A previously healthy 18-year-old girl with no significant medical history presented to her pediatrician in the summer with a sore throat and fatigue. Results of a rapid Streptococcus (strep) screening test and a mononucleosis spot test were both negative, and she was prescribed a 10-day course of amoxicillin for the pharyngitis. One week later, the patient returned with a diffuse rash consisting of small red macules and papules on her trunk, arms, and face, consistent with amoxicillin use in the setting of infectious mononucleosis (IM). Laboratory tests for Epstein-Barr virus (EBV) immunoglobulin G and immunoglobulin M returned positive, the amoxicillin was discontinued, and a 6-day course of prednisone was prescribed in an effort to help manage her symptoms. Ten days later, after completing the course of steroids, the patient visited a dermatologist for painful pustules that had developed on her legs and buttocks. Concerned about infection with methicillin-resistant Staphylococcus aureus (MRSA), her dermatologist cultured the pustules and prescribed topical mupirocin 2% cream and 100 mg twice daily of minocycline for the folliculitis while awaiting culture results (which later returned as methicillin-sensitive S. aureus).

One week after the patient started the minocycline, she noticed a pruritic rash on her legs that spread to her trunk, arms, and face over the next few days. She subsequently developed a fever of 104°F with chills and fatigue; she visited the emergency department, where she was prescribed triamcinolone cream, hydroxyzine, and cetirizine and was discharged. The rash continued to worsen, and the patient developed swelling of her face, lips, neck, hands, and feet. She returned to her primary care physician, now a full month after her initial presentation for sore throat, and was found to have proteinuria (value of 100 mg/dL) and a 30 white blood cell count on urinalysis, in addition to oral ulcers and a diffuse red rash. The minocycline was discontinued, and the patient was directly admitted to the children’s hospital for further evaluation. Laboratory test results revealed a C-reactive protein level of 203.5 mg/L, an erythrocyte sedimentation rate of 38 mm/h, a complete blood cell count with a white blood cell count of 9.3 x 10^9/L and 11.3% eosinophils, nonreactive antinuclear antibody, and a urine protein-to-creatinine ratio of 0.34. Given the timing of the minocycline dose, the diffuse confluent morbilliform rash with fever, the elevated inflammatory markers and eosinophilia, and the oral ulcers and proteinuria, the patient was diagnosed with drug reaction with eosinophilia and systemic symptoms (DRESS), and was closely monitored on the inpatient floor. Luckily, both her clinical condition and her laboratory findings stabilized after a few days off the minocycline, and she was discharged from the hospital on the eve of her sister’s wedding, with a head-to-toe pink-and-purple rash to complement her lavender bridesmaid dress.
In this case, efforts to alleviate a patient’s discomfort led to a cascade of iatrogenic events that culminated in a dangerous and potentially life-threatening drug reaction. This case is an example of low-value care: the quality of the treatment was low, and the cost of the treatment was high. Had careful consideration been given to the safety and effectiveness of the care, the outcome would have been drastically different. Furthermore, the substantial resources spent on treatment could have been avoided. The sequence of events that led to this patient’s misfortune can be broken down into 3 key decision points, which are discussed in detail here. At each juncture, a physician chose an active intervention when watchful waiting or conservative symptom management would likely have constituted higher value care.

The first decision was to prescribe amoxicillin for pharyngitis. In the absence of a positive rapid strep test result, antibiotics are not indicated.1 Indeed, there has been some argument in the literature that in high-resource settings, routine treatment of strep throat should be discontinued.2,3 Adverse reactions to antibiotics occur in 5% to 25% of patients.3 Potential harms of amoxicillin include allergic reaction, gastrointestinal upset, and future development of infections with resistant organisms. A blood draw for EBV-specific antibodies at this junction might have provided a definitive diagnosis, but an appropriate positive test result would not have altered management if amoxicillin was not prescribed. In this patient’s case, the decision to prescribe antibiotics led to an unnecessary prescription, an uncomfortable rash, and an additional physician’s visit.

