiologist in a blinded manner. Statistical analysis was performed using SPSS version 20 (IBM Corp., Armonk, NY, USA) by performing the Mann-Whitney U test for comparison of continuous variables and Fisher's exact test for comparisons of categorical variables at the $P<0.05$ level of significance. Significant continuous variables were analyzed using receiver operating characteristic curves, and the precision of the differential diagnosis was evaluated according to the area under the curve (AUC). Cutoff values yielding the highest sensitivity and specificity were also determined.

Results

The SA group consisted of seven children (three male and four female, mean age: 9.2 months. The affected joints in the patients were: shoulder in one, hip in one, knee in three, and elbow in two. The TS group consisted of seven children (four male and three female, mean age: 83.4 months. The affected joint was the hip in all seven children. There was a significant difference in age between the groups (Table 1).

Bacterial culture identified *Staphylococcus aureus* in four patients (57%), group-B *Streptococcus* in two (26%), and *Haemophilus influenzae* in one (14%) in all SA groups.

Significant differences were observed in the WBC count (mean: 18.2×10^3 cells/μl in the SA group, 13.2×10^3 cells/μl in the TS group) and platelet count (mean: 58.6×10^4 cells/μl in the SA group, 32.6×10^4 cells/μl in the TS group) (P = 0.01 and 0.03, respectively), but the difference in CRP (mean: 9.1 mg/dl in the SA group, 3.9 mg/dl in the TS group) was not significant (P = 0.06). Age, WBC count and platelet count also showed significant differences in AUC (P = 0.04, 0.01 and 0.01, respectively), and the precision of the differential diagnosis was platelet count > WBC count > age (Table 1). Also, the cutoff value with the highest sensitivity and specificity was 9 months for age (sensitivity: 43%, specific-

Table 1. Demographics of the patients included in the study

	SA group	TS group	*P*	AUC (95% confidence interval)	*P*	Cutoff value	Sensitivity (%)	Specificity (%)
Number	7	7						
Age (mo)	9.2 (0.25–24)	83.4 (8–144)	0.01*	0.07 (0.0–0.22)	0.01	9	43	14
Sex	M : 3, F : 4	M : 4, F : 3	0.59**					
Temperature (℃)	38.1 (36.8–39.5)	38 (36.7–39.7)	0.85*					
Involved joint								
Shoulder	1	0						
Elbow	2	0						
Hip	1	7						
Knee	3	0						
Duration of onset (days)	5 (1–19)	2 (1–5)	0.32*					
Laboratory data								
WBC ($\times 10^3$ cells/μL)	18.2 (12.5–22.3)	13.2 (7.8–19.7)	0.03*	0.82 (0.59–1.00)	0.04	17.1	71	86
CRP (mg/dL)	9.1 (1.9–23.6)	3.9 (0–19.5)	0.06*					
Platelets ($\times 10^4$ cells/μL)	58.6 (48–70)	32.4 (17.1–44.9)	0.01*	1.00 (1.00–1.00)	0.01	45.5	100	100
Enhanced MRI								
Enhancement of synovium	yes : 7, no : 0	yes : 5, no : 2	0.23**					
Enhancement of intramuscle tissue	yes : 7, no : 0	yes : 0, no : 7	0.01**					
Osteomyelitis	yes : 1, no : 6	yes : 0, no : 7	0.5**					

*Mann–Whitney U test, **Fisher's exact test

AUC, area under the curve; F, female; M, male; MRI, magnetic resonance imaging; SA, septic arthritis; TS, severe transient synovitis

ity: 14 %), 17.1×10^3 cells/μl for WBC count (sensitivity: 71%, specificity: 86%), and 45.5×10^3 cells/μl for platelet count (sensitivity: 100%, specificity: 100%) (Fig. 1, Table 1).

On contrast-enhanced MRI, a significant difference was observed in contrast enhancement of the muscles surrounding the affected joint (Fig. 2) ($P = 0.01$), but no significant difference was noted in contrast enhancement of the synovial membrane of the affected joint or the presence or absence of osteomyelitis around the affected joint ($P = 0.23$ and 0.5, respectively) (Fig. 2, Table 1).

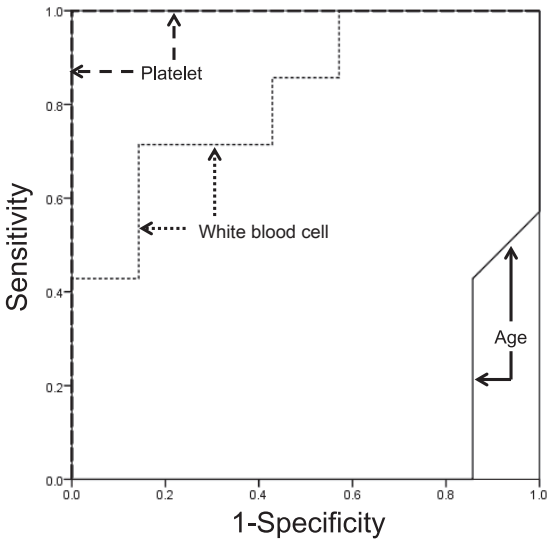

Fig. 1. Receiver operating characteristic curve
The precision of differential diagnosis was high in the order of the Platelet count (thick broken line), White blood cell count (thin broken line), and age (solid line).

