

MEDICAL MYTHOLOGY

Pediatric myth: fever and petechiae

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ABSTRACT

A child presenting with petechiae and fever is assumed to have meningococemia or another form of bacterial sepsis and therefore to require antibiotics, blood cultures, cerebrospinal fluid analysis and hospital admission. A review of the literature challenges this statement and suggests that a child presenting with purpura (or petechiae), an ill appearance and delayed capillary refill time or hypotension should be admitted and treated for meningococcal disease without delay. Conversely, a child with a petechial rash, which is confined to the distribution of the superior vena cava, is unlikely to have meningococcal disease. Outpatient therapy in this context is appropriate. In other children, a reasonable approach would be to draw blood for culture and C-reactive protein (CRP) while administering antibiotics. If the CRP is normal, these children could be discharged to follow-up in 1 day, whereas children with CRP values greater than 6 mg/L would be admitted.

Keywords: meningitis, petechiae, purpura, lumbar puncture, pediatrics

RÉSUMÉ

Un enfant présentant des pétéchies et de la fièvre est soupçonné d'avoir une méningococcémie ou une autre forme de septicémie bactérienne. La prise en charge comprend une antibiothérapie, des hémocultures, l'analyse du liquide céphalorachidien et l'hospitalisation. Une revue de la littérature révèle que cette déclaration est contestée et suggère qu'il faut hospitaliser et traiter sans tarder pour une méningococcie un enfant présentant un purpura (ou des pétéchies), ayant l'air malade, dont le temps de remplissage capillaire est retardé ou manifestant de l'hypotension. Inversement, un enfant présentant un rash pétéchial qui se limite à la distribution de la veine cave supérieure est peu susceptible d'avoir une méningococcie. Un traitement ambulatoire dans ce contexte est approprié. Chez d'autres enfants, il serait raisonnable de faire des prises de sang pour culture et dosage de la protéine C-réactive (PCR) et d'amorcer une antibiothérapie. Si la PCR est normale, ces enfants peuvent obtenir leur congé, avec un suivi le lendemain, alors que les enfants dont la PCR est supérieure à 6 mg/L devraient être hospitalisés.

Myth

Children presenting with fever and a nonblanching rash (petechiae or purpura) require a full sepsis evaluation including a lumbar puncture (LP) and hospital admission.

Introduction

Until proven otherwise, the simultaneous appearance of petechiae and fever is assumed to be meningococemia or another form of bacterial sepsis.¹ Previous investigations

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have determined the incidence of meningococcal disease in children with fever and petechiae to be between 0.5% and 11%.¹⁻⁴ The mortality of meningococcal disease is high (between 3.7% and 17%)^{1,5,6} and increases with delays in diagnosis and initiation of therapy. The incidence of meningococemia peaks in the pediatric and young adult population. Meningococcal meningitis is not usually a diagnostic dilemma, but meningococcal septicemia can be as it may present with subtle findings. A classic early finding is a nonblanchable hemorrhagic (petechial or purpuric) rash. Given the high mortality, its subtle presentation and a reported incidence that can be as high as 11% in children with fever and petechiae, it is a commonly held practice that all children with petechiae and fever need to be evaluated for meningococcal disease. That evaluation consists of immediate antibiotic administration, blood culture, LP and hospital admission while awaiting culture results. Based on the current evidence presented in this manuscript, not all children presenting with petechiae and fever require a full evaluation.

Comment

A 2003 clinical practice guideline on meningococcal disease stated a “golden rule” that “fever plus a petechial rash is meningococemia until proven otherwise.”⁷ However, recent literature has suggested that such a unilateral approach may not always be necessary. Selective evaluation and management of children presenting with fever and petechiae was originally broached by Van Nguyen and colleagues in 1984.¹ They reviewed the records of 129 children admitted to the hospital with fever and petechiae who otherwise appeared well. The authors found 26 patients (20.2%) had culture-proven bacterial infections; 13 (10%) were infected with *Neisseria meningitidis* and 8 (6.2%) had *Hemophilus influenzae* type B. The remaining 5 patients had culture-proven bacterial infections that were secondary to *Streptococcus pneumoniae* (1/26), *Staphylococcus aureus* (2/26) and *Escherichia coli* (2/26). Patients with bacterial infections were found to have higher total absolute leukocyte counts, absolute band counts and an erythrocyte sedimentation rate (ESR). Neither fever nor any sole laboratory finding was sensitive enough to detect all patients with bacterial infections. Sensitivities were 87% for LP and 84.6% for absolute band count. Four patients with bacterial infections had an ESR performed; all 4 were elevated. Not a single patient with a normal white blood cell (WBC) count, absolute neutrophil count, absolute band count, cerebrospinal fluid and with a temperature less than 40°C was found to have an invasive bacterial infection. This investiga-

