Petechiae and Purpura: The Ominous and the Not-So-Obvious?

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Abstract

Petechiae and purpura are among the most alarming findings a pediatrician will commonly observe in the office. Severity of illness can range from a temper tantrum, to common viral infections, to the most deadly infections and diseases. To avoid many of the pitfalls in diagnosis, practitioners will need to be thorough in history taking, assessing fever and immunization status, and physical examination. In addition, a few simple laboratory tests will usually be needed and possibly a manual differential. **[*Pediatr Ann*. 2014;43(8):297-303.]**

Whether the child is febrile, well, or ill, whenever you see a patient with petechiae and/or purpura in your office, you should first take a deep breath. Then your index of suspicion and your pediatric instincts should override everything else in your life or office. You should obtain a full set of vital signs, including blood pressure and oximeter, and make sure your patient does not appear to be acutely ill or prostrate or to have meningismus. If you are observing this scenario, you will then be making immediate arrangements for blood culture, intravenous access, possibly an in-office parenteral dose of ceftriaxone (which is available in nearly all pediatric offices), and emergency transport to your nearest capable emergency department. However, this highly urgent scenario is, fortunately, exceedingly rare in most of our lifetimes.

Instead, typically, you will be encountering a young patient who is non-toxic, who may or may not be febrile, who is alert, is speaking normally, and has normal vital signs. You should first attempt to ensure that you are *not* seeing a case of low-grade early meningococcemia, which could evolve extremely rapidly into full-blown shock. The good news: The former disease has become an increasingly uncommon encounter, with apparently only about 1,000 cases of invasive meningococcal disease (IMD) occurring annually in the United States in recent years.[1] But when you practice in rural Kentucky, any esoteric disease may be lurking.

Next on your list of urgent and potentially devastating diseases are what I term the "big 3" group of very ominous petechial illnesses: 1) renal group: hemolytic uremic syndrome (HUS), 2) cancer/hematology group: leukemia/lymphoma/neuroblastoma/aplastic anemia, and 3) Rocky Mountain spotted fever (RMSF) group, including ehrlichiosis and anaplasmosis.

The next considerations will be three other sometimes not-so-obvious blood/vasculitic disorders: autoimmune thrombocytopenias (eg, idiopathic thrombocytopenia [ITP], systemic lupus erythematosus [SLE]), and the not-so-rare Henoch-Schoenlein purpura (HSP).

But the most common pathogens associated with petechiae/purpura will usually be the more innocuous infectious agents, such as viral infections you commonly see in your practice, including mononucleosis, enterovirus, and parvovirus infections.[2] Schneider and colleagues[3] reported that most cases of petechiae seen in a hospitalized population of German children (average age, 3.8 years) were viral in origin (39 of 58), with a positive blood culture in only one child. However, as a major limitation of the study, they excluded from the report children who had any purpuric lesions. Also, fewer than 10 petechiae were reported in 23% of children in the series as well. Be forewarned, as I have personally seen merely four petechiae, fever, and arthralgia as the initial presenting signs of IMD.[4]

APPROACH TO PETECHIAE/PURPURA

Upper Body Location of Petechiae

Although still ripe with diagnostic pitfalls, a much easier presumptive diagnosis for you will occur when the petechiae are relegated above the nipple line on physical examination. The diagnoses

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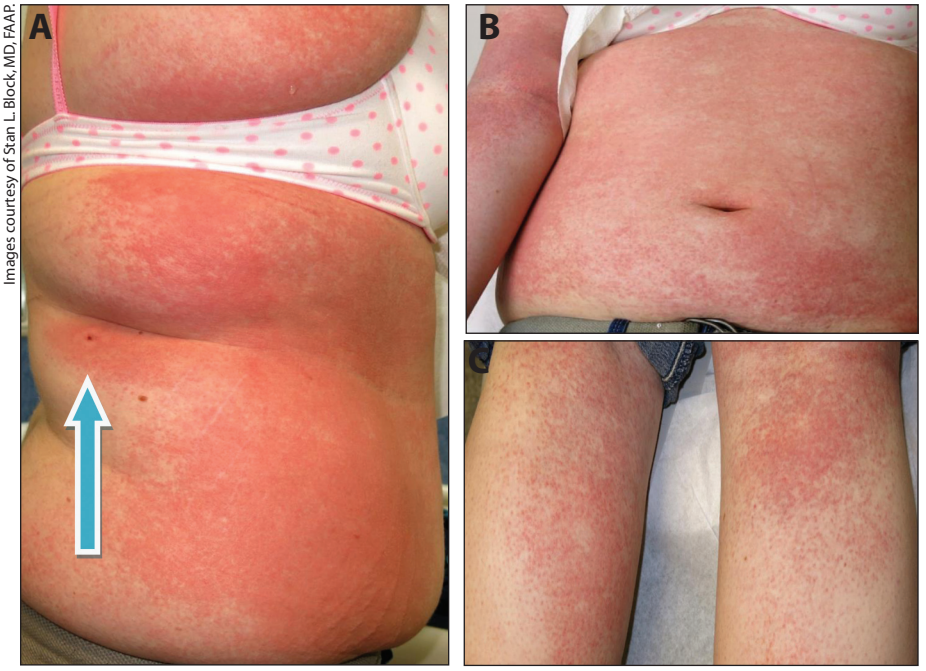

Images courtesy of Stan L. Block, MD, FAAP.

