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The Impact of Fast MIC Evaluation on Antimicrobial Stewardship: A Case Report

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Dealing with Antimicrobial Resistance

Recently antibiotic resistance has become a major public health issue with global dimensions, having a remarkable impact on morbidity, mortality and healthcare associated costs. Due to its increasing relevance, the “antibiotic resistance crisis” has entered the agenda of the WHO and other international agencies, scientific societies, governments and even the UN General Assembly.

Dealing with antimicrobial resistance requires a multitiered approach including the discovery and development of new antibiotics active against multidrug-resistant (MDR) and extremely drug-resistant (XDR) bacteria, the enforcement of effective infection control practices to limit the dissemination of these pathogens, and the implementation of antibiotic stewardship programs to improve patient outcomes while limiting the antibiotic pressure for selection.

Microbiological Diagnosis

Microbiological diagnosis plays an essential role in this complex scenario, by providing information on the presence and the nature of resistant pathogens in clinical specimens, which are crucial to both antimicrobial stewardship and infection control practices. However, the impact of microbiological diagnosis is largely dependent on the speed of results provided by the laboratory, whereby delayed microbiological reports will invariably have minimal impact on the selection/revision of antibiotic treatment. Even in the document addressing the US National Strategy to Combat Antibiotic Resistance, recently issued by the White House, an advancement of the development and use of rapid and innovative diagnostic tests for identification and characterisation of resistant bacteria is considered among the main goals.

The Case Report

An example of the utility of rapid and innovative tests when treating patients with severe bacterial infections is briefly described by the case below.

A 65-year old patient was admitted to the ER with diagnosis of sepsis at 5 pm on day 1. The patient suffered from Type 2 diabetes for several years and had a history of recurrent urinary tract infections due to benign prostatic hyperplasia. The patient had been febrile for six days, and received oral ciprofloxacin as an empiric treatment for five days, with no clinical improvement and eventually a rapid worsening.

Upon hospital admission, blood culturing was performed, and the patient was empirically given meropenem (1 g tid) in consideration of the clinical history and the epidemiological setting, characterised by a high prevalence of ESBL production among Enterobacteriaceae. The patient was then transferred to the general ICU. The blood cultures turned positive after 14 hrs (8 am on day 2), with the presence of Gramnegative bacilli. After Gram-staining, positive blood cultures were processed according to the routine workflow followed in the laboratory (based on fast subculture, followed by MALDI-TOF identification and antibiogram with broth microdilution), and also with the Accelerate Pheno™ system. The Accelerate Pheno™ system returned an identification of Escherichia coli after 2 hrs (10:30 am on day 2), and an antibiogram 5 hours after identification (3:30 pm on day 2) shown in **Table 1.**

The rapid antibiogram revealed a resistance profile suggestive of ESBL production (resistance to cefepime, ceftazidime, ceftriaxone), with resistance also to fluoroquinolones, intermediate susceptibility to amikacin, and susceptibility to gentamicin, piperacillin-tazobactam, carbapenems and colistin. The conventional workflow confirmed the identification (with MALDITOF) after 7 hrs (3:30 pm on day 2), and returned the antibiogram on the following day (day 3). Results of the conventional antibiogram were overall consistent with those provided by the Accelerate Pheno™ system **(Table 1)**.

Contributor's Commentary

In this case, the Accelerate Pheno™ system returned an antibiogram with MIC values for the infecting pathogen isolated from the blood culture on the day after admission, while the routine workflow adopted in the laboratory returned similar results two days after admission, despite using rapid subculture techniques. By comparison, if the laboratory had followed a more conventional approach, such as waiting for the growth of isolated colonies for identification followed by preparing an inoculum for the susceptibility testing, results would not have been available until three days after admission, at the earliest.

The increased speed of the antibiogram allowed de-escalation from empiric treatment to a carbapenem sparing regimen, like piperacilin-tazobactam, to be considered as early as the first day of treatment, offering antimicrobial stewardship advantages. Using conventional diagnostic workflows, the same information would have been available after two or three days of treatment, with a longer carbapenem exposure and a lower likelihood for treatment revision, especially if the patient was already improving.

On the other hand, a molecular test for rapid bacterial identification and detection of resistance determinants, carried out on the positive blood culture, could have returned identification in approximately the same time (1-2 hrs) but would have not provided comparably useful information about antibiotic de-escalation, since susceptibility to piperacillin-tazobactam cannot be directly extrapolated from a molecular antibiogram.

About Professor Gian Maria Rossolini

Gian Maria Rossolini is Professor of Microbiology and Clinical Microbiology at the University of Florence and director of the Clinical Microbiology Unit of Florence Careggi University Hospital. He has served as Chairman of the Department of Molecular Biology and as Dean of the Medical Faculty at the University of Siena. His main research interests are in the field of antimicrobial agents and microbial drug resistance. Prof. Rossolini is author of over 380 scientific articles listed in the PubMed database and inventor in 10 (6 international) patent applications related to diagnostics, antimicrobial agents or host-vector systems for heterologous gene expression. He has served as an Editor for *Antimicrobial Agents and Chemotherapy* and is member of the Editorial Board of several international journals focused on Clinical Microbiology and Antimicrobial Chemotherapy. Prof. Rossolini continues to review and advise on behalf of funding agencies and academic institutions for awarding research grants and academic professorships.

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