When this patient again presented to her physician’s office with a rash after amoxicillin administration, a diagnosis of IM was confirmed with EBV antibody testing, and her physician prescribed a course of prednisone. Corticosteroid use in the treatment of EBV mononucleosis is controversial. A Cochrane review addressing administration of steroids in addition to antibiotics for pharyngitis demonstrated faster relief of pain than in the control group with antibiotics alone. However, these articles were not specific to IM.4 A Cochrane review exploring corticosteroid use in the setting of IM concluded that the evidence is not strong enough to recommend routine use of steroids for IM in the absence of concern for airway compromise.5 The Cochrane review further noted that steroids were not found to benefit a sore throat caused by IM and would thus likely be ineffective for managing dehydration. To date, there is no evidence that steroid treatment has a significant effect on duration or severity of symptoms of IM. As such, absent of any airway compromise, this patient may not have benefited from provision of steroids. The potential adverse effects of oral steroids are numerous, ranging from immunosuppression and drug reactions to malignancy. In longer courses of steroids, dermatologic adverse effects such as acne and infection occur in 5.4% of patients.3 Short courses of oral steroids are usually well tolerated; the most common adverse effect is psychotic or pre-psychotic episodes.1 Thus, the potential benefit of this treatment may have been outweighed even by the low risk for adverse events related to the drug. Unfortunately for our patient, the administration of corticosteroids likely contributed to the development of folliculitis.6,8 Even worse, the patient’s folliculitis afforded another provider the opportunity to prescribe another drug, this time with more serious adverse effects.

The third treatment decision resulting in this patient’s admission to the hospital was to prescribe minocycline for folliculitis. Minocycline is not recommended as a first-line treatment of folliculitis or acne because of its side effect profile.6 Side effects of minocycline include drug hypersensitivity syndrome, DRESS, Stevens-Johnson syndrome, eosinophilic pneumonia, and drug-induced lupus. Although rates of DRESS in patients taking minocycline have not been reported, the drug does increase the risk of autoimmune phenomena eightfold. This patient’s folliculitis may have resolved on its own or alternatively could have been treated with an antibiotic with a more modest side effect profile such as cephalexin.10 It is unclear why the physician suspected MRSA, as this patient had a superficial nonsevere folliculitis without deeper tissue involvement. However, in an effort to prevent complications related to a suspected MRSA abscess, minocycline was prescribed, and a known side effect of the drug—DRESS—resulted. DRESS is a complex multisystem drug reaction with both acute and chronic complications that carries a mortality rate of 5% to 10%.11,12 This patient’s month-long iatrogenic saga included a total of 4 outpatient visits, an emergency department visit, and an inpatient hospitalization, in addition to several rounds of laboratory tests and the administration of 2 rounds of oral antibiotics, a topical antibiotic, and oral and topical steroids. The patient experienced significant physical discomfort and stress from this cascade of events that all began with a very common viral illness that would likely have resolved on its own. Even if her primary care physician had ordered no testing and provided no medications, this patient likely would have been fine.

Patients often expect physicians to act: to order the tests, to get the laboratory findings, to prescribe the medication. And as physicians, we worry that by not treating we are not doing enough for our patients. We want to help, so we use everything in our arsenal to alleviate the symptoms, cure the disease, or prevent complications. And in our litigious society, we have become increasingly conscious of what might happen if we miss something, and thus are now even more likely to act “just in case.” We figure we might as well, since a short course of steroids or a round of antibiotics seems an obvious choice given the complications that might arise if we do not treat. As this case illustrates, however, what we might consider benign treatments for benign diseases can have significant repercussions. We need to incorporate more evidence-based medicine into our decisions and weigh the benefits of the treatment against the costs. Because, in the end, it is just as important to shield our patients from potential adverse effects of tests and medications as it is to protect them from potential sequelae of disease.
Sometimes the best action is no action at all.

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