Differentiating *Kingella kingae* Septic Arthritis of the Hip from Transient Synovitis in Young Children

Pablo Yagupsky, MD[1], Gal Dubnov-Raz, MD, MSc[2,3], Amadeu Gené, MD[4], and Moshe Ephros, MD[5], on behalf of the Israeli-Spanish *Kingella kingae* Research Group*

Objective To conduct a retrospective multicenter study to assess the ability of a predictive algorithm to differentiate between children with *Kingella kingae* infection of the hip and those with transient synovitis.

Study design Medical charts of 25 Israeli and 9 Spanish children aged 6-27 months with culture-proven *K kingae* arthritis of the hip were reviewed, and information on the 4 variables included in the commonly used Kocher prediction algorithm (body temperature, refusal to bear weight, leukocytosis, and erythrocyte sedimentation rate) was gathered.

Results Patients with *K kingae* arthritis usually presented with mildly abnormal clinical picture and normal serum levels of or near-normal acute-phase reactants. Data on all 4 variables were available for 28 (82%) children, of whom 1 child had none, 6 children had 1, 13 children had 2, 5 had 3, and only 3 children had 4 predictors, implying ≤40% probability of infectious arthritis in 20 (71%) children.

Conclusions Because of the overlapping features of *K kingae* arthritis of the hip and transient synovitis in children younger than 3 years of age, Kocher predictive algorithm is not sensitive enough for differentiating between these 2 conditions. To exclude *K kingae* arthritis, blood cultures and nucleic acid amplification assay should be performed in young children presenting with irritation of the hip, even in the absence of fever, leukocytosis, or a high Kocher score. *(J Pediatr 2014;165:985-9)*.

Young children who come to medical attention because of limping pose a common and serious diagnostic challenge, and differentiating between septic arthritis of the hip and transient synovitis is of paramount clinical and therapeutic importance. If inadequately diagnosed and treatment delayed, pediatric septic arthritis may result in major morbidity, including joint destruction, necrosis of the femoral head, and permanent disability.[1] Transient synovitis, in contrast, is a benign and self-limited condition requiring only rest and analgesic therapy, and does not lead to orthopedic sequelae.[2] Erroneous misclassification of transient synovitis as septic arthritis may result in unnecessary hospitalization, surgery, and antibiotic therapy. To assist in differentiating between these 2 conditions, an algorithm combining clinical information and laboratory data was developed by Kocher et al.[3] This predictive guideline is based on clinical criteria (body temperature >38.5°C and refusal to bear weight) and blood inflammatory markers (white blood cell [WBC] count >12 000 cells/mm^3 and erythrocyte sedimentation rate [ESR] >40 mm/h), complemented by the presence of >50 000 WBCs/mm^3 in synovial fluid, when joint aspiration is performed.[3] The risk of suppurative arthritis directly correlates with increasing number of positive predictors, and transient synovitis is characterized by low scores. The performance of this diagnostic algorithm and similar guidelines based on Kocher original clinical prediction model with slight modifications has been evaluated and validated in many studies that included pediatric patients with bacterial arthritis caused by traditional pathogens such as *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumonia*, and *Haemophilus influenzae* type b.[3-8]

As the result of increasing use of improved culture methods and sensitive nucleic acid amplification (NAA) assays, *K kingae*, a gram-negative component of the normal pharyngeal flora, is increasingly recognized as an important human pathogen and the most common etiology of joint infections in children aged 6-48 months in widespread geographic populations.[9-11] The clinical presentation of patients with *K kingae* arthritis is often subtle, requiring a high index of suspicion: the body temperature and levels of acute phase reactants may be normal or only mildly elevated, and leukocytosis is frequently absent.[9,12-15] *K kingae* usually affects large weight-bearing joints and in a large multicenter study comprising 140 children with culture-proven *K kingae* arthritis, the hip was involved in 20 (14.3%) patients and represented the third most commonly infected site in this series.[15] Although Kocher decision-making algorithm has gained

CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
NAA	Nucleic acid amplification
WBC	White blood cell

From the [1]Clinical Microbiology Laboratory, Soroka University Medical Center, Beer-Sheva, Israel; [2]Edmond and Lily Safra Children's Hospital, Chaim Sheba Medical Center, Tel-Hashomer, Israel; [3]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [4]Molecular Microbiology Department, University Hospital Sant Joan de Deu, Barcelona, Spain; and [5]Pediatric Infectious Diseases Unit, Carmel Medical Center, and the Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

*List of members of the Israeli-Spanish *Kingella kingae* Research Group is available at www.jpeds.com (**Appendix**).

The authors declare no conflicts of interest.

http://dx.doi.org/10.1016/j.jpeds.2014.07.060

general acceptance for differentiating between septic hip joints and transient synovitis,[16] it was developed when the role of *K kingae* in pediatric septic arthritis was unrecognized. As none of the patients included in the original and subsequent validation studies had a proven infection caused by this organism, the performance of this tool for diagnosing such infections remains unknown. A retrospective multicenter study, comprising Israeli and Spanish patients, was conducted to assess the ability of Kocher diagnostic algorithm to correctly categorize children with *K kingae* infection of the hip as having septic arthritis.

