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BRIEF REPORT

Defining Variability in Evaluation and Management of Children with Chronic Osteomyelitis

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Pediatric chronic osteomyelitis is a rare, debilitating condition lacking management guidelines. In a national survey of 162 pediatric infectious disease physicians through the Emerging Infections Network, tremendous variability in diagnostic approaches and management was noted, highlighting a need for a prospective study to better define the spectrum of pathogens and disease.

Key words. diagnosis; management; pediatric chronic osteomyelitis; prospective studies.

INTRODUCTION

Though rare, chronic osteomyelitis (COM) in children may have serious consequences, including limb length discrepancies, draining sinus tracts and pathologic fractures often requiring prolonged courses of antibiotics [1, 2]. Acute hematogenous osteomyelitis (AHO) guidelines define COM as a protracted, indolent disease process with: (1) presence of a sequestrum; and/or (2) relapse of infection in the same bone weeks to years after apparently successful treatment of initial infection in that site [3]. COM may arise from AHO, but may also complicate hardware-associated infections, occur after trauma or arise from contiguous spread of an infection (eg, decubitus ulcers) [4–7]. The microbiology of COM is partly dependent upon the etiology of infection. COM due to *Staphylococcus aureus* more commonly follows AHO, while enteric and polymicrobial infections are more common in COM associated with contiguous foci and implant-associated processes [7]. Clinically, COM may have a variable presentation and often occurs in patients with medical comorbidities [1, 2, 8]. COM may also be mistaken for chronic nonbacterial osteomyelitis, an inflammatory bone disorder, particularly in children with prolonged or culture-negative disease.

Proposed definitions of COM, such as the one above, may not be widely adopted nor reflective of historical interpretations of COM (eg, many large series of COM in children describe a majority of cases without a sequestrum or occurring without previous infection in involved bone) [1, 7–9]. Determination of microbiologic etiology is hindered by low culture yield from COM specimens (≥30% sterility in some series) [7, 10]. Varied clinical presentations, lack of an accepted definition for the disease, and scarcity of prospective studies assessing treatment are persistent gaps in knowledge, potentially contributing to a lack of standardized management.

To address these gaps in knowledge, we surveyed pediatric infectious diseases (PID) physicians via the Infectious Diseases Society of America Emerging Infections Network (EIN) to better understand current approaches used nationally for diagnosing, defining, and managing COM in children, in hopes of identifying and clarifying issues requiring future prospective study [11].

METHODS

A 14-question, confidential, web-based survey link was distributed to 387 PID physician members of the EIN and remained open between April 19, 2022 and May 12, 2022 (Supplementary Material). Non-responders received two reminders, 1 week apart. Respondents were characterized by region of the United States and Canada, years of experience after fellowship (<5 years; 5–24 years; and >25 years), and practice setting (eg, community- or academic-based). An initial screening question identified respondents self-identifying as caring for children with suspected COM. These subjects were then presented with multiple choice and "choose all that apply" questions to assess their diagnostic approach, comfort diagnosing and treating COM (grouped as comfortable, neutral, or uncomfortable), and standard surgical and antibiotic management. Descriptive statistics and chi-square analyses assessed for associations between diagnosis and management decisions and provider characteristics, including time since fellowship and practice setting. Statistical analyses were performed using SAS version 9.4 (Cary, NC, USA).

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RESULTS

Of 387 EIN PID physician members who received the survey, 194 responded (50%); 30 members who had not responded to any prior surveys were excluded from the denominator. Full survey results are available online: https://ein.idsociety.org/media/surveys/report/2022/FinalReport_PedsChronicOsteo.pdf. A majority of respondents had >5 years of experience since infectious disease fellowship (81%) and worked in an academic medical setting (59%). Respondents originated from all major geographic regions of the United States and Canada. Of the 194 respondents, 162 (84%) cared for children with COM and were included in the analyses.

