

CASE REPORT

A health care-associated pneumonia case due to colistin resistant *Acinetobacter baumannii*

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ABSTRACT

A 78 year old male was hospitalized in neurology clinic with a diagnosis of encephalopathy. On 13th day of imipenem treatment for ventilator-associated pneumonia (VAP), a new VAP episode was diagnosed based on physical examination, laboratory and radiological findings. Cefoperazone-sulbactam 2x2 gr/day IV was started empirically. In the 3rd day of treatment *Acinetobacter baumannii* was identified from endotracheal aspirate culture that was resistant to all other antibiotics including colistin except cefoperazone-sulbactam (intermediate) and tigecycline (MIC: 4 mg/L, intermediate) by VITEK and E-test. Tigecycline 2 x 50 mg (after loading dose of 100 mg) IV, colistin IV 2 x 150 mg and colistin inhaler 2 x 75 mg were added to the cefoperazone-sulbactam 2 x 2 gr IV. Clinical findings were improved under this combination and completed to 14 days. The patient was discharged from hospital with neurological sequel after three months. This case has been presented to emphasize that colistin resistant *Acinetobacter baumannii* is becoming a problem for our country. *J Microbiol Infect Dis* 2014; 4(3): 111-113

Key words: *Acinetobacter baumannii*, colistin resistant, pneumonia, multidrug resistant

Kolistin dirençli *Acinetobacter baumannii*'ye bağlı sağlık bakımı ile ilişkili bir pnömoni vakası

ÖZET

Yetmiş sekiz yaşındaki erkek hasta ensefalopati tanısı ile nöroloji bölümüne yatırıldı. Ventilator ilişkili pnömoni (VİP) nedeniyle başlanan imipenem tedavisinin 13. gününde fizik muayene, laboratuvar ve radyolojik bulgulara dayanarak yeni bir VİP tanısı kondu. Ampirik olarak sefoperazon sulbaktam 2 x 2 gr/gün IV tedavisi başlandı. Tedavinin 3. gününde endotrakeal aspirat kültüründe hem Vitek hem de e-testle sefoperazon-sulbaktam (orta duyarlı) ve tigesiklin (MIC: 4 mg/L, orta duyarlı) hariç diğer tüm antibiyotiklere (kolistin dahil) dirençli *Acinetobacter baumannii* üremesi oldu. Sefoperazon-sulbaktam 2 x 2 gr/gün IV tedavisine tigesiklin 2 x 50 mg/gün (100 mg yükleme dozunu takiben) IV, kolistin 2 x 150 mg/gün IV ve kolistin 2 x 75 mg/gün inhaler eklendi. Bu kombinasyon tedavisi altında hastada klinik yanıt alındı ve tedavi 14 güne tamamlandı. Hasta 3 ay sonra nörolojik sekel ile hastaneden taburcu edildi. Bu olgu kolistin dirençli *Acinetobacter baumannii* olgularının ülkemiz için bir sorun haline gelmeye başladığını göstermek amacıyla sunulmaktadır

Anahtar kelimeler: *Acinetobacter baumannii*, kolistin direnci, pnömoni, çoklu ilaç direnci

INTRODUCTION

Resistance to all major classes of antibiotics (except polymyxins) in *Acinetobacter baumannii* has substantially increased worldwide in the past decade. *A. baumannii* is now regarded as one of the most difficult nosocomial pathogens to treat and control.¹ In many cases, the available therapeutic options for MDR *A. baumannii* infection include colistin (polymyxin E) or polymyxin B. A relationship between the

increasing rate of colistin usage and colistin resistance in *A. baumannii* has been reported.² Herein, a case of healthcare-associated pneumonia due to colistin resistant *A. baumannii* is presented.