Figure 1. An 18-year-old female with history of "possible spider bite" punctum on right lower rib area (A, blue arrow). Forty-eight hours after the initial bite, she has developed marked confluent erythroderma on the lateral trunk, in contrast with the more maculo-papular pinpoint rash on the abdomen, as well as a thick, scarlet fever–like rash on the abdomen, neck, and elbow creases (B). At 96 hours, the rash has progressed. It is more petechial and pruritic on the knees (C), despite 48 hours of oral clindamycin and 24 hours of doxycycline therapy to cover for potential methicillin-resistant *Staphylococcus aureus*-related surgical scarlet fever and Rocky Mountain spotted fever, respectively, from the insect bite. Are you more concerned that the bite may have initially been from a tick instead?

are more likely to be benign: *s*treptococcal pharyngitis, forceful vomiting, severe cough.[5] But still be very cautious when making this assumption in any febrile child. For these patients, I would still consider obtaining a complete blood count (CBC), possibly with a manual differential, along with close follow-up within the next 24 hours by phone and/or in the office the next day.[6]

History

You will want to ascertain most of the following factors in your history: level of fever, tick bites in the last 3 weeks, recent travel, recent camping trips, constitutional symptoms such as weight loss and fatigue, urine output and color, vaccination status, sore throat, headaches, and joint aches.

Physical Examination

Vital signs should be assessed, along with oximetry. You should inspect the skin carefully for distribution of petechiae and purpura and other types of rashes—especially for lesions below the nipple line, any elevation and nonblanching of lesions, and sclera icterus. The patient's general demeanor and level of alertness and toxicity are important to note. A thorough physical examination is essential, including at minimum: most node regions, neck suppleness, pharynx, heart, lungs, liver, spleen, abdomen, and joints.

Laboratory Assessments

I suggest the following basic and simple laboratory assessments for patients with petechiae and/or purpura:

- CBC with a manual differential (can be performed by capillary stick). Certain abnormalities suggest meningococcemia, RMSF, ehrlichiosis, HUS, and cancer group, and will usually eliminate the diagnosis of HSP.
- Urine analysis (UA). Certain abnormalities suggest HUS, rarely RMSF group or HSP

In the more ill or febrile child consider:

- Complete metabolic panel (CMP; ie, electrolytes, renal and liver functions). Certain abnormalities suggest the RMSF group, mononucleosis, HUS, or meningococcemia.
- Blood culture.
- Lumbar puncture. Primarily performed for any stable child with nuchal rigidity or altered mental status; however, it will likely be too difficult to obtain in the office setting for all but infants and toddlers.

Then make a calculated guess whether to:

- Initiate empiric antibiotics (orally or parenterally).
- Use doxycycline to cover for the RMSF group and/or ceftriaxone to cover for meningococcemia.
- Hospitalize your patient.
- Send home with careful follow-up.

You must be keenly aware that the earliest finding and only good clue for IMD in nearly one third of infected patients was an elevated band count on the manual differential of the CBC.[6] Regarding the "RMSF triad," as I discussed in my July 2014 article,[7] most patients with RMSF will, initially or over a few days, have at least one or more of the three following laboratory manifestations: low leukocyte count with a high band count, thrombocytopenia, and/or hyponatremia.[8] In addition, those with Ehrlichiosis will usually have elevated hepatic transaminases. An empiric course of doxycycline should be considered.

These medical decisions are among the most difficult for both experienced and novice practitioners. Remember that almost no in-office hematology machine and leukocyte counter can perform a band count or examine a peripheral blood smear for "blasts" or hemolysis.

CASE 1

At 48 hours after a possible "spider bite," an 18-year-old female presents with a fulminant erythroderma (**Figure 1A**) mixed with a scarlet fever–like rash (**Figure 1B**) on her lateral torso and abdomen, respectively. Unlike most cases of alleged spider bites seen in the office, which are usually staphylococcal pyodermas not associated with a bite, a small bite punctum is actually present on her side (**Figure 1A,** arrow). She is afebrile, affable, and feels fine. Her physical examination and vital signs are normal. Because you are concerned that this may be a *Staphylococcus aureus* "surgical scarlet fever" reaction, you initiate oral clindamycin therapy. When seen 24 hours later, the rash is still spreading, so you initiate doxycycline therapy for possible tick-borne illnesses.