Diagnosis of COM

Most respondents (85%) reported caring for one to six patients with COM annually. A total of 137 respondents (84%) reported feeling very comfortable or somewhat comfortable recognizing COM, while only 12 respondents (7%) felt somewhat uncomfortable or very uncomfortable. Despite this confidence, there was substantial variability in factors considered necessary to make a diagnosis of COM (Figure 1). In total, 77% of respondents reported that prolonged symptom duration was necessary for diagnosis, with an average of 4.8 weeks (range 1–12 weeks, median 4.0 weeks). Abnormal plain films at presentation (48%), normal or near normal acute inflammatory markers (45%), histopathological evidence of chronic inflammation in bone (40%), and patient risk factors (eg, prior trauma, retained orthopedic implants) (35%) were also commonly considered. Few respondents required evidence of sequestrum or involucrum (18% and 14%, respectively). The most frequent constellation of findings (provided by only 12 respondents, 7%), was a combination of: (1) normal or near normal acute inflammatory markers; (2) abnormal plain film; and (3) prolonged duration of symptoms. A total of 34 respondents (21%) reported using no specific diagnostic criteria. Respondents reported an array of most common etiologies for COM including: in the setting of orthopedic implants (44%), after progression from AHO (22%), with contiguous foci of infection (8%), after penetrating trauma (7%), as chronic recurrent nonbacterial osteomyelitis (6%), and as primary hematogenous chronic osteomyelitis (4%). Respondents differentiated sub-acute osteomyelitis from COM primarily based on shorter duration of symptoms (61% of respondents; exact duration not assessed).

Management of COM

Respondents reported that typical patients with COM had 1 (42%) or 2 (24%) debridement surgeries. Most respondents reported feeling either very comfortable (54, 33%) or somewhat comfortable (83, 51%) treating COM in a child. Despite this confidence, the duration of intravenous (IV) antibiotic therapy prior to transition to oral therapy (assuming all necessary surgical debridement occurred) ranged from 0 to greater than 6 weeks (Figure 2A). Physician demographics, including the setting of practice or time since fellowship graduation, were not associated with either comfort treating COM or duration of IV antibiotics.

Respondents noted several factors influencing the timing of transition to oral antibiotics (Figure 2B). Typical duration of oral therapy was 3–6 months (52%) in patients with COM without retained orthopedic implants; however, respondents noted variability based on the clinical scenario. In children with retained orthopedic implants, many respondents reported treating with oral antibiotics until implants were removed (44%), and if treating for a fixed duration, typically for 3–6 (39%) or 6–12 months (51%).

DISCUSSION

Pediatric COM is a complex entity that lacks accepted diagnostic criteria, thereby complicating the design of prospective

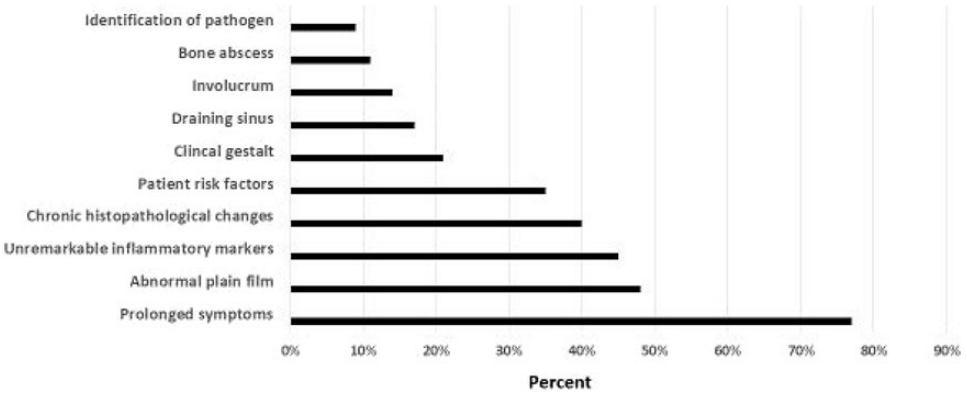

Figure 1. Factors used to diagnose chronic osteomyelitis in children. Factors used for diagnosis of chronic osteomyelitis in children by 162 pediatric infectious disease physician survey respondents. No respondents stated they were unsure of the necessary diagnostic criteria. Four respondents provided additional criteria, including the use of magnetic resonance imaging (MRI; $n = 2$) and the exclusion of alternative diagnoses ($n = 2$). Abbreviations: MRI, magnetic resonance imaging.