tion concluded that there would be very little probability of children defined by these criteria having an invasive bacterial infection. They still recommended a full workup on all children with fever and petechiae or purpura.

Kuppermann and colleagues⁸ performed a retrospective review over a 9-year period at 4 centres seeking to evaluate whether clinical and laboratory parameters commonly used in the evaluation of fever could identify children with unsuspected meningococcal disease. They identified 381 children ultimately diagnosed with meningococcal disease, of which 45 (12%) were unsuspected. Of the 45 children with unsuspected meningococcal disease, 37 (82%) were between the ages of 3 and 36 months. These 45 patients were then compared with 6414 culture-negative patients. The authors determined via multivariate analysis that those with unsuspected meningococcal disease were younger (8.9 v. 14.2 mo) and had a higher band count. The positive predictive value of an elevated band count was determined to be very low and therefore the authors did not recommend screening all young febrile children with a complete blood count. They did, however, recommend screening with a band count in patients with known meningococcal disease contact, during meningococcal outbreaks and in children with fever and a petechial rash. The authors did not determine a difference in temperature, WBC count or absolute neutrophil count between the unsuspected meningococcal disease group and the culture-negative group.

Brogan and Raffles⁹ performed a retrospective and prospective audit of 55 children presenting with fever and petechiae. The objectives of this investigation were to identify risk factors predictive of significant bacterial sepsis in children with fever and petechiae, and to establish a set of clinical guidelines. Proposed risk factors for significant bacterial sepsis were shock (capillary refill > 2 s, hypotension or both), irritability, lethargy, abnormal WBC count (< 5000 or > 15 000) and elevated C-reactive protein (CRP) (> 5 mg/L). Of the 55 children enrolled, 5 were found to have significant bacterial sepsis. Brogan and Raffles then defined the “ILL” criteria (i.e., irritability, lethargy, low capillary refill). They concluded that patients who lack the “ILL” criteria in conjunction with a normal WBC count and CRP could be observed for a least a 4-hour period and then reassessed. If there was no evidence of clinical deterioration, then outpatient care could be recommended. Children who had negative “ILL” criteria but a laboratory abnormality could be treated for meningococcal disease pending blood cultures. Finally, those who had the presence of 1 or more of the “ILL” criteria and who had an abnormal WBC count or CRP could be treated for meningococcal sepsis with intensive care referral. It should

be noted that Brogan and Raffles did not report information regarding CRP values in the nonsignificant bacterial sepsis population. It was not the authors' intention to assess the screening test characteristics of any single factor in isolation, but to provide an assessment tool using a combination of risk factors.

In the first prospective study of patients presenting with fever and petechiae, Mandl and colleagues⁴ conducted a cohort study of 411 patients (357 of whom appeared well) presenting to a pediatric emergency department. Consecutive patients with fever and petechiae were enrolled over an 18-month period. Of the 411 patients, 8 patients had bacteremia or clinical sepsis. Six of the 8 had a serious bacterial illness diagnosed. Two children had *Streptococcus pneumoniae* bacteremia. None of the 8 had a positive CSF result. Meningococcal disease was found in 2 of the 8 patients. All patients with serious bacterial illness appeared ill at the attending physician's initial assessment, had petechiae below the nipple line and had purpura (> 2 mm) as well as petechiae. The authors concluded that "confirmation of normal laboratory values, an observation period to evaluate for progressive petechiae and empiric antibiotics to selected patients may permit management of well-appearing children with fever and petechiae as outpatients."⁴