After 48 hours of antibiotics, the rash has progressed, now covering her lower extremities in a highly petechial but pruritic rash (**Figure 1C**). The petechiae can now be seen on her palms (**Figure 1E**), as well as on her face. Her leukocyte count has increased to 18,500, with 90% segmented neutrophils. Her serum chemistries and urine analysis are normal. Upon further questioning, you surmise that she may have actually been bitten by a brown recluse spider. She is still smiling, although with some generalized malaise.

Diagnosis

You are now concerned that the progression of the rash may indicate either an indolent meningococcemia or RMSF infection from a tick bite instead. You hospitalize her at your children's hospital, where the infectious disease consultant elects to go "mostly" with your first diagnosis of a spider bite, secondarily infected with bacteria such as *S. aureus* or others. They initiate high-dose intravenous clindamycin and ampicillin/sulbactam. However, hedging their bets, they also continued doxycycline intravenously. Within 48 hours, the patient is feeling much better, and her rash is fading rapidly. The RMSF and ehrlichiosis titers that you obtained earlier were negative. She recovers uneventfully.

Diagnosis: Petechiae/purpura secondary to brown recluse spider bite.

Discussion

Brown recluse spider bites can cause systemic toxicity, including fever, chills, nausea, malaise, and a diffuse macular rash with petechiae.[9,10] Hemolysis, coagulopathy, and renal failure have also been reported in children. In one series of adult patients, 5% were hospitalized, 3% required surgical debridement, and 9% received Dapsone antibiotic (not for children).[10]

CASE 2

An 11-year-old male who was being treated with amoxicillin for a typical streptococcal pharyngitis, develops a morbilliform measles-like dermatitis 4 days into therapy (**Figure 2A**). He still has a sore throat and remains febrile at 101°F; his cervical lymph nodes and abdomen are normal; his leukocyte count is normal.

His rapid test for mononucleosis is positive today. Thus, you assume this is just the purported "typical" mononucleosis rash triggered by amoxicillin and not a drug hypersensitivity reaction or other complication. The rash is non-pruritic and not urticarial. Four days after you switch his antibiotics to oral cephalexin, he has now developed a petechial and lumpy purpuric rash over his entire body (**Figures 2B-2C**). He is non-toxic, talkative, and feels fine. He is afebrile with normal vital signs and physical examination.

Diagnosis

Although he has classic palpable purpura, the distribution of the rash is too extensive to be typical for HSP or immunoglobulin A (IgA) vasculitis. Or is it?

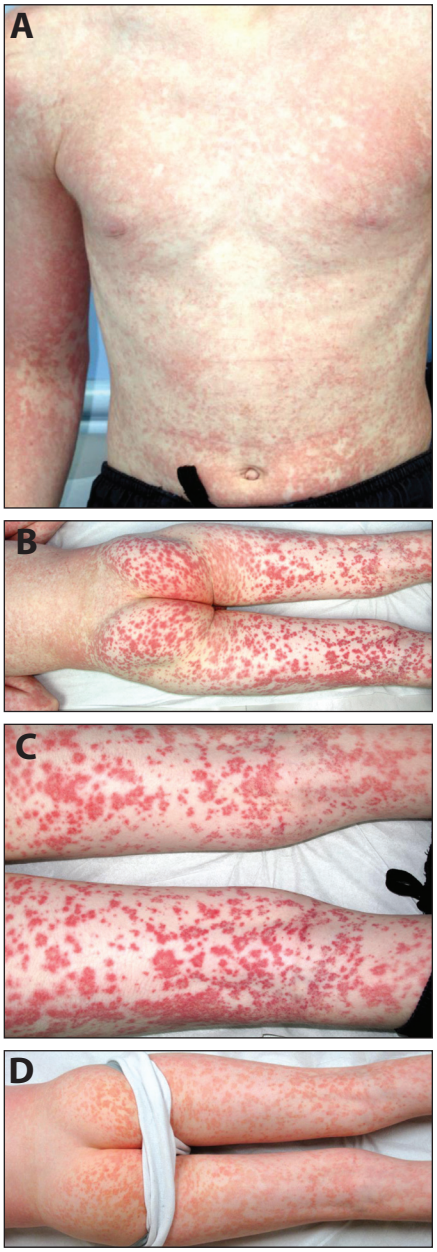

Figure 2. An 11-year-old White male who developed this morbilliform measles-like rash 4 days into treatment with amoxicillin for streptococcal pharyngitis (A). His fever is still 101°F, his lymph nodes and abdomen are normal, and his leukocyte count is normal. Further testing? When the patient showed a positive monospot test, his doctor switched him off amoxicillin and substituted oral cephalexin. Four days later, the patient developed this full-body "lumpy" purpuric rash (B, C). He is now afebrile and has minimal other symptoms. Allergic reaction? Refer? Hospitalize? Treatment? The morbilliform purpuric rash in the 11-year-old male has markedly dissipated 24 hours after being treated with which drug (D)? (Answer can be found in the text.)