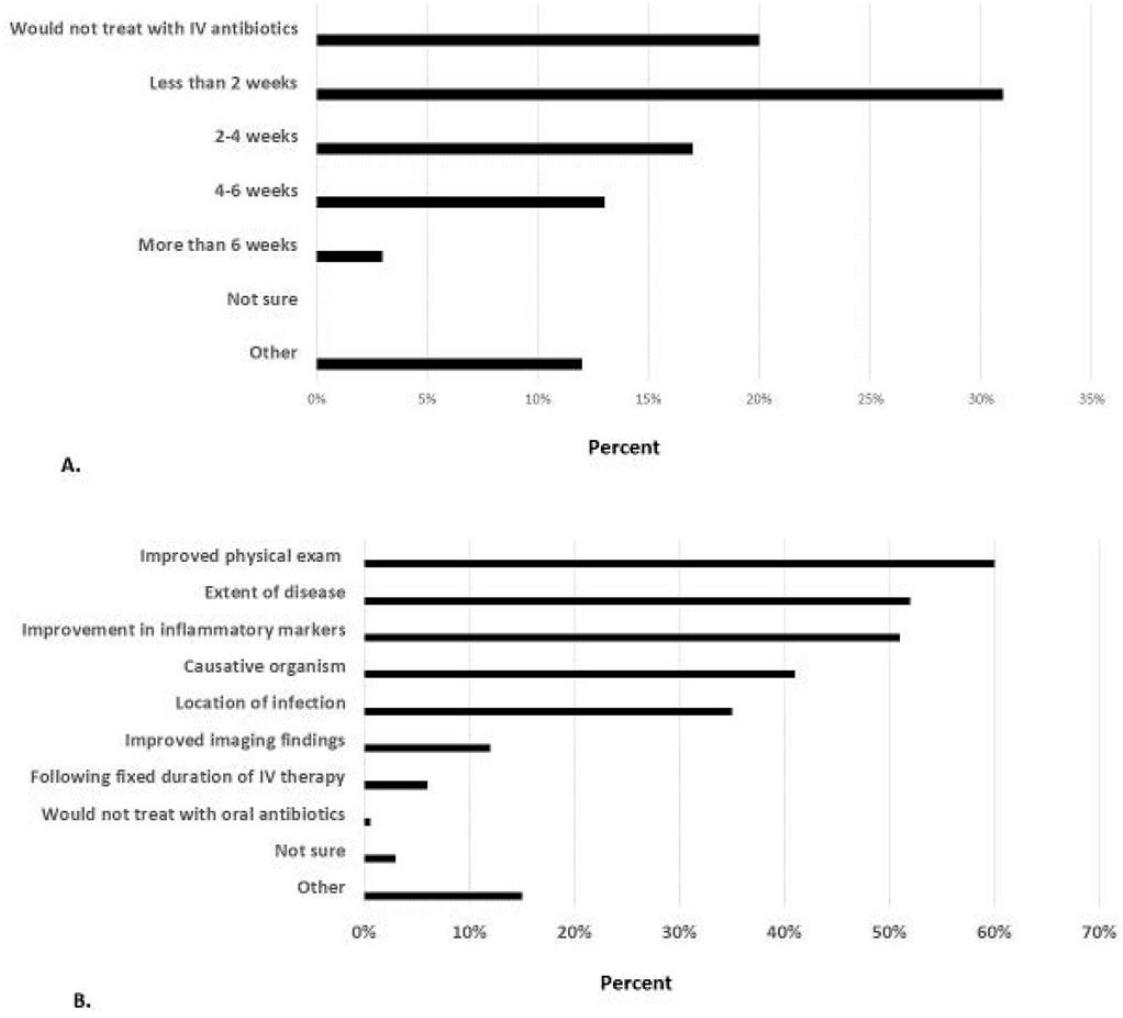

Figure 2. IV and oral antibiotics. (A) Physician-reported preference for initial use of intravenous (IV) antibiotics in children with chronic osteomyelitis. "Other" free text responses summarized as follows: transition from IV to oral was highly variable or dependent on patient factors ($n = 17$); emphasized a quick transition from IV to oral antibiotics ($n = 7$). Missing data for this question for five respondents. (B) Physician-reported criteria for conversion from IV to oral antibiotics in children with chronic osteomyelitis. "Other" free text responses summarized as follows: dependent on patient factors ($n = 18$); would not use any IV therapy and treat only with oral antibiotics ($n = 12$). Missing data for this question for two respondents. Abbreviations: IV, intravenous.

studies and resulting in significant management heterogeneity. We found substantial variability in the diagnosis and management of COM among PID physicians, emphasizing the importance of standardizing definitions and designing studies to guide management, particularly for children with foreign material remaining in presumed or documented infected tissue space (the most commonly reported etiology of COM in our survey, presumably due to orthopedic contraindications for removal).

Diagnosis of COM may be difficult, as symptoms are often vague and more indolent than in AHO. From our survey, consensus appears to support the use of symptom duration, abnormal plain films, and unremarkable inflammatory markers at presentation, along with chronic histopathological inflammatory changes of bone as diagnostic criteria. Nevertheless, this approach is not infallible, as fewer than half of respondents reported using the last three criteria. In addition, although chronic inflammatory changes of bone may be histopathological findings in COM [7, 8], recent evidence suggests up to 30% of bone samples from children with clinical suspicion of COM may have either normal histopathological results (20%) or evidence of only acute inflammatory changes (10%), despite prolonged symptoms (median 6 months) [7]. Though evidence of bony necrosis may be seen on imaging, findings of involucrum and sequestrum may be less common in industrialized countries and are not always present [9]. Few of our respondents required evidence of an involucrum (14%) or sequestrum (18%) for diagnosis. In designing prospective studies of COM, the establishment of widely accepted and evidence-based diagnostic criteria will be essential.