CASE REPORT

A 78 year-old male was hospitalized in the neurology clinic with a diagnosis of encephalopathy. The patient was transferred to the Intensive Care Unit

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(ICU) because of cardiopulmonary arrest on the 18th day of hospitalization. Colistimethate sodium (Colimycin, Kocak Farma, Turkey) intravenous (IV) 2 x 150 mg was administered empirically for three days with a diagnosis of ventilator-associated pneumonia (VAP). Colistin treatment was switched to imipenem after isolation of *Enterobacter cloacae* (106 colony forming unit/mL) in an endotracheal aspirate fluid. On the 13th day of imipenem treatment, fever of 38.4°C with increased purulent respiratory secretion was detected. On the physical examination, bilateral rales were auscultated. The laboratory findings revealed that white blood cells (WBC) 12.8 K/ μ L, hemoglobin 8.6 g/dL, hematocrite 25.2%, platelet count 241 K/ μ L, sedimentation rate 82 mm/h, and C-reactive protein (CRP) 134 mg/L. Postero-anterior lung radiography revealed a pulmonary infiltration on the right lung. After obtaining endotracheal aspirate culture, imipenem was stopped, and cefoperazone-sulbactam 2 x 2 g/day was started empirically. On the 3rd day of treatment, *A. baumannii* ($\geq 10^5$ colony forming unit/mL) was identified in the endotracheal aspirate fluid culture. The isolate was resistant to all of the antibiotics, including colistin, except for cefoperazone-sulbactam (intermediate) and tigecycline (MIC=4 mg/L, intermediate) by VITEK and E-test. Colistin resistance was confirmed twice with E-test. Colistimethate sodium IV 2 x 150 mg plus colistimethate sodium inhaler 2 x 75 mg were added to the cefoperazone-sulbactam 2 x 2 g IV. On the 3rd day of this treatment, there was no growth from repeated endotracheal aspirate culture, but his fever persisted and no clinical or laboratory response was achieved. Tigecycline was added to the therapy as 2 x 50 mg IV (after 1 x 100 mg IV loading dose), although tigecycline was not approved for pneumonia. On the 6th day of cefoperazone-sulbactam, 4th day of colistin and 2nd day of tigecycline, the patient's clinical findings were improved, WBC decreased to normal range, and CRP levels declined. Antimicrobial therapy was stopped on the 14th day of colistin. The patient was discharged from the hospital with neurological sequelae after three months.

DISCUSSION

A substantial increase in MDR in *A. baumannii* has forced clinicians to use colistin alone or in combination with some other antibiotics.³ Tigecycline is a therapeutic option; however, besides the potential for toxicity. On the other hand, a high percentage (78%) of resistance to tigecycline among MDR *A. baumannii* isolates has been reported from Israel

despite tigecycline has never been used.⁴ Several combinations with carbapenems, beta-lactam, doxycycline, rifampicin, or azithromycin have been investigated for treatment of *A. baumannii* infections.⁵ In a study by Kalin et al.⁶, clinical cure rates and bacteriological clearance rates were reported to be better in the colistin/sulbactam combination group than in colistin monotherapy, but the difference did not reach statistical significance.

Colistin resistance among *Acinetobacter* strains, especially in *A. baumannii*, is increasing. In different parts of the world, colistin-resistant *Acinetobacter* strains have been identified.⁷ In the literature, the most common risk factor was reported as previous colistin usage. In our case, colistin was used for three days with a diagnosis of VAP two weeks before colistin-resistant *Acinetobacter* growth in the endotracheal aspirate culture. This might have led to the colistin resistance.

The pathogenesis of the emerging resistance in *Acinetobacter* is not well identified. Mutations in two genes that constitute a two-component system (PmrAB) involved in the modification of lipid A, the major constituent of the LPS membrane, and mutations, deletions, or insertions in genes essential for the synthesis of lipid A were suggested as the possible mechanisms.⁸

Synergism was demonstrated between colistin and sulbactam, imipenem and rifampicin.^{8,9} In a study by Mutlu Yılmaz et al.¹⁰, despite detection of in-vitro synergistic activity, which was proven by the efficacy on bacterial counts in the lung tissue, the authors could not find any statistically significant difference between colistin, tigecycline and combination treatments. However, we preferred to continue cefoperazone-sulbactam to obtain a synergistic effect.

On the basis of our experience, a clinical response was observed on average five days later, even for colistin-susceptible MDR *Acinetobacter* infections (unpublished data). Thus, in this case, the clinical response might have been obtained due to the combined use of colistin and cefoperazone-sulbactam. However, it is thought that tigecycline might also have an additional effect on this response because of its synergistic effect with colistin, which was shown in a recent article.⁹

In conclusion, taking advantage of this synergic effect seems to be the most reasonable approach in the treatment of patients infected with MDR *A. baumannii*.

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