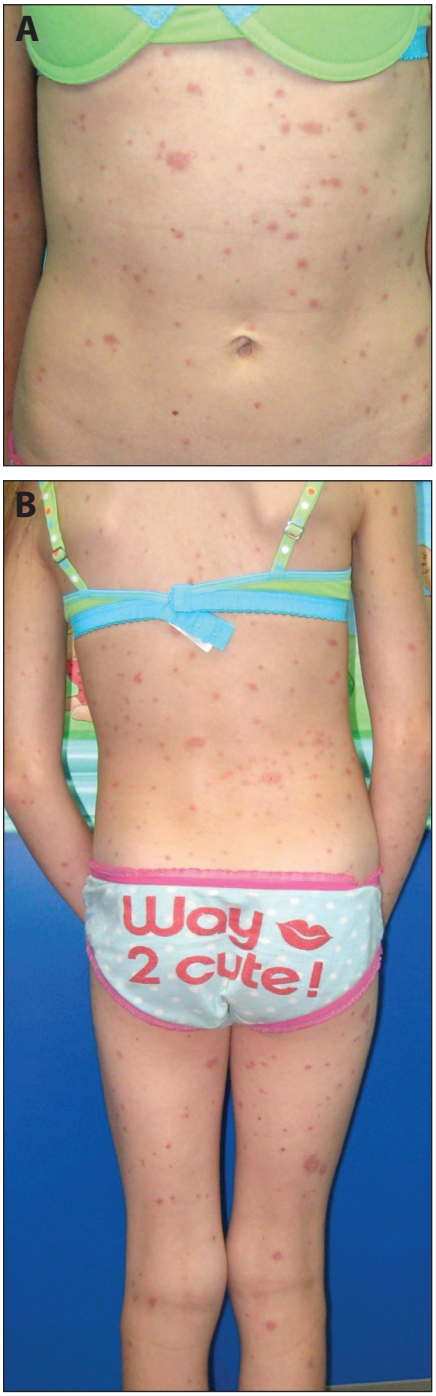

Figure 3. Note the full body (A) and arm (B) distribution of the lumpy purpuric rash in this 13-year-old white female who is afebrile and has no other symptoms.

After all, you have been taught that the rash rarely goes superior to the waistline or on the arms. But one of the keys to this diagnosis is the usual lack of any systemic illness signs or fever.

You obtain a CBC, UA, and CMP to ensure you are not witnessing a case of early meningococcemia or hemolytic uremic syndrome, ITP, or SLE. All laboratory tests are normal, thus you default to the HSP diagnosis.

How common is HSP? You audited your charts for the diagnosis of either anaphylactic purpura of HSP over the past 5 years. In your busy, seven pediatrician private practice of children and adolescents, you found 27 cases within the 60-month interval—about one episode every 2 months may occur in your office. Only three patients were adolescents.

You are well aware that the IgA vasculitis can primarily affect (early on or later) four other organ systems besides the skin, such as: 1) glomerulonephritis, 2) abdominal pain (rarely along with intussusception), 3) arthritis, and 4) orchitis/oophoritis. Although these sequelae have been reported in 50% to 75% of children[9] (who were mostly hospitalized), they are actually uncommon (< 5%-10%) in your experience with outpatients in the general pediatrics office. You are quite attuned to possible secondary nephritis, which may have particularly severe long-term sequelae. However, in fact, you have only seen this occur in two patients during 30 years of general pediatric practice. Both patients are doing well, but both still require antihypertensive medication. And, you learned this week in the office, one young girl had just finished receiving immune suppressants for more than 3 years. Only a few of your patients have also experienced severe abdominal pain to the point of requiring surgical evaluation and hospitalization. In one of these patients who was febrile, despite 48 hours of an initial diagnosis of HSP and the later development of a typical HSP rash, the blood culture obtained in the emergency department revealed that she actually had a meningococcal serogroup B infection. So be very careful with the diagnosis of HSP in the febrile child. A continued physical and laboratory evaluation is very important.

Monitoring in HSP

Careful follow-up over the first few weeks is still essential, despite the low incidence of nephritis. In the otherwise uncomplicated afebrile case after HSP diagnosis is made, you may typically recommend: 1) two additional visits within the first week, and then two more weekly visits; and 2) to return at any time if the family notices the child has developed puffy eyes, bad headaches, off-colored urine, decreased urine output, abdominal/genital/joint pain or swelling; 3) at each visit, a CBC, UA, and serum chemistries as well as obtaining weight, vital signs (blood pressure especially), and a physical examination.

Treatment of HSP

This is a fairly controversial area, but the literature suggests a possible role for steroid therapy, at least in hospitalized patients. I think that two recent studies conducted by Weiss et al,[11,12] have shown that steroids may cause a modest reduction in renal disease and significant reductions in surgery (odds ratio: 0.39), endoscopy (odds ratio: 0.27), and abdominal imaging (odds ratio: 0.5).

