

To the Editors:

## Isolation of inducible Amp C $\beta$ -lactamase producing *Enterobacter aerogenes* from a diabetic foot ulcer

$\beta$ -lactamases are a major cause of resistance to the  $\beta$ -lactam antibiotics. Many classes of  $\beta$ -lactamases have been described depending on substrate specificity and susceptibility to inhibitors [1]. Amp C  $\beta$ -lactamases are able to hydrolyse all penicillins and cephalosporins and are not inhibited by clavulanic acid. Bacteria that produce these enzymes are resistant to all penicillins including  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations and all cephalosporins [2].

Amp C enzymes may be constitutively expressed or inducible (expressed only in the presence of the antibiotic). When these enzymes are inducible, the organism will appear sensitive to the newer penicillins and third-generation cephalosporins on antibiotic sensitivity testing (ABST) and be misreported.

A 60 year old female was admitted to the National Hospital of Sri Lanka with an infected diabetic foot ulcer. Wound curettings yielded a growth of two "coliforms". One of these showed a blunting of the cefotaxime zone near the coamoxyclav disc in the ABST and it was suspected that this could be an Amp C  $\beta$ -lactamase producer. A screening test using ceftioxin confirmed this suspicion. Therefore, we reported it resistant although the isolate appeared sensitive to cefotaxime on ABST. The isolate was speciated as *Enterobacter aerogenes*.

Inducible Amp C enzymes are found in most *Enterobacter*, *Serratia* and *Providencia* spp and in *Morganella morganii* and *Citrobacter freundii* [1]. First generation cephalosporins and amoxicillin strongly induce Amp C enzymes and are destroyed by them, and this is readily detectable on ABST. Third generation cephalosporins and cefuroxime are labile but induce weakly. Therefore, on routine testing, the strains appear susceptible but there will be clinical failure when these drugs are used for therapy.

There are no standard tests for identification of inducible Amp C producers [3]. They may be detected by using an inducing antibiotic to induce the enzyme [4]. This induction of resistance is the basis for the ceftioxin /

cefotaxime disc antagonism test. In this test the ceftioxin disc acts as an inducer of the enzyme and the induced enzyme is able to destroy cefotaxime, blunting the zone of susceptibility around the disc on that side. Clavulanic acid is a weak inducer of Amp C enzymes, which is why a blunting of the zone of inhibition around cefotaxime adjacent to coamoxyclav was seen on the initial ABST.

In the absence of a standardised method for detection of inducible Amp C production it is recommended that all *Enterobacter*, *Serratia* and *Providencia* spp and *Morganella morganii* and *Citrobacter freundii* are reported resistant to all third generation cephalosporins [2,4] i.e. the best method for detecting Amp C  $\beta$ -lactamase inducible bacteria is accurate speciation. However most laboratories in Sri Lanka do not have the facilities to speciate Enterobacteria and they are usually reported as 'coliforms'. In these circumstances Amp C producing bacteria which are resistant to third generation cephalosporins may be reported as sensitive with resulting treatment failure.

Until a standard laboratory method of detection of Amp C mediated resistance is available, clinicians need to be aware of the possibility of Amp C production in isolates of 'coliforms' from serious infections when prescribing antibiotics and monitoring response to antibiotic therapy.

### References

1. Livermore D.  $\beta$ -lactamases in laboratory and clinical resistance. *Clinical Microbiology Reviews* 1995; **8**: 557-84.
2. Jacoby GA. AmpC  $\beta$ -lactamases. *Clinical Microbiology Reviews* 2009; **22**: 161-82.
3. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 19th informational supplement. CLSI document M100-S19. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.
4. Livermore DM, Brown DFJ. Detection of  $\beta$ -lactamase-mediated resistance. *Journal of Antimicrobial Chemotherapy* 2001; **48** (Supp): 59-64.

E M Corea<sup>1</sup>, P L L Bandara<sup>2</sup>

<sup>1</sup>Department of Microbiology, and <sup>2</sup>Trainee MD (Medical Microbiology), Postgraduate Institute of Medicine, University of Colombo, Sri Lanka.

Correspondence: EC, e-mail <enokacorea@hotmail.com>. Received 6 October 2009 and revised version accepted 5 February 2010. Competing interests: none declared.