When antibiotics experts say no to antibiotics

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Abstract

Overuse or misuse of antibiotics is one reason for the emergence of antibiotic resistance. Here, we present four cases where antibiotics were started (or proposed) although they were not needed. The first case was asymptomatic bacteriuria where antibiotic therapy was initiated but then stopped after the case was referred to the infectious diseases (ID) service. The second case was a cholangiocarcinoma patient in whom four antibiotics were continued after completing the treatment for a remote infection. Hence, the ID team discontinued the unneeded therapy after considering that the inflammatory process was due to malignancy. The third case was a patient who was diagnosed with pneumonia in whom both antibiotics and an antiviral were initiated. However, antibiotic therapy was continued despite the lack of bacterial growth in the respiratory culture. Thus, it wasn't until the ID team evaluated the case and decided that the pneumonia was viral in nature that antibiotic therapy was discontinued. The last case was for a patient who presented with dry cough presumed to be a pneumonia and was about to be started on antibiotics. The ID team noticed the patient had a history of decompensated congestive heart failure causing the cough. Antibiotics were not initiated when lack of clinical findings suggestive of pneumonia was also confirmed. These cases represent an example of daily occurrences of antibiotics overuse. Healthcare providers are encouraged to augment their knowledge regarding the safe and judicious use of antibiotics, as well as consulting an ID expert if doubts concerning the necessity of antibiotics arise.

Keywords **Antibiotics, infectious diseases, infection, stewardship.**

Introduction

Antibiotics have been used to treat infectious diseases since the discovery of penicillin in 1928.[1] The first case of bacterial penicillin resistance was reported in 1965, followed by the emergence of different patterns of resistance by different bacterial species. This resistance is most often characterized by the production of extended-spectrum β-lactamase (ESBL), carbapenemases, and aminoglycoside modifying enzymes, as well as different resistance mechanisms at the cellular level.[1,2] One reason for the emergence of antibiotic resistance is the overuse or misuse of antibiotics.[2] In the United States, about 30% of hospitalized patients receive antibiotics that are deemed to be unnecessary, the elimination of which could save 10-30% of the pharmacy costs by antimicrobial stewardship programs.[3] Another negative consequence of the overuse of antibiotics is the risk of superinfections mainly *Clostridioides difficile*.[4] Such consequences are collectively termed "collateral damage."[4]

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When speaking about the use of antibiotics, it is important to differentiate between a "colonization" and an "infectious disease." A colonization is simply defined as the establishment of a microorganism on or within a host. This may cause no harm or only low gain to either participant. On the other hand, an infectious disease results when such interaction causes damage to the host in the form of altered physiology leading to clinical signs and symptoms.[5] Antibiotic therapy is indicated for the latter but not the former.

The concept of antimicrobial stewardship has been introduced in the last decade and is defined as "coordinated interventions designed to improve and measure the appropriate use of antibiotic agents by promoting the selection of the optimal antibiotic drug regimen including dosing, duration of therapy, and route of administration".[6] Antimicrobial stewardship has two major goals: to optimize clinical outcomes of infections while reducing the harm caused by unnecessary antibiotic use and to decrease healthcare costs while maintaining the same quality of care.[7]

Here, we present four cases in which antibiotics were started (or proposed) but were not needed when their use was reviewed by an infectious diseases (ID) specialized healthcare provider, a consultant (attending physician), specialist, or clinical pharmacist. At the time of the evaluation of these cases, an antimicrobial stewardship program was not yet established (it was established at our institution in September 2020). Nonetheless, some of the broad-spectrum antibiotics (such as piperacillin/tazobactam, cefepime, and carbapenems) required prior authorization from the ID team for prescribing or continuation of therapy within 48 hours of initiation (depending on the level of restriction of the antibiotic). In such case, the patient's case would be referred to the ID service where the ID clinicians would evaluate the case for the need of antibiotic therapy or lack thereof, as well as suggest dose and duration in case antibiotic therapy was deemed necessary. While our institution, as an academic medical center, held weekly ID grand rounds (where an ID topic or case is presented), no formal education or training on antimicrobial stewardship was offered to hospital staff.