When the child with HSP did not have severe abdominal pain, I have personally only used oral steroids in an outpatient setting one time—in this case. And, the results appeared to be dramatic within 24 hours of initiation of oral steroids (**Figure 2D**). My rationale was based on the severity of his vasculitic rash in this case and the fact that steroids have also shown a modest benefit in some cases of severe mononucleosis. The earlier steroids are started in more severe cases of HSP, the greater the benefit will be, in my opinion. Obviously, I did not want to wait for severity requiring hospitalization.

Mononucleosis Rash Due to Amoxicillin

I believe this may be one of the most unsubstantiated "factoids" in pediatric medicine; and any entrenched mythol-

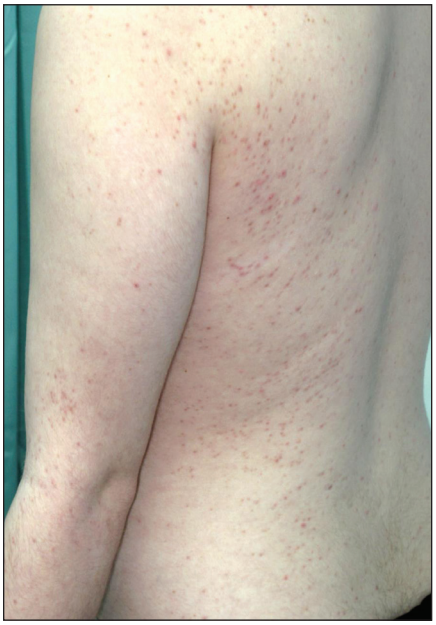

Figure 4. Note the petechiae on the trunk and upper extremity in this 12-year-old white male who is afebrile and has no other symptoms. Is further testing needed?

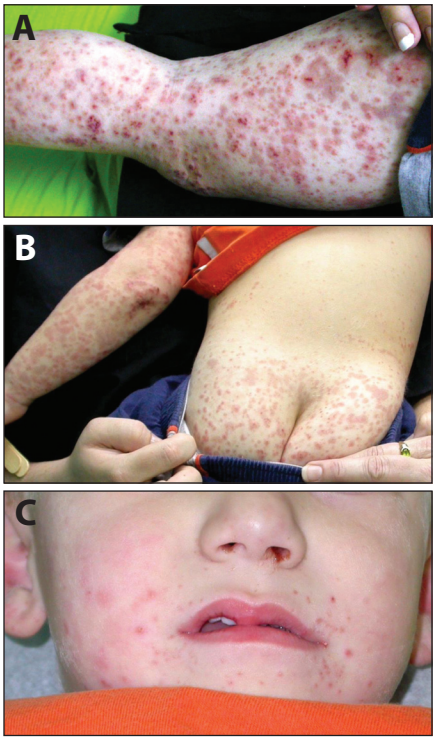

Figure 5. An irritable, unhappy 2-year-old white male who has developed this alarming petechial and purpuric rash on the legs (A), arm and below the waistline (B), and peri-orally (C). Is further testing needed?

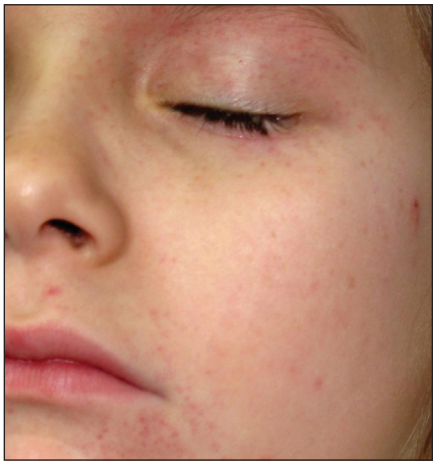

Figure 6. Eight-year-old female with strep throat and fever to 102°F, who has developed this peri-oral and peri-orbital petechial rash.

ogy is hard to extinguish. For years in our office, we have been treating streptococcal pharyngitis with amoxicillin as the first-line agent. We observe probably 50 to 100 cases of mononucleosis annually, of which at least 5% are co-infected with streptococcal pharyngitis, and several will also develop acute otitis media or sinusitis, which we have almost uniformly treated with amoxicillin, as well. We rarely ever have observed a rash in this group of children. A recent report regarding Israeli children seems to confirm our anecdotal findings. Among children with mononucleosis, the incidence of rash was not any different for children who had received amoxicillin versus those who had not (29.5% vs 23%).[13]

Diagnosis: Petechiae/purpura secondary to HSP; possibly related to mononucleosis or group A *Streptococcus*.[14]

CASES 3, 4, AND 5

Each of these children (ages 13 [**Figure 3**], 12 [**Figure 4**], and 2 years old [**Figure 5**], respectively), who were otherwise healthy and afebrile, shows the uncharacteristic distribution of the palpable purpuric and petechial rash in HSP. Cases 3 and 4 were distributed all the way up the back and onto the arms. Case 5 shows another alarmingly diffuse HSP rash that appeared not only on the arms but also the face. The rash may be associated with pruritus and excoriations. In each of the cases, the CBC and platelet counts were normal. The child in Case 5 was also the most worrisome due to his difficult examination in the office and the severity of his rash. A blood culture was obtained in his case, but no antibiotics were started in light of his normal CBC and other laboratory findings.