Discussion

This study showed that a platelet count of 45.5×10^4 cells/μl, WBC count of 17.1×10^3 cells/μl, age of 9 months, and contrast enhancement of muscles around the affected joint were practical predictive factors contributing to the differentiation between severe TS and SA, and that contrast enhancement of muscles around the affected joint had the highest precision for differential diagnosis.

In a retrospective study, Kocher et al.[3] reported that TS and SA could be differentiated at an accuracy of 99.6% using the following cri-

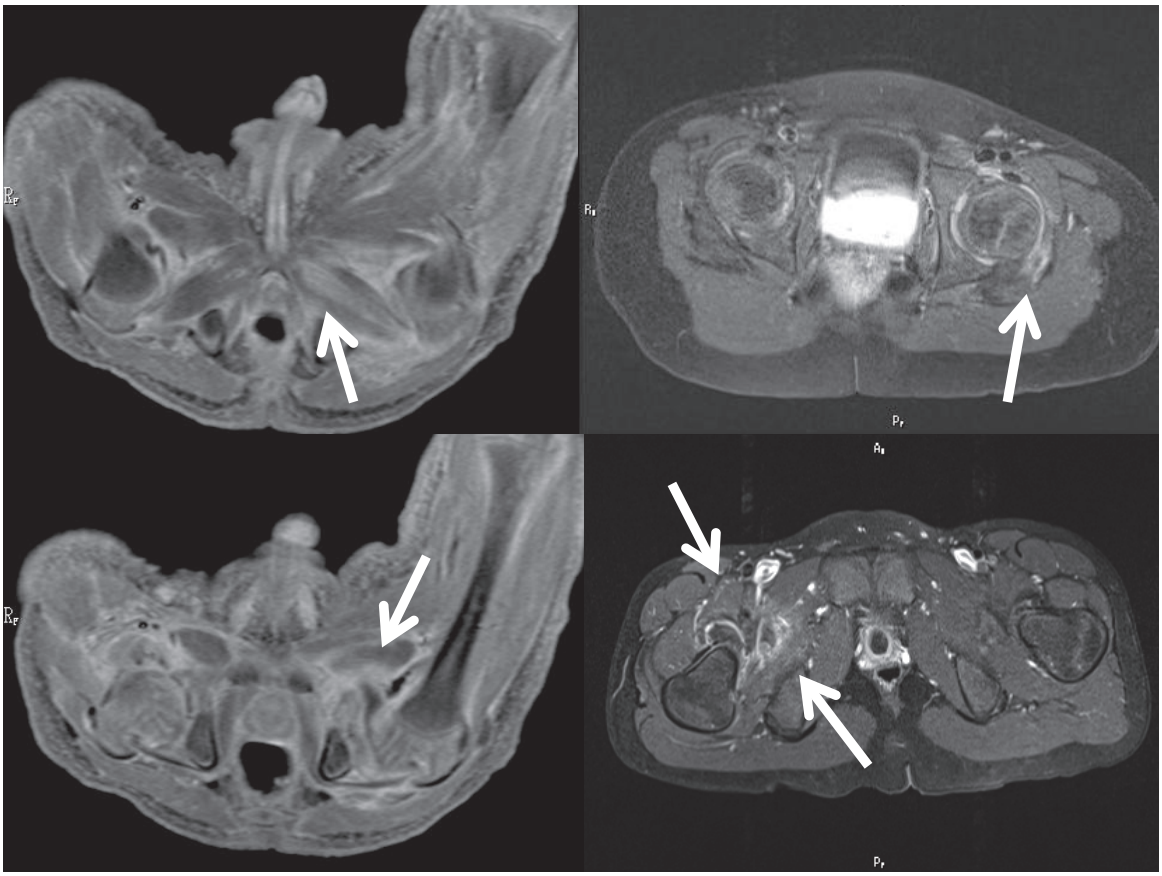

Fig. 2. Contrast-enhanced magnetic resonance image (left: septic arthritis group; right: transient synovitis group). Left: contrast enhancement was observed in the muscles around the affected joints (white arrows). Right: contrast enhancement was observed only in the synovial membranes and not in the muscles around the affected joints (white arrows).

