Case report
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Case report of acute type 2 respiratory failure secondary to Colistin

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Abstract We report an elderly patient who developed type 2 respiratory failure after receiving Colistimethate (CMT). The patient has chronic kidney disease, and was admitted to Medical Intensive Care Unit with Pneumococcal pneumonia. However, he had nosocomial *Acinetobacter baumannii* urinary tract infection, which was only sensitive to colistin. Unfortunately, 72 h after initiation of Colistimethate, his consciousness deteriorated. 5 days later, he passed into acute type 2 respiratory failure. All investigations were done and no cause was found so, Colistin-induced respiratory failure was presumed hence, the drug was withdrawn, and his condition improved within 48 h and was extubated 4 days later.
Keywords Colistin, neurotoxicity, respiratory failure.

Introduction

Polymyxins were discovered in 1947 from different species of *Bacillus polymyxa*.[1,2] This class of antibiotics consists of five chemically different compounds, polymyxin A, B, C, D, and E (colistin). Only polymyxins B (PMB) and E have been used in clinical practice.[3] Both of them exert a bactericidal effect on the cell wall of Gram-negative bacteria, causing permeability changes in the cytoplasmic membrane leading to cell death.[4] Their use was abandoned in 1970s and replaced with other antibiotics because of concerns related to toxicity (kidney and neurotoxicity).[3,5] However, there was a renewed interest into colistin use due to multidrug-resistant(MDR) Gram-negative bacteria, in particular *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Klebsiella pneumoniae*.[6,7] Our patient had *Acinetobacter baumannii* which was MDR, so this is the reason colistin was chosen.

Case Report

A 73-year-old male presented with fever, cough of yellowish sputum of 4-day duration. He is a known case of type 2 diabetes, hypertension, chronic kidney disease, ischemic heart disease and old cerebrovascular accident with left-sided hemiplegia.

On examination: he was cyanosed with a pulse rate of 121/min, blood pressure of 90/45 mm Hg, temperature of 38.5°C. His investigations shown in table revealed evidence of multiorgan failure and his chest X-ray showed bilateral pneumonia (picture). His condition necessitated intubation and he was commenced on ringer lactate, nor adrenaline 0.09 µg/kg/min, fentanyl infusion 30 µg/h and Amoxicillin/Clavulanic acid in a dose of 1.2 intravenously 8 h according to blood culture with other lines of septic shock management. Luckily, 4 days following initiation of treatment, his general condition improved, inotrope was withdrawn and his renal function got better. By the sixth day, he was extubated while antibiotic was continued for a total of 8 days. Unfortunately, a week later, he ran a continuous fever of more than 38°C, CRP steeped up, urine culture grew *Acinetobacter buamanii* resistant to all conventional antibiotics. In addition, meropenem minimum inhibitory concentration (MIC) >32 µg/mL, and there was an intermediate susceptibility to Tigecycline of (MIC = 8 µg/mL, but sensitive to colistimethate (MIC < 1 µg/mL). Hence, colistimethate was given in a dose of 2.5 mg/kg per day in two divided doses according to his glomerular filtration rate and his fever remitted after 48 h. However, 3 days later, he became weaker then, he showed a labored pattern of breathing. Moreover, his consciousness deteriorated and became unable to communicate. On clinical assessment, his vitals were normal (blood pressure of 144/82 mm Hg, pulse rate of 102/min and temperature of 36.8°C), neurologically, he had decreased gag reflex although he was off-fentanyl. However, there was no neck stiffness and both pupils were equal and reacting to light. He also had equivocal plantar reflexes and preserved peripheral reflexes in all limbs. His arterial blood gases showed acute type 2 respiratory failure (pH of 7.26, pCO2 of 62.6 mm Hg, and PaO2 of 60 mm Hg .on FiO2 of 100%). So he was re-intubated. Investigations were done to rule out septic, metabolic or a vascular cause, all cultures were negative, no electrolyte or metabolic changes were found (Table 1). Chest radiograph was normal (picture-2), electrocardiogram showed tachycardia. His echocardiogram showed normal right ventricular diameters and normal pulmonary artery pressure and his non contrast CT of his head showed old changes with no bleeds, new infarction or edema. It was suspected that colistimethate was the culprit therefore, it was discontinued. Having reviewed tigecycline trials in urinary tract infections in literatures, it was started instead. Within 48 h, his consciousness improved then, he started to communicate, and retain muscle power thence, he was extubated. A week later, he was discharged from the Medical Intensive Care in a stable condition.

Discussion

The interaction of colistin with neurons, which have high lipid content, has been associated with the occurrence of neurotoxicity.[8]

Similarly, neuromuscular blockade presenting as a myasthenia-like syndrome or as respiratory muscle paralysis producing apnea has been reported.[9,10] The possible mechanism is a non-competitive myoneuronal presynaptic blockade of acetyl-cholinesterlase that may be enhanced by hypocalcemia-induced prolongation depolarization.[11] Calcium infusion has been proposed to reverse paralysis but no benefit from neostigmin.[12] Lindesmith et al described 21 cases of reversible

Table 1.

Labs	On admission	One week after admission	After colistin & before second intubation	Before Discharge from ICU
White blood cell	21 x10*3/uL	9.8 x10*3/uL	12.2 x10*3/uL	6.5 x10*3/uL
C-reactive protein	224.45 mg/L	98 mg/L	117 mg/L	36 mg/L
Creatinine	289 umol/L	172 umol/L	200 umol/L	167 umol/L
Potassium	4.4 mmol/L	3.8 mmol/L	4.3 mmol/L	4.1 mmol/L
Magnesium	0.86 mmol/L	0.69 mmol/L	0.72mmol/L	0.76 mmol/L
Corrected calcium	2.46 mmol/L	2.2 mmol/L	2.3 mmol/L	2.4 mmol/L

respiratory paralysis in 1968; 15 cases were associated with CMS and 6 cases with PMB therapy.[13,14,15,16,17,18,19]

Concomitant drug therapies including other anesthetics, muscle relaxant, corticosteroids, and narcotics probably increase the risk of CMS neurotoxicity.[8] Our patient has no new neurological insult such as stroke and he did not received muscle relaxants or steroids but Fentanyl. His calcium, potassium, and magnesium were normal, there were no tetany, arrhythmia, seizure, or involuntary movements.

The majority of respiratory failure related to polymyxin-associated neuromuscular blockade was described in patients with chronic kidney disease.[19] Likewise, our patient has chronic kidney disease and received intravenous colistin which may have lead to apnea 5 days after commencing the medicine .This can readily be supported by his normal parameters including serum electrolytes, white cell differential, chest X-ray, echocardiography and brain CT. A more confirmatory finding; his consciousness, breathing as well as arterial blood gases and renal functions returned back to their base line once the medication was stopped.

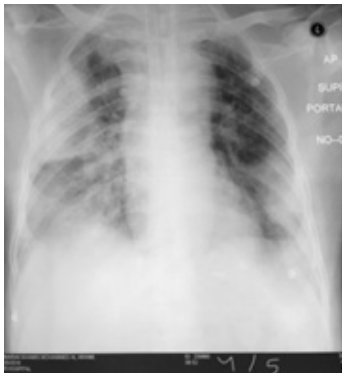

Fig. 1

Conclusion

Due to presence of MDR bacteria and re-usage of colistin, the awareness of colistin-induced respiratory failure must be kept in mind as this is serious side effect. Patients receiving these drugs should have regular reviews for drug–drug interactions, as well as renal and neurological assessments.[8] Vigilance of the shortness of breath can facilitate the diagnosis of colistin-mediated respiratory failure in a patient with shortness of breath of unknown cause.

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