However, the young boy in Case 4 with the least alarming rash was one of the only two children in our practice over 30 years who actually developed renal complications of azotemia and hypertension. His renal condition has resolved, but he still requires an antihypertensive daily.

Diagnosis: Petechiae and purpura secondary to HSP.

CASES 6 AND 7

Each of these photographs (**Figures 6 and 7**) shows some of the most common presentations of petechiae in otherwise healthy white children who have streptococcal pharyngitis and fever. Neither child had a history of cough or vomiting. Note the facial distribution of petechiae without any other body petechiae in each case. Because of the fever and illness, these children usually need more careful evaluation and follow-up the next day or two, even though they both have a documented case of streptococcal pharyngitis. You will usually still perform a CBC, preferentially with a smear for a manual band count, platelets, and evidence of hemolysis. Note that the leukocyte and band count both may be elevated notably in children with streptococcal pharyngitis, creating some consternation on your part. Occasionally, you may be worried enough initially to perform a blood culture and sometimes even to administer parenteral ceftriaxone, if you have significant suspicion for early meningococcemia despite your positive rapid strep test. To make your overall assessment even more complex, remember that some of

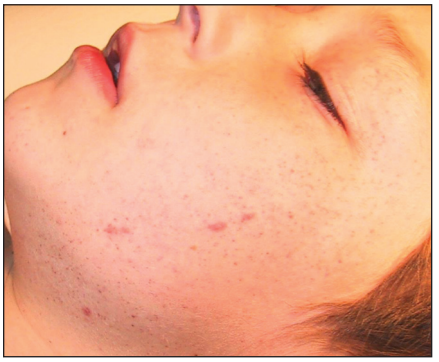

Figure 7. Six-year-old male with *Streptococcal pharyngitis,* lymphadenitis, and fever 101°F, who has developed this petechial rash on his face.

these children with a positive streptococcal pharyngitis test, may actually be streptococcal carriers.

Diagnosis: Petechiae secondary to strep throat.

CASE 8

This toddler had such a severe screaming temper tantrum the night before the office visit that she developed this highly concentrated localization of petechiae from the clavicle to the scalp line (**Figure 8**). She was not ill otherwise; she had absolutely no history of vomiting, cough, or pharyngitis. Her CBC and platelets were also normal. Without any spread or other triggers of petechiae, could this be a case of early ITP or leukemia? The petechiae dissipated moderately over the next 48 hours when she was seen back in the office, and she has remained well and without any evidence of petechiae over the next month.

Diagnosis: Petechiae secondary to the "terrible two's."

CASES 9 AND 10

These two patients with streptococcal pharyngitis show a worrisome distribution of petechiae (ie, on the feet and palms, extending up to the knee) (**Figures 9-10**). Because RMSF classically presents with a rash starting on the hands and feet, which spreads centripetally, you must be particularly attuned

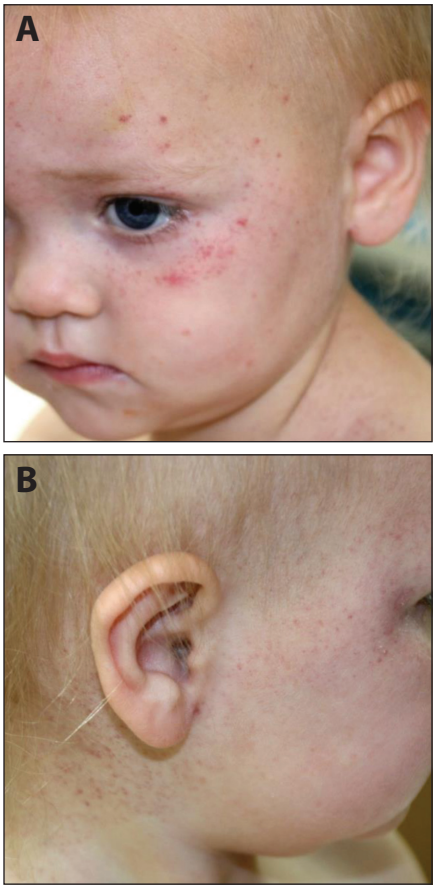

Figure 8. Afebrile toddler in the full throes of the "terrible two's", who has no cough, vomiting, or illness. You are perplexed as to the cause of her facial petechiae. She is certainly not happy that you are visiting with her today.

to this diagnosis and carefully assess for a history of any tick bites. This is summertime, after all. You think that a CBC, serum chemistries, and UA are a prudent starting point in the evaluation.