Similarly, Wells and colleagues¹⁰ prospectively enrolled a group of 233 pediatric patients presenting to the emergency department with petechiae or purpura. Patients presenting without a fever were included (111/233). Fifteen patients were excluded for alternative diagnoses such as Henoch-Schonlein purpura, idiopathic thrombocytopenic purpura, hemolytic uremic syndrome, acute leukemia and clotting disorders. Of the remaining 218 patients, 24 (11%) had meningococcal disease. The petechiae in 74 (34%) patients were confined to the distribution of the superior vena cava (SVC); none of these patients had meningococcal infection. Additionally, CRP values were obtained on all patients. None of the children with meningococemia had a CRP less than 6 mg/L (100% sensitive, 54% specific). Most patients diagnosed with meningococcal infection were ill-appearing on presentation (19/24). These data suggest that if petechiae are confined to the distribution of the SVC (i.e., above the nipple line) or if the CRP is less than 6 mg/L the child is unlikely to have meningococcal disease.

Nielsen and colleagues,¹¹ in a prospective study of 264 children hospitalized with fever and petechiae, found that 39 (15%) had proven or probable meningococcal disease and an additional 6 had another invasive bacterial infection. In this population, universal distribution of petechiae, which is defined as the presence of petechiae below the nipple line, had a sensitivity of 92% and a

specificity of 40%. The median CRP of patients with meningococcal diseases was 109 mg/L. Nielsen and coauthors used a general condition score (an observation score) based on a 3-point scale for 3 variables (level of consciousness, spontaneous motor activity and skin colour/circulation). The authors concluded that there were 5 clinical variables that were independently able to predict the presence or absence of meningococcal disease:

1. skin hemorrhages characteristic of meningococcal disease,
2. universal distribution of skin hemorrhages,
3. one or more skin lesions with a maximal diameter of greater than 2 mm (i.e., purpura),
4. a poor general condition score,
5. nuchal rigidity.

If 2 or more of the aforementioned variables were present, the probability of identifying a patient with meningococcal disease was 97%.

These studies indicate several features that may guide the clinician when examining a child with petechiae and fever. All children in the studies by Mandl and colleagues⁴ and Wells coauthors,¹⁰ and all but 3 of the children in the Nielsen and coworkers¹¹ study who had petechiae confined to the area of distribution of the SVC ultimately did not have a diagnosis of meningococcal disease. Furthermore, no patient in the study by Wells and colleagues who was ultimately diagnosed with meningococcal disease had a CRP of less than 6 mg/L. Additionally, although not reported in Nielsen and coauthors' paper, all patients diagnosed with meningococemia also had a CRP greater than 6 mg/L (H.E. Nielsen: personal communication, 2007).

In the aforementioned studies, most children diagnosed with meningococemia appeared ill at presentation, but in both Wells and colleagues¹⁰ and Kuppermann and coauthors⁸ patient groups there was a significant portion of children who appeared well when they initially presented. Additionally, the presence of purpura was helpful, with a sensitivity of 83% (95% confidence interval [CI] 68–98) and a specificity of 88% (95% CI 84–93) for meningococcal disease.

A reasonable approach for evaluating a child with a non-blanching rash would appear to be:

1. If there is the presence of purpura, ill appearance, delayed capillary refill time or hypotension, the child should be admitted and treated for meningococcal disease without delay.
2. If the rash is confined to the distribution of the SVC, the "ILL" criteria are not present, nuchal rigidity is absent, the WBC and CRP are within normal limits, and the child looks well after a careful evaluation and period of

observation, the child is unlikely to have meningococcal disease. In this group, age-appropriate fever guidelines should direct management and disposition.

3. In children with petechiae below the nipple line who otherwise appear well, a reasonable approach would be to draw blood for culture, CBC and CRP, and proceed with a fever evaluation based on the patient's age, while administering antibiotics and observing the child. If the CRP is normal and these children appear well after a 4-hour observation period they could be discharged with close follow-up (within 1 d), whereas children with CRP values greater than 6 mg/L or clinical deterioration should be admitted to hospital.

Conclusion

Not all children presenting with fever and petechiae warrant a complete evaluation for meningococcal disease. However, a careful and thorough clinical evaluation must always be undertaken. For the well-appearing child, the above management strategy allows for careful evaluation but may prevent routine testing, admission or both for a select group of patients.

Competing interests: None declared.

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