teria as predictors: (1) fever of 38.5°C; (2) being incapable of standing or walking; (3) WBC count of ≥12×10^9 cells/l; and (4) an erythrocyte sedimentation rate of ≥40 mm/h. They subsequently validated this algorithm in a prospective study, and reported that differentiation was possible at an accuracy of 93.0%[4]. However, Luhmann et al.[6] re-examined the validity of this algorithm in a retrospective study, and reported that the four predictors were in agreement in only 59 % of cases. Thereafter, Caired et al.[1] added CRP to these four predictors and reported that differentiation was possible in 98 % of the patients with this combination. However, according to a retrospective study by Sultan et al. to validate this[9], the five predictors were in agreement in only 59.9 % of the patients. This discrepancy in the precision of prediction among reports is considered to be due to the difference in the number of TS and SA patients and the inclusion of all cases of TS from mild to severe[10]. Singhal et al.[8] studied outpatients who visited because of irritable hip, and reported that a combination of being unable to stand up, walk, or move the joint passively and CRP ≥2 mg/dl was related to SA. However, in actual clinical practice, the differentiation of severe TS from SA in patients who are unable to stand up, walk, or move the joint passively is the most difficult. The results of our present study indicate

that the possibility of SA is high when platelet count is ≥45.5×10^4 cells/μl, WBC count is ≥17.1×10^3 cells/μl, age is ≤9 months, and when contrast enhancement is noted in the muscles around the affected joint on contrast-enhanced MRI. The cause in infants aged ≤9 months is unknown. These infants might be referred to our hospital because it specializes in children. Tanaka et al.[11] have reported that WBC count undergoes age-related change in Japanese children. The high WBC count in SA might be related to age. The cause of high platelet count is also unknown. Ikeda et al.[2] reported that platelet count increased secondarily during treatment of SA in infants and toddlers. However, there was no significant difference in duration of onset. Tanaka et al.[11] have reported platelet count undergoes age-related change in Japanese children. The high platelet count in SA might also be related to age. We did not validate this algorithm as a predictor with four combinations in a prospective study. We need to validate this algorithm using a prospective study in the future.

The limitations of this study were that there were only 7 patients in each group and that the joints affected by SA varied.

In this study, severe TS and SA could be differentiated using the algorithm as predictors with combination of (1) platelet count ≥45.5×10^4 cells/μl; (2) WBC count ≥17.1×10^3 cells/μl; (3) age ≤9 months; and (4) contrast enhancement is noted in the muscles around the affected joint on contrast-enhanced MRI. We consider that arthrotomy and lavage might be performed promptly in such patients.

REFERENCES

1) Caird M, Flynn JM, Leung YL et al: Factors distinguishing septic arthritis from transient synovitis of the hip in children. J Bone and Joint Surg Am **88**：1251–1257, 2006.
2) Ikeda T, Minamisawa I, Kobayashi A et al: Clinical result of suppurative arthritis of the hip joints in infancy and childhood. Kanto J Orthop and Trauma **26**：397–401, 1995. (In Japanese)
3) Kocher MS, Zurakowski D, Kasser JR: Differentiating between septic arthritis and transient synovitis of the hip in children: an evidence-based clinical prediction algorithm. J Bone and Joint Surg Am **81**：1662–1670, 1999.
4) Kocher MS, Mandiga RM, Zurakowski D et al. Validation of a clinical prediction rule for the differentiation between septic arthritis and transient synovitis of the hip in children. J Bone and Joint Surg Am **86-A**：1629–1635, 2004.
5) Lee SK, Suh KJ, Kim YW et al: Septic arthritis versus transient synovitis at MR imaging: preliminary assessment with signal intensity alterations in bone marrow. Radiology **211**：459–465, 1999.
6) Luhmann SJ, Jones A, Schootman M et al: Differentiation between septic arthritis and transient synovitis of the hip in children with clinical prediction algorisms. J Bone and Joint Surg Am **86-A**：956–962, 2004.
7) Nouri A, Walmsley D, Pruszczynski B et al: Transient synovitis of the hip: a comprehensive review. J Pediatr Orthop **B 23**：32–36, 2014.
8) Singhal R, Perry DC, Khan FN et al: The use of CRP within a clinical prediction algorithm for the differentiation of septic arthritis and transient synovitis in children. J Bone and Joint Surg Br **93**：1556–1561, 2011.
9) Sultan J, Hughes P: Septic arthritis or transient synovitis of the hip in children: the value of clinical prediction algorithms. J Bone Joint Surg Br. **92**：1289–1293, 2010.
10) Taekema HC, Landham PR, Maconochie I: Distinguishing between transient synovitis and septic arthritis in the limping child: how useful are clinical prediction tools? Arch Dis Child **94**：167–168, 2009.
11) Tanaka T, Yamashita A, Ichihara K: Reference intervals of clinical tests in children determined by a latent reference value extraction method. J Jpn Pediatr Soc **112**：1117–1132, 2008. (In Japanese)
12) Yang WJ, Im SA, Lim GY et al: MR imaging of

transient synovitis: differentiation from septic arthritis. Pediatr Radiol **36**：1154–1158, 2006.