Patient cases

Case 1

In the first case, a 60-year-old woman with a history of congestive heart failure (CHF) and diabetes mellitus presented to the emergency department complaining of shortness of breath with a productive cough and yellow sputum for two days. Upon examination, the patient had a fever of 39°C with bilateral basal crepitations. The white blood cell (WBC) count was normal at 8.75 cells/mm^3. The patient was admitted with a diagnosis of community-acquired pneumonia (CAP) with respiratory failure and started on 4.5 g intravenous (IV) piperacillin/tazobactam every 8 hours with bilevel positive airway pressure. A respiratory culture was ordered but not collected. Upon admission, a urine culture was collected as a clean catch, which revealed ESBL-producing *Escherichia coli* with a bacterial count of >100,000 CFU/mL (colony-forming units per milliliter). As a result, the primary team decided to upgrade the antibiotic to 1 g IV meropenem every 8 hours in order to cover both infections. The patient was then referred to the ID team for evaluation of the infections. The patient's record was reviewed, and the patient was physically examined and asked about the presence of any symptoms indicating a urinary tract infection, such as dysuria, urinary frequency and hesitancy, and suprapubic pain. Notably, the patient denied such symptoms. Therefore, the ID team decided that the urine culture represented a typical case of asymptomatic bacteriuria. Additionally, as the patient's respiratory function was improving on meropenem, the ID team decided to de-escalate the empiric coverage for CAP to 1 g IV ceftriaxone every 24 hours for two days to complete a total duration of five days of therapy (piperacillin/tazobactam was given for two days and meropenem was given for one day). Coverage for atypical bacteria was considered unnecessary since the patient was improving on β-lactam therapy.

Case 2

The second case involved a 64-year-old woman who had undergone renal transplantation and was on immunosuppressive therapy composed of tacrolimus, mycophenolate mofetil, and prednisolone. Upon presentation, the patient was complaining of fever, severe upper right abdominal pain, jaundice, and diarrhea. After extensive medical investigation, the patient was diagnosed with acute cholangitis and obstructive jaundice secondary to cholangiocarcinoma. The patient underwent left biliary plastic stenting and hepatic external biliary drainage, which was sent for a microbiological culture. A stool sample was sent for *C. difficile* toxin enzyme immunoassay. The biliary culture showed *Stenotrophomonas maltophilia* susceptible to trimethoprim/sulfamethoxazole and levofloxacin, and the *C. difficile* toxin assay returned positive. Thus, the patient was started on an IV of trimethoprim/sulfamethoxazole (at 960 mg of trimethoprim component) every 12 hours and 125 mg of oral vancomycin every 6 hours. Three weeks later, while still on both antibiotics, the patient spiked a fever at 38.5°C with a WBC count of 14.6 cells/mm^3 (up from 7.5 cells/mm^3 two days prior). Blood and urine cultures showed no growth. The patient was empirically started on 500 mg IV imipenem/cilastatin every 6 hours and 4.5 million units of IV colistin every 12 hours. After two weeks of being on all four antibiotics, the patient was seen by the ID team. After a careful review of the patient's condition and despite a slight fluctuation of the WBC count above the upper limit of normal, the ID team decided to discontinue vancomycin since the patient had already completed a 10-day course (the primary team had maintained it for potential prophylaxis against *C. difficile* infection). The ID team also discontinued the other three antibiotics since the patient was clinically stable and they had determined that the inflammatory process presented by the slight elevation in WBC counts was due to the malignancy. Of note, the patient developed acute kidney injury demonstrated by significantly elevated serum creatinine ten days after colistin was initiated, which was another indication for its discontinuation.