Methods

The medical records of pediatric patients with culture-proven *K kingae* hip arthritis, defined as presence of a painful hip joint and from whom the bacterium was recovered by culture of synovial fluid and/or blood, diagnosed in 7 Israeli hospitals and 1 large Spanish medical center located in the city of Barcelona, dating from 1989-2013, were examined. Patients were identified through the clinical microbiology laboratory databases of participating hospitals. Blood and synovial fluid specimens obtained from Israeli patients were processed using the Bactec blood culture system (Becton Dickinson), whereas the BacT/Alert (bioMérieux) was employed in the Spanish medical center. Medical records were reviewed and relevant demographic and clinical information was extracted using a uniform data collection form. Some patients were included in previous reports in the medical literature. Data retrieval was approved by the local Institutional Review Boards of each medical center.[15] Information, thus, collected included the clinical variables (body temperature on admission and refusal to bear weight) and laboratory data (blood WBC count and ESR) of Kocher predictive algorithm. The number of predictors (score) recorded for each patient was calculated, and the likelihood of a child having septic arthritis was interpreted according to Kocher original study model: from 0.2% when none was present, 3% for 1 predictor, 40% for 2 predictors, 93.1% for 3 predictors, and 99.6% if all 4 criteria were met.[3] Additional information included demographic data (age, sex), clinical data (duration of symptoms), laboratory results (leukocyte count in joint aspirate [$>$ or $\leq$50 000 WBCs/mm^3 in synovial fluid]), and, if performed, joint drainage modality (aspiration/arthrotomy).

Statistical Analyses

The study examined the distribution of the individual clinical and laboratory components of Kocher diagnostic algorithm among children with bacteriologically-proven *K kingae* arthritis of the hip, and the sensitivity of Kocher algorithm to correctly assign children with culture-proven *K kingae* infection of the hip to the septic arthritis category. The statistical significance of the differences between continuous variables was assessed by the Mann-Whitney test and that of categorical variables by the χ^2 test. A P value of $<.05$ was considered significant for all calculations.

Results

Thirty-four children (25 Israeli, 9 Spanish) with culture-proven *K kingae* arthritis were studied retrospectively (**Table I**). The patients' mean ± SD age was 15.0 ± 5.9 months (median: 15.5 months, range: 5-27 months, 95% CI: 12.9-17.1 months), and 23 (68%) were males. On admission, patients had been ill for 2.6 ± 2.6 days (mean ± SD, median: 2 days, range: 1-14 days, 95% CI: 1.8-3.4 days). Israeli and Spanish children were similar in terms of age, sex distribution, and duration of symptoms ($P > .05$ for all variables). All patients were previously healthy and had no significant underlying medical problem.

K kingae was isolated from a synovial fluid specimen in 22 (65%) children (from a seeded blood culture vial in 21 children and from direct plating on routine solid media in one). In the remaining 12 children, the organism was recovered from blood culture. None of the 34 cases had the organism isolated from both blood and synovial fluid.

Fifteen patients (44%) underwent open arthrotomy and another 2 (6%) closed needle aspiration of the affected joint. In 17, no drainage of the affected joint was performed. Two children (patients 3 and 13 in **Table I**) who presented with an irritable hip joint and from whom *K kingae* was isolated from blood culture recovered without antibiotic therapy, indicating a self-limited clinical course. All other patients were administered a variety of β-lactam antibiotics.

Although body temperature on admission was recorded in 33 of 34 children and blood WBC counts on admission were available for all children, ESR determination was performed in only 28 (82%). Because of the patients' young age, refusal to bear weight could not be assessed in 2 infants aged 5 and 6 months. Therefore, results for the 4 variables of Kocher algorithm were available for 28 (82%) children, 3 variables were evaluable in 4 (12%) children, and only 2 variables in the remaining 2 (6%) children. The 2 patients who did not receive antibiotics had Kocher scores of 0 and 1, respectively. Spanish children presented with a significantly lower body temperature (median: 38.5°C), compared with Israeli children (median: 38.9°C [$P = .023$]), and lower erythrocyte sedimentation rate values (median values: 19 mm/h and 35 mm/h, respectively [$P = .029$]), but the 2 populations did not have significantly different WBC counts in peripheral blood. Results of the leukocyte count in joint fluid were available for 7 (21%) children, and the Gram-stain examination of the fluid was negative for bacteria in all 7 specimens.

Table I shows the patients' demographic, clinical, and laboratory results recorded on admission. **Table II** summarizes the results of the individual variables and their sensitivity for correctly identifying children with culture-proven *K kingae* septic arthritis. The **Figure** depicts the patients' Kocher algorithm score of the total number of evaluable variables. The mean ± SD score of the 28 children with 4 evaluable variables was 2.1 ± 1.0, of whom 20 (71%) had scores $\leq$2, indicating that nearly three-quarters of children with proven *K kingae* infection would