Diagnosing Septic Arthritis in the Synovial White Cell Count “Gray Zone”

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Received: 30 July 2015/Accepted: 20 October 2015/Published online: 30 November 2015
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Abstract Differentiating septic arthritis of the pediatric hip from other causes of hip pain and effusion continues to present a diagnostic challenge for the clinician. Although septic arthritis traditionally has been reported to have a synovial white blood cell count of 75,000 cells/mm³ or greater, lower counts can be seen in this condition. In cases where a synovial sample has been obtained and the cell count falls in the intermediate range between 25,000 and 75,000 cells/mm³, it is unclear what proportion of these cases may be truly septic hips. In this evidence-based review, we examine Heyworth et al’s study focusing on the predictive value of this intermediate white cell count range in a Lyme-endemic region.

Keywords pediatric septic hip · synovial white cell count

Introduction

Distinguishing septic arthritis of the pediatric hip (SAH) from innocuous pathologies such as transient synovitis of the hip (TSH) continues to present a diagnostic challenge for clinicians. The stakes are high because missing a joint infection can lead to devastating effects including damage to the articular cartilage, osteomyelitis, and systemic infection including septic shock. Despite these sequelae, overtreatment is not ideal as surgical debridement coupled with empiric antibiotic treatment is not without risks and morbidities. For these reasons, diagnostic accuracy is paramount when septic joint is on the differential diagnosis.

Electronic supplementary material The online version of this article (doi:10.1007/s11420-015-9480-6) contains supplementary material, which is available to authorized users.

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Over the course of time, the physical exam alone has demonstrated limited ability to distinguish between SAH and TSH. Ancillary studies including serum white cell counts and serum inflammatory markers were later added to the diagnostic armamentarium in order to increase the diagnostic accuracy. It was not until 1999 when a landmark retrospective study [1] introduced four variables (serum WBC count >12,000/mm³, refusal to bear weight, ESR > 40 mm/h, oral temperature >38.5°C) that provided cumulative predictive value for diagnosing septic arthritis. Later, a prospective study [2] demonstrated the added benefit of a fifth factor, C-reactive protein (>2.0 mg/dL) to the predictive algorithm. Since their inception, these risk factors have been used as a tool to guide management with hip aspiration and synovial fluid analysis in cases when multiple risk factors are present. After an aspiration has been performed, it has generally been accepted that a synovial white cell count greater than 100,000 cells/mm³ likely [3] represents a septic hip requiring surgical management. Values between 25,000 and 75,000 cells/mm³ represent a “gray zone” where professional opinion and management differs among treating physicians.

Reviewed here, Heyworth et al. assessed the utility of the five risk factors previously described in predicting SAH and examined the proportion of SAH cases that arise from this specific synovial white cell range. The specific aims of this review are (1) to examine the methodological rigor of the above study and (2) to evaluate the validity of the authors’ recommendations in light of their findings.

The Article

Management of Pediatric Patients with Synovial Fluid White Blood-Cell Counts of 25,000 to 75,000 Cells/mm³ After Aspiration of the Hip. Heyworth BE, Shore BJ, Donohue KS, Miller PE, Kocher MS, Glotzbecker MP. J Bone Joint Surg Am. 2015 Mar 4;97(5):389-95.

At their tertiary care children's hospital, the authors retrospectively examined children who underwent hip aspirations for suspected SAH over an 8-year period. One hundred eighty-one total aspirations were performed during the study period but after excluding patients with white cell counts either greater than 75,000 or less than 25,000 cells/mm³, older than 19 years old, or with a history of any immunologic, oncologic, or rheumatologic disorders, only 46 patients were included in the analysis. Each patient's eventual clinical diagnosis was determined and grouped into one of four categories: SAH, Lyme arthritis, transient synovitis of the hip (TSH), and a fourth category encompassing all other named diagnoses. Septic arthritis was defined as either blood or synovial fluid culture growth of an organism not deemed to be a contaminant or in culture-negative cases when the treating physicians came to a consensus that it was a bacterial etiology. The diagnosis of Lyme arthritis was based upon a positive synovial fluid Western blot or polymerase chain reaction (PCR) for *Borrelia burgdorferi*. The category of named immunologic and infectious etiologies included cases of poststreptococcal arthritis, psoriatic arthritis, pelvic osteomyelitis, obturator and iliacus pyomyositis, pauciarticular inflammatory arthritis, chronic recurrent multifocal osteomyelitis, and Henoch-Schonlein purpura. TSH was a diagnosis of exclusion. The authors used univariate and multivariate regression analyses to determine the association between the pre-established risk factors and SAH.