Case 3

The third case involved a 68-year-old man who had been diagnosed with idiopathic pulmonary fibrosis 3.5 years prior to presentation, for which he had been receiving pirfenidone, prednisolone, and home oxygen for 1.5 years. He also had a history of diabetes managed by oral hypoglycemics. He presented to the emergency department with respiratory symptoms, including progressive shortness of breath for five days, chest pain, paroxysmal nocturnal dyspnea, night sweating, and weight loss. He reported no gastrointestinal or urinary symptoms, history of travel, fever, or sick contacts. The patient was vitally stable, but his WBC count was elevated at 18.73 cells/mm^3. Chest radiograph showed bilateral infiltration. The patient was suspected to have pneumonia; however, it was unknown whether it was bacterial or viral. During admission, an influenza test (polymerase chain reaction) was not available and a respiratory culture was not collected. Blood culture showed no growth. As such, the patient was admitted to the medical ward and was started empirically on 1 g ceftriaxone every 8 hours (this was escalated a day later to 4.5 g IV piperacillin/tazobactam every 6 hours), 500 mg azithromycin orally every 24 hours, and 75 mg oseltamivir orally every 12 hours. Vancomycin was added two days later (1 g IV every 12 hours). Two days post admission and initiation of antibiotics, the case was referred to the ID team, and they requested a measurement of the procalcitonin level, which can help differentiate between bacterial and viral infections. Upon checking the patient's laboratory results, the team noticed that the procalcitonin level has already been ordered upon admission and was low (within reference range). As such, bacterial pneumonia was ruled out and all antibiotics were stopped immediately. The patient continued the full course of oseltamivir for five days. The patient's condition improved and he was discharged.

Case 4

The fourth patient was a 68-year-old woman with a past medical history of CHF, hypertension, ischemic heart disease, and diabetes mellitus. Eight days before the admission described here, the patient had undergone surgery for subdural hemorrhage. At this admission, the patient was brought in by her daughter due to an altered mental status. Three days post admission, the patient developed a dry cough for which she was referred to the ID team for investigation of potential respiratory infection and initiation of antibiotics for suspected CAP. Moreover, the primary team suspected that the patient also had oral thrush (oral candidiasis), for which she was started on 200 mg IV fluconazole every 24 hours. When the patient was evaluated, she was afebrile, had a normal WBC count, normal chest radiograph, normal respiration (besides the nonproductive cough), and no oral thrush was observed. Upon further investigation, the patient had an echocardiography a month prior to the current admission showing an ejection fraction of 22.2%. Furthermore, a relative of the patient recalled a similar episode of dry cough the previous year when the patient was first diagnosed with CHF (ejection fraction was 25-30%). Based on these findings, the ID team decided that the patient's cough was due to her progressive CHF rather than a lower respiratory tract infection, especially given the lack of clinical findings suggestive of pneumonia. Hence, no antibiotic therapy was initiated and fluconazole was discontinued.

Conclusions

While the determination to discontinue unnecessary antibiotics in the aforementioned examples was made by the intervention of the ID service, healthcare providers are encouraged to augment their knowledge regarding the safe and judicious use of antibiotics. This is especially important for clinical trainees, such as residents and fellows, in order to establish a good antibiotic prescribing practice early in their careers, which can be carried out to the next generation of clinicians. Several studies from different countries reported the issue of the lack of knowledge on antibiotics and resistance among young clinicians resulting in improper attitude towards antibiotic prescribing.[8-13] As a general concept, if the case does not meet the criteria for referral to the ID service, physicians are encouraged to consult an ID clinical pharmacist, if available, in order to receive an advice regarding the appropriate selection of antibiotic, dose, duration, as well as checking for any potential drug interactions. However, referral to the ID service is advisable if doubts arise concerning the necessity of the use of antibiotics.

Authors' contributions statement: AKT supervised the work, participated in manuscript drafting, and revised the final version of the manuscript. SAT, SAA, EAT, LFB, and DWS collected the patient cases and participated in manuscript drafting. All authors read and approved the final version of the manuscript.

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