But these two patients do not appear ill. Thus, if you were to carefully assess the oropharynx of these two patients, you have a distinct likelihood of uncovering some red, round, yellow-centered blisters in the posterior pharynx or on the lips. Remember that the peak season for very commonly encountered enteroviral infections is also summer, and enteroviral infections can also cause petechiae,[14] which it did in these cases.

Diagnosis: Enteroviral infection.

CASE 10

The 10-year-old male in this photo-

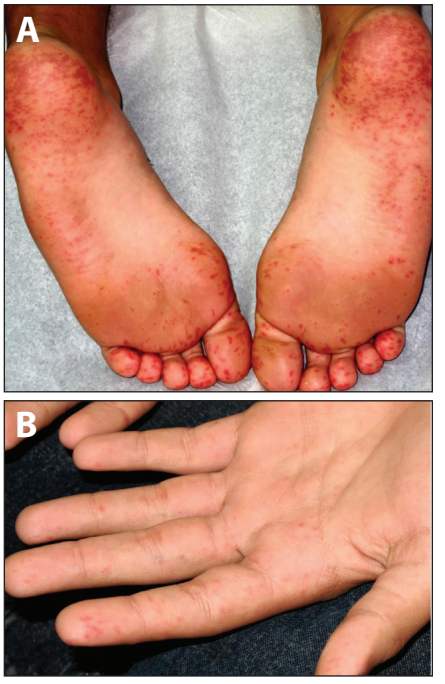

Figure 9. Worrisome petechiae rash on the soles (A) and palms (B) of a 13-year-old male who has sore throat and fever (102.5°F). It is summer, and he has been camping, but the mother can recall no tick bites recently. Further testing? Or a more thorough physical examination?

graph (**Figure 11**) is more ill appearing and sleepy. He has been previously healthy and has no history of tick bites or travel. He has had a fever for the past 2 days (101.3°F today), headache, moderate photophobia, no nuchal rigidity, and some lower extremity joint aches. He also has moderate abdominal pain, so you are also worried about the vasculitis of HSP. The rash is scarlet fever–like with macule-papules interspersed with petechiae.

Discussion

In your office, you obtain a CBC, UA, and serum chemistries, which only show a low leukocyte count. Because your automated office hematology machine does not perform a leukocyte differential, you send the bloodwork to the hospital. Although you were not initially certain of the severity of his illness, when the band results (28%) arrive a few hours later, you call the patient back in to the office. You have observed enough.

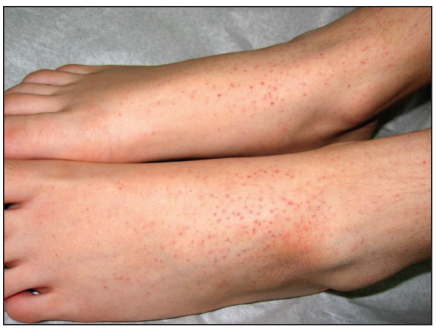

Figure 10. A worrisome petechial rash on the dorsum of the feet and up to the knees (not shown) in an afebrile 14-year-old female who only reports a sore throat. A careful physical examination may reveal the causative pathogen.

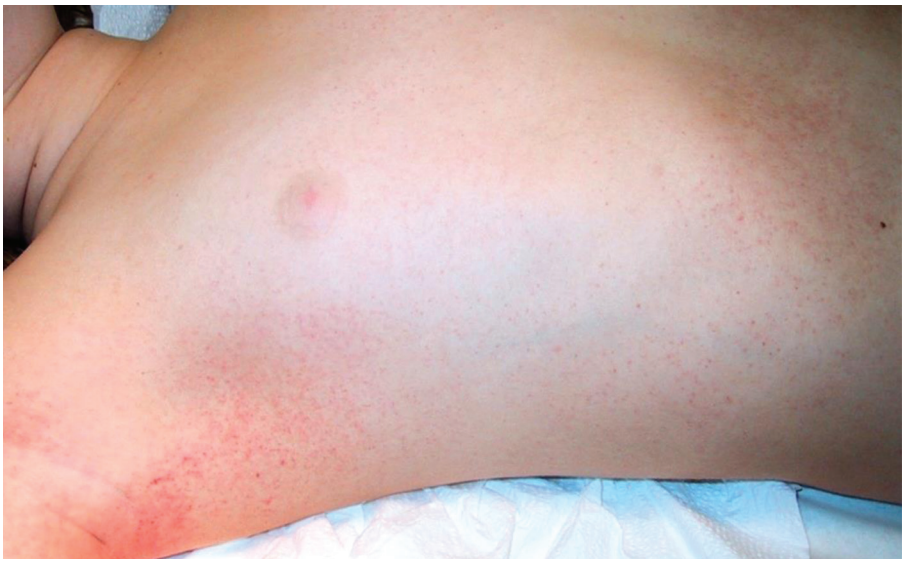

Figure 11. In April, this 10-year-old male developed headache, abdominal pain, generalized arthralgias, and fever (101.3°F) along with these petechiae all over the trunk in a scarlet fever–like distribution. In your practice, does this series of cases remind you of the fable of the little boy who cried wolf too many times? Is further testing needed?