As a whole, our survey respondents did not conceptualize COM as a single entity, but instead as arising from multiple different etiologies. Perhaps partly as a result of this belief, we

found the management of COM was highly variable. The lack of evidence basis for the management of COM was highlighted in a 2013 Cochrane review of adult COM [12]. Limited evidence suggests that outcomes are similar with oral versus parenteral treatment, as long as organisms are susceptible to the oral antibiotic selected [9, 12]. No studies were identified that compared differing durations of antibiotic treatment for COM, and no prospective pediatric studies address this question. In a recent single-center retrospective study of pediatric COM, all patients received IV therapy, with a median duration of 12 days and no association between the duration of IV therapy and treatment failure [7]. Partially due to a lack of prospective trials assessing the duration of IV therapy, historical durations of 6 weeks or more are reported, and one-third of our respondents were treated with intravenous antibiotics for more than 2 weeks [8]. McNeil described a prolonged and variable total antibiotic treatment duration (median 210 days; Q1 150 days, Q3 367 days) [7]. Among our respondents, 15% were treated for more than 6 months with oral therapy.

This study has several limitations. Our survey data are subject to response and recall bias, and given our 50% response rate, may not be representative of the entire EIN network. The survey did not collect patient-level data, rendering assessment of outcomes by management practice and consideration of regional variations in incidence and severity impossible. Finally, the sample of PID physicians enrolled in EIN may differ from PID physicians not part of EIN.

CONCLUSIONS

Significant variability exists among PID physicians regarding the diagnosis and management of COM. Creating a formal definition for this entity is required to facilitate prospective research to standardize care for children with this disease.

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Potential conflicts of interest. All authors: No reported conflicts.

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