Throughout the entire cohort, 33% were diagnosed with SAH, 38% Lyme arthritis, 17% TSH, and 22% another diagnosis. In synovial WBC counts greater than 50,000 cells/mm³, 48% were diagnosed with SAH, whereas in those less than 50,000 cells/mm³, 17% were diagnosed with SAH. For those with WBC counts between 50,000 and 75,000 cells/mm³, each additional risk factor increased the odds of SAH nearly fourfold. There was no correlation in the lower WBC range.

The authors conclude that there remains a substantial percentage of SAH in those patients with synovial WBC counts between 25,000 and 50,000 cells/mm³ and that the established predictors did not appear to be useful in predicting SAH in this population.

Commentary

The purpose of this review is to critically examine Heyward et al's retrospective analysis of hip aspirations with synovial fluid white cell counts between 25,000 and 75,000 cells/mm³ and their conclusions regarding likelihood of septic arthritis and potential risk factors within this cell count range. To our knowledge, the authors are the first to focus on this "gray zone" of the synovial white cell count that gives rise to significant clinician uncertainty in addition to differing treatment philosophies. In their study, they aim to provide some evidence to supplement a primarily subjective decision-making process.

The study's primary strength lies in its identification of a relevant problem and sound methodological rigor in examining it. Not only is the catchment of the specific study population large as it encompasses a major pediatric medical center's experience with this disease entity over nearly a

decade but the data is also complete with respect to both risk factors and clinical outcomes as no patients were excluded from the analysis for absent clinical data.

Despite its strengths, the study has a number of flaws, the greatest of which being the small sample size, which ultimately limits the strength of the conclusions drawn. Furthermore, performing multivariable logistic regression analyses to examine risk factors and the diagnosis of SAH may not be warranted. The statistical "rule of ten" suggests that in regression analyses, the ratio of predictive variables to events should approach 1:10. This study examines 5 variables with only 15 SAH events, a ratio of only 1:3. Secondly, likely due to the retrospective nature of their review, the authors offer no rationale or clinical criteria that prompted the aspirations. Knowing such rationale would have offered a more standardized and reproducible study group for later investigation. Thirdly, the generalizability of the study may be limited as the study was performed in a region where Lyme disease is prevalent, accounting for 28% of the cases. Eliminating the 13 cases of Lyme from the analysis increases the proportion of SAH diagnoses from 33% (15/46) to 45% (15/33). In a different region where the percentage of SAH cases is potentially higher, a similar study may result in different conclusions. Fourthly, given that animal studies have demonstrated significant changes of synovial white cell counts within hours following joint infections [4], drawing important conclusions based upon a synovial white cell count range is potentially flawed with no information regarding the time of aspiration relative to the time since infection. Finally, how the authors dealt with culture-negative cases deserves special attention. Despite being consistent with some previously reported culture-negative SAH rates reported in the literature [1, 2], the 50% rate is high enough to warrant further investigation before being labeled as SAH, especially given the multiple diagnostic tests available to identify Lyme arthritis and other potential forms of inflammatory or rheumatologic arthritides. A workup including gram stain, PCR, and/or serologic testing can often identify the pathogen in culture-negative arthritides.

In spite of some drawbacks, most notably small size and retrospective nature, the study provides the reader with an important takeaway that can immediately influence clinical practice: In suspected cases of pediatric hip septic arthritis within Lyme endemic regions that present with synovial white cell counts between 25K and 75K, the risk of septic arthritis is considerable and the traditional risk factors may not have the same predictive value in this subset of patients. In such cases, the most prudent course includes close clinical observation with serial exams, repeat aspirations if warranted, and low threshold to proceed to the operating room.

Compliance with Ethical Standards

Conflict of Interest: Joseph J. Ruzbarsky, MD, Brian P. Gladnick, MD and Emily Dodwell, MD, MPH, have declared that they have no conflict of interest.

Human/Animal Rights: This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed Consent: N/A

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

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