You decide to admit him to the hospital for blood culture and parenteral ceftriaxone antibiotics. His mental status and neck suppleness remain unchanged over the next several hours, so you do not think a lumbar puncture is worthwhile. He does not have meningitis, so you do not think that he initially needs either vancomycin or steroids as well.[15] Within 24 hours, most of his fever and illness symptoms have dissipated, except for the joint aches. His blood culture is now growing a gram-negative cocci. Your index of suspicion was correct: He was affected by both the ominous and not-so-obvious—early meningococcemia.

Diagnosis: Early meningococcemia.

CONCLUSION

Petechiae and purpura are among the most alarming findings a pediatrician will commonly observe in the office. The severity of the cause of illness can range from a simple temper tantrum, to common viral infections, to the most deadly of infections (meningococcemia) and diseases (HUS). Although no cases of the following were presented here, I have seen several cases of ITP, aplastic anemia, and leukemia present in similar manner as these cases.

To avoid many of the pitfalls in diagnosis, practitioners will need to be thorough in history taking, assessing fever and immunization status, and physical examination. Also, you will usually need to resort to a few simple laboratory tests and possibly request a manual differential, paying meticulous attention to the details in all these reports. Index of suspicion and clinical gestalt are key as well. Be especially wary of any child who has fever with his petechiae/purpura. Petechiae and purpura will test your mettle!

REFERENCES

1. U.S. Centers for Disease Control and Prevention. Meningococcal disease: causes and transmission. http://www.cdc.gov/meningococcal/about/causes-transmission.html. Accessed July 22, 2014.
2. Edmonson MB, Riedesel EL, Williams GP, DeMuri GP. Generalized petechial rashes in children during a parvovirus B19 outbreak. *Pediatrics*. 2010;125:e787-e792.
3. Schneider H, Adams O, Weiss C. et al. Clinical characteristics of children with viral single- and co-infections and a petechial rash. *Pediatr Infect Dis J*. 2013;32(5):e186-e191.
4. National Public Broadcasting Network. The Best Doctors in the World are Making House Calls on Public Television: Healthy Body Healthy Mind TV Series: 2204 Catching a Killer: Preventing Meningococcal Disease. 2012. Episode 2204 [DVD].
5. Wells LC, Smith JC, Weston VC, Collier J, Rutter N. The child with a non blanching rash: how likely is meningococcal disease?. *Arch Dis Child.* 2001;85:218-222.
6. Demissie DE, Kaplan SL, Romero JR, et al. Altered neutrophil counts at diagnosis of invasive meningococcal infection in children . *Pediatr Infect Dis J*. 2013; 32:1070-1072.
7. Block SL. Spots and lumps: treacherous tick-borne illnesses. *Pediatr Ann*. 2014;7:256-261.
8. Mandell GL, Wilfert CM. *Atlas of Infectious Diseases. Pediatric Infectious Diseases*. Philadelphia, PA: Churchill Livingstone; 1999.
9. Kliegman RE, Stanton B, St. Geme J, Schor NF, Behrman RE. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia: Saunders Elsevier; 2011.
10. Wright SW, Wrenn KD, Murray L, Seger D. Clinical presentation and outcome of brown recluse spider bite. *Ann Emerg Med*. 1997;30:28-32.
11. Weiss PF, Feinstein JA, Luan X, Brunham JM, Feudtner C. Effects of corticosteroid on Henoch-Schonlein purpura: a systematic review. *Pediatrics*. 2007;120:1079-1087.
12. Weiss PF, Klink AJ, Localio R, et al. Corticosteroids may improve clinical outcomes during hospitalization for Henoch-Schonlein purpura. *Pediatrics*. 2010;126:674-681.
13. Chovell-Sella A, Tov AB, Lahav E. Incidence of rash after amoxicillin treatment in children with infectious mononucleosis. *Pediatrics*. 2013;131:e1424-e1427.
14. Paller AS, Mancini AJ, eds. *Hurwitz Clinical Pediatric Dermatology: A Textbook of Skin Disorders of Childhood and Adolescence*. 4th ed. Philadelphia, PA: Elsevier/ Saunders; 2011.
15. AAP Committee on Infectious Diseases; Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2012. Report of the Committee on Infectious Diseases (Red Book Report of the Committee on Infectious Diseases).* 29th edition. Elk Grove Village, IL. American Academy of Pediatrics; 2012.